Acute pancreatitis.

1. Anatomy and physiology information about pancreas.

2. Acute pancreatitis: definition , etiology, pathogenesis, pathological anatomy.

3. Classification of acute pancreatitis.

4. Laboratory and instrumental methods of diagnosing acute pancreatitis.

5. Conservative treatment of acute pancreatitis.

6. Complications of acute pancreatitis, diagnosing, conservative and surgical treatment.

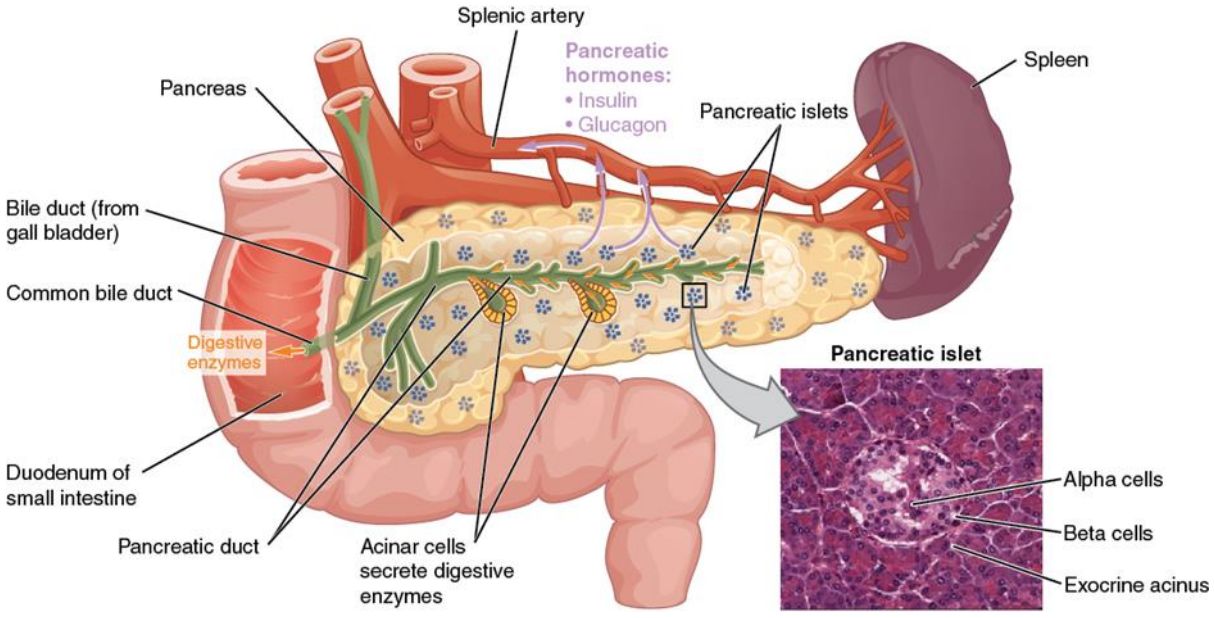
Anatomy and physiology information about pancreas.

The pancreas is a gland located in the upper posterior abdomen. It is responsible for insulin production (endocrine pancreas) and the manufacture and secretion of digestive enzymes (exocrine pancreas) leading to carbohydrate, fat, and protein metabolism. Approximately 80% of the gross weight of the pancreas supports exocrine function, and the remaining 20% is involved with endocrine function. The focus of this article is on the exocrine function of the pancreas.

The pancreas accounts for only 0.1% of total body weight but has 13 times the protein-producing capacity of the liver and the reticuloendothelial system combined, which together make up 4% of total body weight. Digestive enzymes are produced within the pancreatic acinar cells, packaged into storage vesicles called zymogens, and then released via the pancreatic ductal cells into the pancreatic duct, where they are secreted into the small intestine to begin the metabolic process.

In normal pancreatic function, up to 15 different types of digestive enzymes are manufactured in the rough endoplasmic reticulum, targeted in the Golgi apparatus and packaged into zymogens as proenzymes. When a meal is ingested, the vagal nerves, vasoactive intestinal polypeptide (VIP), gastrin-releasing peptide (GRP), secretin, cholecystokinin (CCK), and encephalins stimulate release of these proenzymes into the pancreatic duct.

The proenzymes travel to the brush border of the duodenum, where trypsinogen, the proenzyme for trypsin, is activated via hydrolysis of an N-terminal hexapeptide fragment by the brush border enzyme enterokinase. Trypsin then facilitates the conversion of the other proenzymes into their active forms.



The pancreatic islets each contain four varieties of cells:

The **alpha cell** produces the hormone glucagon and makes up approximately 20 percent of each islet. Low blood glucose levels stimulate the release of glucagon.

The **beta cell** produces the hormone insulin and makes up approximately 75 percent of each islet. Elevated blood glucose levels stimulate the release of insulin.

The **delta cell** accounts for four percent of the islet cells and secretes the peptide hormone somatostatin. Recall that somatostatin is also released by the hypothalamus, stomach and intestines. An inhibiting hormone, pancreatic somatostatin inhibits the release of both glucagon and insulin.

The **pancreatic polypeptide cell** (PP cell) accounts for about one percent of islet cells and secretes the pancreatic polypeptide hormone. It is thought to play a role in appetite, as well as in the regulation of pancreatic exocrine and endocrine secretions. Pancreatic polypeptide released following a meal may reduce further food consumption; however, it is also released in response to fasting.

The exocrine pancreas is a gland that produces digestive enzymes and bicarbonate. It is an essential organ for the survival, adaptation, and restoration of the organism. The exocrine pancreas' function must be evaluated in relationship to the endocrine pancreas, stomach, intestines, liver, gallbladder, lungs, skin, joints, immunity, central nervous system, autonomic nervous system, and endocrine system. It affects or is solicited by each of these areas of the organism. From this arises the role of the exocrine pancreas in the precritical and critical terrain of numerous disorders from immunity to athropathies, from digestive to mental. There are numerous signs and symptoms according to the theory of endobiogeny that indicate the level of insufficiency of oversolicitation of the exocrine pancreas. The pancreas contains exocrine glands that produce enzymes important to digestion. These enzymes include trypsin and chymotrypsin to digest proteins; amylase for the digestion of carbohydrates; and lipase to break down fats. When food enters the stomach, these pancreatic juices are released into a system of ducts that culminate in the main pancreatic duct. The pancreatic duct joins the common bile duct to form the ampulla of Vater which is located at the first portion of the small intestine, called the duodenum**.** The common bile duct originates in the liver and the gallbladder and produces another important digestive juice called bile. The pancreatic juices and bile that are released into the duodenum, help the body to digest fats, carbohydrates, and proteins.

Acute pancreatitis: definition , etiology, pathogenesis, pathological anatomy.

Acute pancreatitis may occur when factors involved in maintaining cellular homeostasis are out of balance. The initiating event may be anything that injures the acinar cell and impairs the secretion of zymogen granules; examples include alcohol use, gallstones,

and certain drugs. Once a cellular injury pattern has been initiated, cellular membrane trafficking becomes chaotic, with the following deleterious effects:
1) Lysosomal and zymogen granule compartments fuse, enabling activation of trypsinogen to trypsin
2) Intracellular trypsin triggers the entire zymogen activation cascade
3) Secretory vesicles are extruded across the basolateral membrane into the interstitium, where molecular fragments act as chemoattractants for inflammatory cells

Activated neutrophils then exacerbate the problem by releasing superoxide (the respiratory burst) or proteolytic enzymes (cathepsins B, D, and G; collagenase; and elastase). Finally, macrophages release cytokines that further mediate local (and, in severe cases, systemic) inflammatory responses. The early mediators defined to date are tumor necrosis factor-alpha (TNF-α), interleukin (IL)-6, and IL-8.

These mediators of inflammation cause an increased pancreatic vascular permeability, leading to hemorrhage, edema, and eventually pancreatic necrosis. As the mediators are excreted into the circulation, systemic complications can arise, such as bacteremia due to gut flora translocation, acute respiratory distress syndrome (ARDS), pleural effusions, gastrointestinal (GI) hemorrhage, and renal failure.

The systemic inflammatory response syndrome (SIRS) can also develop, leading to the development of systemic shock. Eventually, the mediators of inflammation can become so overwhelming that hemodynamic instability and death ensue.

In acute pancreatitis, parenchymal edema and peripancreatic fat necrosis occur first; this is known as acute edematous pancreatitis. When necrosis involves the parenchyma, accompanied by hemorrhage and dysfunction of the gland, the inflammation evolves into hemorrhagic or necrotizing pancreatitis. Pseudocysts and pancreatic abscesses can result from necrotizing pancreatitis because enzymes can be walled off by granulation tissue (pseudocyst formation) or via bacterial seeding of pancreatic or peripancreatic tissue (pancreatic abscess formation).

Etiology

Biliary tract disease

One of the most common causes of acute pancreatitis in most developed countries (accounting for approximately 40% of cases) is gallstones passing into the bile duct and temporarily lodging at the sphincter of Oddi.

Alcohol

Alcohol use is a major cause of acute pancreatitis (accounting 35% of cases). At the cellular level, ethanol leads to intracellular accumulation of digestive enzymes and their premature activation and release. At the ductal level, it increases the permeability of ductules, allowing enzymes to reach the parenchyma and cause pancreatic damage. Ethanol increases the protein content of pancreatic juice and decreases bicarbonate levels and trypsin inhibitor concentrations. This leads to the formation of protein plugs that block pancreatic outflow.

Endoscopic retrograde cholangiopancreatography

Pancreatitis occurring after endoscopic retrograde cholangiopancreatography (ERCP) is probably the third most common type (accounting for approximately 4% of cases). Whereas retrospective surveys indicate that the risk is only 1%, prospective studies have shown the risk to be at least 5%.

Trauma

Abdominal trauma (approximately 1.5%) causes an elevation of amylase and lipase levels in 17% of cases and clinical pancreatitis in 5% of cases. Pancreatic injury occurs more often in penetrating injuries (eg, from knives, bullets) than in blunt abdominal trauma (eg, from steering wheels, horses, bicycles). Blunt injury to the abdomen or back may crush the gland across the spine, leading to a ductal injury.

Drugs

Considering the small number of patients who develop pancreatitis compared to the relatively large number who receive potentially toxic drugs, drug-induced pancreatitis is a relatively rare occurrence (accounting for approximately 2% of cases) that is probably related to an unknown predisposition. Fortunately, drug-induced pancreatitis is usually mild.

Classification of acute pancreatitis.

The Atlanta classification is the new, clinically based classification of acute pancreatitis.

Acute pancreatitis

- mild
- severe

Interstititial edematous pancreatitis is characterized by interstitial edema associated infrequently with fat necrosis. *necrotizing pan creatitis*
sterile
infected
The main feature is necrosis of the pancreas and/or peripancreatic tissues. Necrosis can be sterile or infected.
Fluid collections are defined as collections occurring early in the course of pancreatitis with no defined wall. More than half of these fluid collections disappear spontaneously in the course of the disease.
Post-acute pseudocysts are defined as a collection of pancreatic juice limited by a fibrotic wall. *Pancreatic abscess* is a circumscribed collection of pus with minimal or no necrotic debris, developed in the peripancreatic spaces

Type of Pancreatitis	Fluid Collections
< 4 Weeks after Onset	
IEP	APFC
	Sterile
	Infected
Necrotizing Pancreatitis	ANC
	Parencymal necrosis alone
	Sterile
	Infected
	Peripancreatic necrosis alone
	Sterile
	Infected
	Pancreatic and peripancreatic necrosis
	Sterile
	Infected
≥ 4 Weeks after Onset	
IEP	Pancreatic pseudocyst
	Sterile
	Infected
Necrotizing Pancreatitis	WON
	Sterile
	Infected

Table 2. Revised Atlanta Classification [4].

A. Mild acute pancreatitis:
(i) No organ failure
(ii) No local or systemic complications
B. Moderately severe acute pancreatitis:
(i) Organ failure that resolves within 48 h (transient organ failure) and/ or
(ii) Local or systemic complications without persistent organ failure
C. Severe acute pancreatitis : Persistent organ failure (> 48 h)
(i) Single organ failure
(ii) Multiple organ failure

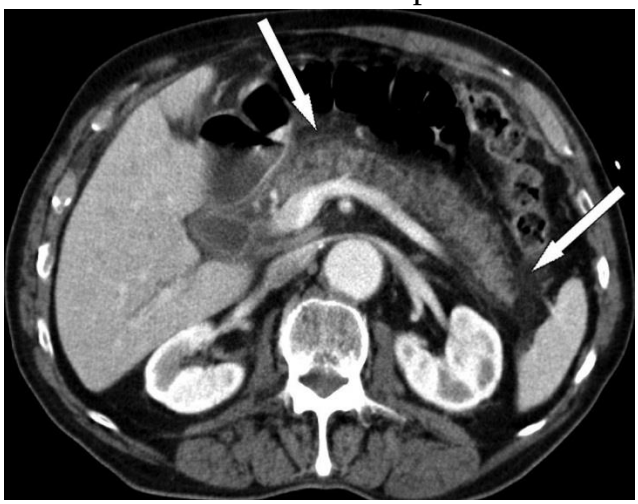
Phases of Acute Pancreatitis

In pathophysiologic terms, acute pancreatitis is divided into early and late phases. The early phase occurs in the 1st week after onset, with the disease manifesting as a systemic inflammatory response. At this time, clinical severity and treatment are mainly determined on the basis of type and degree of organ failure. The late phase, which generally starts in the 2nd week and can last for weeks to months, occurs only in patients with moderately severe or severe pancreatitis, as defined by persistent organ failure and by local complications.

Definition of types of acute pancreatitis: interstitial oedematous pancreatitis and necrotising pancreatitis.

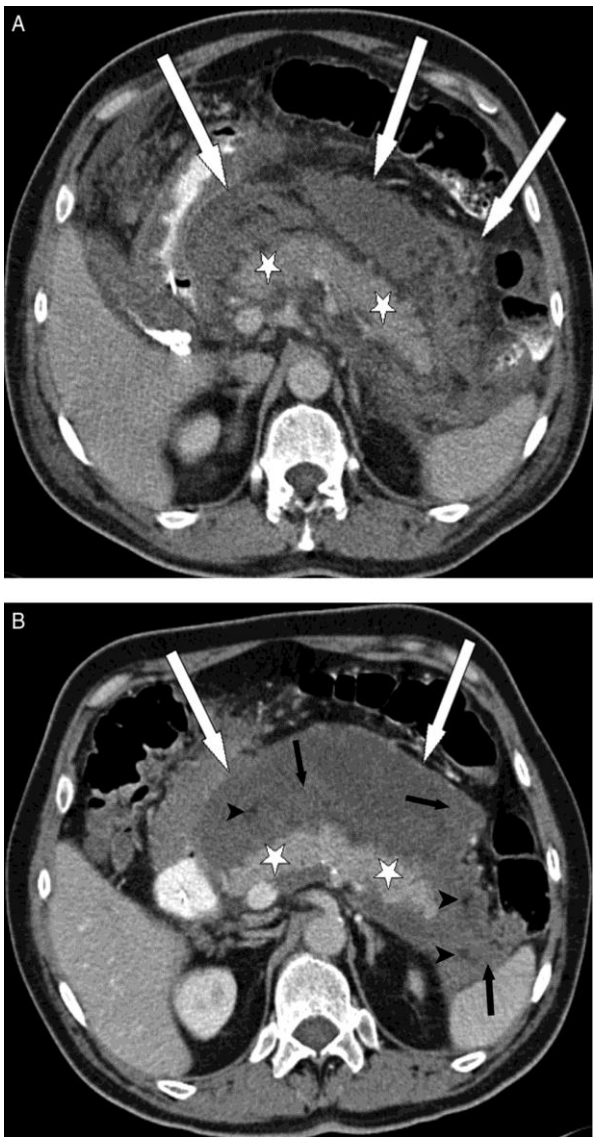
Interstitial oedematous pancreatitis Patients with acute pancreatitis have diffuse (or occasionally localised) enlargement of the pancreas due to inflammatory oedema. On

CECT, the pancreatic parenchyma shows relatively homogeneous enhancement, and the peripancreatic fat usually shows some inflammatory changes of haziness or mild stranding. There may also be some peripancreatic fluid. The clinical symptoms of interstitial oedematous pancreatitis usually resolve within the first week.



Necrotising pancreatitis

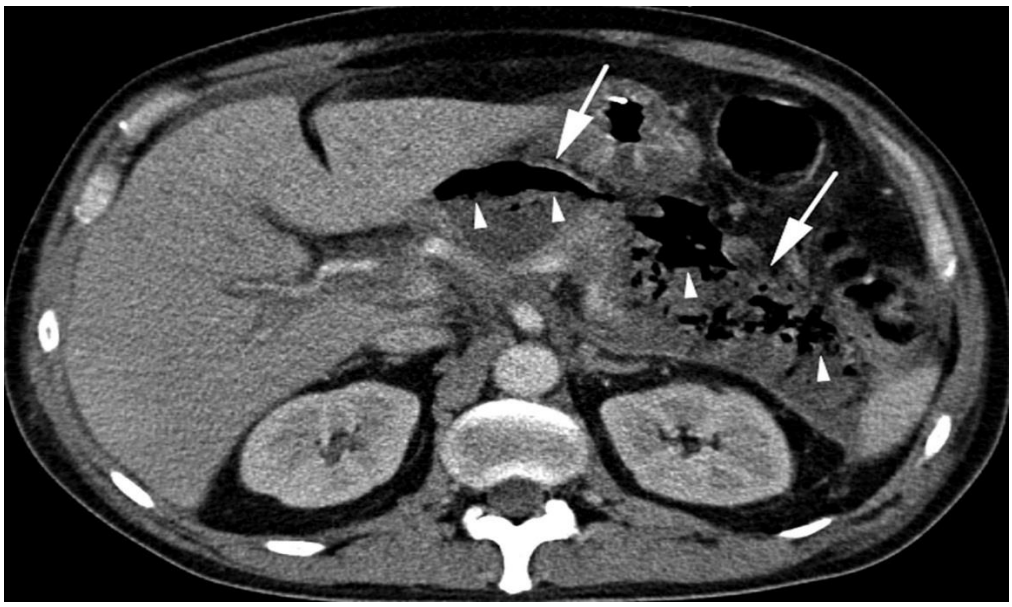
About 5–10% of patients develop necrosis of the pancreatic parenchyma, the peripancreatic tissue or both (see below, Definition of pancreatic and peripancreatic collections) Necrotising pancreatitis most commonly manifests as necrosis involving both the pancreas and peripancreatic tissues and less commonly as necrosis of only the peripancreatic tissue, and rarely of the pancreatic parenchyma alone.



Infected pancreatic necrosis

Pancreatic and peripancreatic necrosis can remain sterile or become infected; most of the evidence suggests no absolute correlation between the extent of necrosis and the risk of infection and duration of symptoms. Infected necrosis is rare during the first week.

The presence of infection can be presumed when there is extraluminal gas in the pancreatic and/or peripancreatic tissues on CECT for bacteria and/or fungi on Gram stain and culture. There may be a varying amount of suppuration (pus) associated with the infected pancreatic necrosis, and this suppuration tends to increase with time with liquefaction.



The revised Atlanta classification requires that two or more of the following criteria be met for the diagnosis of acute pancreatitis: *(a)* abdominal pain suggestive of pancreatitis, *(b)* serum amylase or lipase level greater than three times the upper normal value, or *(c)* characteristic imaging findings.

Laboratory and instrumental methods of diagnosing acute pancreatitis.

Symptoms

Abdominal pain is the cardinal symptom. It occurs in about 95% of cases. Typically it is generalized to the upper abdomen, but it may be more localized to the right upper quadrant, epigastric area, or, occasionally, left upper quadrant. The pain typically occurs acutely, without a prodrome, and rapidly reaches maximum intensity. It tends to be moderately to intensely severe and tends to last for several days. The pain typically is boring and deep because of the retroperitoneal location of the pancreas. It often radiates in a bandlike manner to the lower thoracic region of the back. The pain tends to be steady but is exacerbated by eating or drinking, especially the drinking of alcohol. Patients may lean forward or even curl upin a knee-to-chest (fetal position) to decrease the pain by decreasing the stretch of the pancreas. With biliary pancreatitis, the pain may be more localized to the right upper quadrant, more gradual in onset, and more variable in intensity over time because of the contribution of biliary colic. Although patients who have gastrointestinal perforation tend to be motionless, patients who have acute pancreatitis may be restless and agitated. About 90% of patients have nausea and vomiting, which can be severe and unremitting. The vomiting is related to peripancreatic inflammation extending to the posterior gastric wall and a localized or generalized ileus.

Physical examination

The severity of the physical findings depends on the severity of the attack. Mild disease presents with only mild abdominal tenderness. Severe disease presents with severe abdominal tenderness and guarding, generally localized to the upper abdomen. Rebound tenderness is unusual. Hypoactive bowel sounds, accompanied by epigastric distention, may be caused by peripancreatic spread of the inflammatory process that produces a generalized ileus, localized spread of the inflammation to the adjacent small intestine that produces a sentinel loop, or localized spread of the inflammation to the adjacent transverse colon that produces a colon cut-off sign. Tachycardia and mild hypotension may result from hypovolemia from sequestration of fluid in the pancreatic bed. About 60% of patients develop low-grade pyrexia from peripancreatic inflammation without evident infection. Patients may have shallow, rapid respirations from diaphragmatic inflammation, pleural effusions, and respiratory compromise. Uncommon physical findings reflect specific complications. Unilateral dullness to percussion and decreased breath sounds at a lung base indicatea pleural effusion. Subcutaneous fat necrosis, or panniculitis, typically presents as tender, palpable, subcutaneous, red nodules that are 0.5 to 2 cm indiameter and most commonly occur along the distal extremities. Ecchymoses in the flanks, called ‘‘Gray-Turner’s sign,’’ indicate retroperitoneal hemorrhage from hemorrhagic pancreatitis, whereas ecchymoses in the periumbilical region, called ‘‘Cullen’s sign,’’ indicate intra-abdominal hemorrhage. Jaundice suggests choledochal obstruction from gallstone pancreatitis.

Laboratory tests

Leukocytosis is common because of a systemic inflammatory response. Mild hyperglycemia is common because of decreased insulin secretion and increased glucagon levels. The serum aspartate aminotransferase (AST) and alanine aminotransferase (ALT) levels sometimes are mildly elevatedin alcoholic pancreatitis but frequently are significantly elevated in biliary pancreatitis. An ALT level higher than 150 IU/L (approximately threefold or more above normal) therefore suggests biliary rather than alcoholic pancreatitis. In a meta-analysis, a serum ALT level higher than 150 IU/L had a positive predictive value of 95% in diagnosing acute gallstone pancreatitis.

Serum lipase

The serum lipase level generally is the primary diagnostic marker for acute pancreatitis because of high sensitivity and specificity. The serum lipase assay has become more reliable with the recent incorporation of colipase. Serum lipase now is more than 90% sensitive for acute pancreatitis. The serum lipase level rises early in pancreatitis and remains elevated for several days. It may increase up to twofold above normal with renal failure, however, because of decreased renal excretion and increase up to threefold

with intestinal inflammation or perforation because of leakage of lipase from the intestine.

Serum amylase

The serum amylase level was the traditional, standard diagnostic blood test. The serum amylase level increases during acute pancreatitis from leakage from the inflamed pancreas into the bloodstream and from decreased renal excretion. Although serum amylase is a very sensitive diagnostic test, hyperamylasemia has insufficient specificity. Many disorders cause mild to moderate hyperamylasemia, but an amylase level more than three times above normal is highly specific for pancreatitis. The serum amylase level is insensitive in three uncommon situations: in delayed clinical presentation, because the serum amylase normalizes after several days of pancreatitis; in pancreatitis resulting from hypertriglyceridemia, which typically produces minimally or mildly elevated serum amylase levels, possibly because of the dilutional effects of the lipemia; and in acute-on-chronic alcoholic pancreatitis in which the amylase level rises only modestly because of pre-existing pancreatic injury. Macroamylasemia produces hyperamy lasemia without clinical pancreatitis because of large multimers of amylasecomplexed with immunoglobulin A. These large molecules are not filtered and excreted by the kidney, so the urinary amylase level and fractional excretion of amylase is low.

Other serum tests

Other pancreatic enzymes that leak from the pancreas during pancreatitis and accumulate in the serum include phospholipase A, trypsin, trypsinogen-2, and carboxyl ester lipase. The acutely inflamed pancreas also overproduces pancreatitis-associated protein and trypsinogen activation peptide.

Radiologic tests

Abdominal radiography

Any patient who has unexplained, severe abdominal pain should undergo supine and upright chest and abdominal radiographs or, if available, abdominal CT. Abdominal radiographs are performed mainly to exclude alternative abdominal diseases, such as gastrointestinal perforation, but may indicate findings suggestive of pancreatitis. Intestinal loops may be generally dilated from a generalized ileus. A severe ileus may produce multiple air-fluid levels. In a sentinel loop, bowel is focally dilated proximally because of spasm of distal bowel overlying the inflamed pancreas. Similarly, in the colon cut-off sign the mid-transverse colon is dilated focally because of extension of peripancreatic inflammation and bowel spasm at the splenic flexure. Edema and inflammation of the pancreatic head may manifest as widening of the C-loop (descending duodenum) that frames the medial border of the pancreas. Occasionally,

visualization of calcifications in the gallbladder suggests gallstone pancreatitis. The chest rengenogram may reveal a pleural effusion that is more common on the left side. Other abnormalities on a chest roentgenogram include elevation of the left hemidiaphragm, basal atelectasis, and pulmonary infiltrates.

Abdominal ultrasonography

Abdominal ultrasonography is the primary imaging study for abdominal pain associated with jaundice and for excluding gallstones as the cause of acute pancreatitis. It has the advantages of low cost, ready availability, and easy portability for bedside application in very sick patients. It thus is ubiquitous in the evaluation of pancreatitis. When adequately visualized, an inflamed pancreas is recognized as hypoechoic and enlarged because of parenchymal edema. The pancreas is visualized inadequately in 30% of cases, however, either because of the presence of overlying intestinal gas, particularly with a localized ileus, or because the presence of fat in the abdominal wall limits penetration of the acoustic waves. Abdominal ultrasound is about 95% sensitive for the detection of cholecystolithiasis but is only about 50% sensitive for the detection of holedocholithiasis. Abdominal ultrasound is less accurate than CT in delineating peripancreatic inflammation and detecting intrapancreatic necrosis.

Abdominal CT

Patients who present with severe pancreatitis or who present initially with mild to moderate pancreatitis that does not improve after several days of supportive therapy should undergo abdominal CT. For optimal sensitivity, patients should receive both intravenous and oral contrast. Intravenous contrast is contraindicated in the presence of renal insufficiency. Abdominal CT is highly useful to determine the severity and complications of pancreatitis. Pancreatic inflammation is recognized reliably as pancreatomegaly, a smooth pancreatic margin, parenchymal inhomogeneity, peripancreatic fluid, or peripancreatic inflammation visualized as peripancreatic streakiness or‘‘dirty’’ fat. Most importantly, dynamic CT demonstrates necrotic or poorly perfused pancreatic parenchyma as areas that fail to enhance, with a density of less than 50 Hounsfield units, after intravenous contrast administration. The severity of abnormalities on an unenhanced CT is graded quantitatively and is combined with the severity of pancreatic necrosis on an enhanced CT to form the CT severity index. This index has important prognostic implications.

Nonstandard imaging tests

MRI has had limited application for diagnostic imaging of acute pancreatitis because it is less available, more cumbersome, and more expensive than CT. It has advantages in selected patients, however, such as those who are pregnant (because of the radiation teratogenicity of CT), those who are allergic to the contrast used for enhanced CT, and those who have renal insufficiency that can be exacerbated by the iodinated contrast used for enhanced CT. It has advantages in all patients, in that magnetic resonance

cholangiopancreatography (MRCP) delineates the bile and pancreatic ducts better than CT and has a higher sensitivity in detecting choledocholithiasis. In a recent meta-analysis, MRCP had 90% sensitivity and 95% specificity for detecting choledocholithiasis. MRI may prove to be superior to CT in the characterization of pancreatic fluid collections. MRCP is used currently to detect choledocholithiasis before therapeutic endoscopic retrograde cholangiopancreatography (ERCP). Endoscopic ultrasound is somewhat more sensitive than MRCP in detecting choledocholithiasis. It is useful in patients who are pregnant because of its relative safety during pregnancy and in patients who cannot undergo MRCP, such as patients who have internal metallic devices. ERCP with sphincterotomy is essential for the diagnosis and therapy of symptomatic choledocholithiasis and is valuable for determining the cause of recurrent acute pancreatitis of unknown origin. Cholescintigraphy is highly useful to diagnose acute cholecystitis, where it is the test of choice, but it provides limited information about the bile ducts and is not indicated in the evaluation of suspected choledocholithiasis.

Clinical predictors of diseases severity

Determination of the severity of pancreatitis is important for early recognition of pancreatic complications, triage of patients to higher levels of care such as an ICU, therapeutic decisions, and prognostication. The serum lipase and amylase levels are poorly correlated with disease severity and lack prognostic significance. The experienced clinicians' clinical impression, based on their informal evaluation of the vital signs, respiratory distress, renal insufficiency, other evidence of organ failure, and abnormal laboratory tests, is fairly specific but relatively insensitive in determining disease severity and predicting complications. Laboratory values that suggest severe disease include leukocytosis, elevated C-reactive protein, and elevated trypsinogen activation peptide. Formal clinical scoring systems improve the accuracy of determining disease severity.

The Ranson criteria distinguish between mild and severe pancreatitis with about 80% accuracy. The Ranson criteria, however,require evaluation of 11 parameters over 48 hours.

The APACHE II scale has advantages in that it can be performed on admission, can be reevaluated at any time during the patient's hospitalization, and is applicable to any medical illness. It incorporates 11 physiologic variables in addition to the patient's age, organ insufficiency, neurologic status (as determined by the Glasgow coma scale), and postoperative state. It is a fairly reliable indicator of disease severity and is a robust predictor of complications. It is cumbersome to use clinically.

The CT severity index includes findings of inflammation with noncontrast CT and findings of necrosis with contrast CT. It provides important information about the severity of pancreatitis and the prediction of complications and mortality. Gurleyik and

colleagues found a sensitivity of 85% and a specificity of 98% in predicting severe pancreatitis based solely on this index. In one study, patients who had a severity index less than three had only a 4% morbidity rate and no mortality, whereas patients who had a severity index of more than six had a 92% morbidity rate and a 17% mortality. In other studies, patients who had a CT severity index greater than five were eight times more likely to die, 17 times more likely to have a prolonged hospital course, and 10 times more likely to require necrectomy than patients who had a severity index less than five.

Conservative treatment of acute pancreatitis.

A team approach with specialist consultation and referral helps optimize the management of severe and complicated pancreatitis. The intensivist manages the general ICU care including invasive hemodynamic monitoring, aggressive fluid hydration, and management of cardiovascular, pulmonary, or renal failure. The radiologist can grade the severity of the pancreatitis according to the CT severity index. The gastrointestinal endoscopist performs ERCP with sphincterotomy as necessary. The gastrointestinal surgeon performs necrosectomy for infected pancreatic necrosis. An infectious disease specialist is involved in selecting the antibiotics for pancreatic infections. Ideally, a dedicated pancreatologist coordinates and supervises the care of severe pancreatitis at tertiary referral centers. Almost all patients who have acute pancreatitis should be hospitalized for supportive therapy and optimal management, especially for the first episode of pancreatitis, in which there is a need to determine the specific cause. Occasionally patients who have chronic pancreatitis may be able to manage a smoldering episode of recurrent pancreatitis at home. Patients exhibiting early signs of organ failure should be monitored in an ICU. The three goals of therapy for acute pancreatitis are general supportive therapy to prevent complications, directed therapy for specific causes of pancreatitis, and early recognition and aggressive treatment of complications.

General supportive therapy

Patients who have acute pancreatitis generally are severely intravascularly depleted on presentation from the profound loss of intravascular fluid into the inflamed pancreas and abdomen. This hypovolemia can manifest clinically as hemoconcentration, hypotension, tachycardia, dry mucous membranes, poor skin turgor, and oliguria. Decreased pancreatic perfusion from hypovolemia can exacerbate pancreatic necrosis and can cause acute tubular necrosis. Patients who have pancreatitis often are relatively young and do not have cardiac disease. Such patients should be hydrated intravenously aggressively with 250 to 300 cm3/h of crystalloid solutions for the first 48 hours after admission. The hematocrit may decline mildly with rehydration because of hemodilution. Inpatients who have mild to moderate pancreatitis, rehydration does not require invasive monitoring. In patients who have severe pancreatitis and unstable vital signs, a Foley catheter should be inserted to monitor urine output, and a central line

should be used to monitor central venous pressure. Patients who have borderline cardiac function or respiratory failure may require a Swann-Ganz catheter to monitor fluid balance during aggressive hydration. Patients without prior diabetes mellitus may experience moderate hyperglycemia during severe pancreatitis. The serum glucose level should be monitored carefully. Insulin should be administered cautiously because of volatility in the serum glucose level, the potential for a blunted pancreatic release of glucagon in response to hypoglycemia, and the frequently transient nature of the serum glucose abnormalities. Hypocalcemia commonly occurs with acute pancreatitis, particularly when the attack is severe.

Analgesia is essential. Traditionally, opiates are used because of their potency. Ideally, the administered opiate should not induce sphincter of Oddi hypertension that could exacerbate the pancreatitis. Morphine traditionally has been disfavored for acute pancreatitis because it increases the sphincter of Oddi pressure. Meperidine can be administered safely for a few days but should not be administered long term at high dose (O100 mg/3 h) because the accumulation of the metabolite normeperidine can cause agitation and, rarely, seizures. Hydromorphone or fentanyl is a useful alternative in this situation. The dose of analgesia should be monitored and titrated to achieve pain relief without somnolence or hypoventilation. Nasogastric tube aspiration traditionally was used to prevent pancreatic stimulation induced by gastric distention and acid secretion. Multiple clinical trials, however, have demonstrated no benefit from nasogastric aspiration. For example, in a prospective, randomized trial of 60 patients who had mild to moderate pancreatitis, patients receiving nasogastric aspiration tended to resume oral feedings later and remain hospitalized longer than patients not receiving nasogastric aspiration. Nasogastric aspiration is reserved for patients who have a severe ileus pattern on abdominal rengenograms, severe abdominal distention on abdominal examination. The oxygen saturation should be maintained at 95% or higher, with supplemental oxygen administered by nasal cannulae as necessary to main tain pancreatic oxygenation and prevent pancreatic necrosis. An oxygen saturation below 90% may require delivery of supplemental oxygen by a face mask. Endotracheal intubation and assisted ventilation should be performed early if the patient remains hypoxic despite these measures, has severe pulmonary disease, or experiences respiratory fatigue. Hypoxemia in the absence of pre-existing pulmonary disease may be an early sign of the adult respiratory distress syndrome (ARDS) caused by interstitial edema from increased alveolar capillary permeability. The pulmonary venous wedge pressure characteristically is normal with ARDS. Chest rengenogram may reveal multilobar pulmonary infiltrates. ARDS is treated by endotracheal intubation and mechanically assisted ventilation using high positive end-expiratory pressures.

Patients initially should receive nothing by mouth to rest the pancreas. Patients who have mild to moderate and uncomplicated pancreatitis usually are managed solely by intravenous hydration without initiating parenteral feeding, because they typically can resume oral feedings within several days when the patient has no more abdominal pain, nausea, vomiting, and abdominal distention. The diet is advanced slowly to minimize the risk of postprandial pain and recurrent pancreatitis. The diet initially consists of clear liquids and then is advanced sequentially to full liquids, soft solids, and full solids,

as tolerated. The diet initially consists mostly of carbohydrates with some proteins and small amounts of fat added gradually as tolerated. Initially intake is limited to small amounts of kcal/d that are increased gradually as tolerated. Mild to moderate residual elevations of the serum amylase or lipase level are not contraindications to oral feeding, but an amylase or lipase level that is more than threefold above the normal range signals a moderately increased risk of inducing abdominal pain with refeeding. Patients who have severe pancreatitis typically cannot resume oral feedings for many days after presentation because of persistent ileus, abdominal pain, or unresolved pancreatitis that is exacerbated by eating. These patients, however, particularly benefit from nutritional supplementation for tissue repair after tissue catabolism from pancreatic necrosis and the systemic inflammatory response. Total parenteral nutrition (TPN) was used traditionally for patients who had severe pancreatitis to provide nutrition efficiently without stimulating the pancreas and reactivating the pancreatitis. Prolonged TPN, however, is associated with significant risks of direct complications including line sepsis, local abscess, localized hematomas, pneumothorax, venous thrombosis, and venous air embolism, as well as indirect complications involving the kidneys, bones, liver, and biliary tract from metabolic abnormalities.

Peritoneal lavage to remove toxic necrotic compounds no longer is recommended for severe pancreatitis. But peritoneal lavage did not reduce morbidity or mortality significantly.

Prophylactic administration of antibiotics for severe pancreatitis, in the absence of a specific infection, is controversial because of highly variable and contradictory study results. Antibiotics selected for pancreatic infections should be bactericidal and produce adequate therapeutic levels within pancreatic tissue. Such antibiotics include imipenem, third-generation cephalosporins and piperacillin. Broad-spectrum antibiotic prophylaxis increases the risks of fungal infection.

Complications of acute pancreatitis, diagnosing, conservative and surgical treatment.

Treatment of local complications

Early extensive pancreatomies have been abandoned because of an unacceptable mortality rate (30–50%) and because they did not reach their aim that was to prevent initial systemic complications by resection of the necrotic pancreas, nor late local infectious complications. Resection of sterile pancreatic necrosis is unnecessary and may aggravate the prognosis.

At present, the indication for surgical drainage is infection of necrosis.

The diagnosis of local infection is difficult. Clinical parameters do not allow to discriminate between sterile and infected necrosis. Hyperleucocytosis, fever, organ failures resulting from the inflammatory response, can be observed in sterile pancreatic necrosis. The diagnosis of infection relies on bacteriological studies of aspirates yielded

by percutaneous aspiration under CT scan or ultrasonography guidance. Percutaneous aspiration gives the right bacteriological status in 90% of cases. When several collections or pancreatic areas of hypodensity are present all of them must be examined unless there is a technical impossibility (interposition of digestive or vascular structures). Percutaneous aspirations can be performed systematically every 3 or 4 days or when clinical signs of sepsis are present.

Several techniques of drainage have been proposed:

- Percutaneous drainage: it is best indicated for the treatment of infected fluid collections, especially for pancreatic abscesses. Nonetheless, the presence of necrotic debris, often associated with fluid collections, justify the use of large drains (> 20 french). It has no indication in the treatment of sterile fluid collections because of an almost constant occurrence of superinfection.
- Surgical drainage: it must remove all necrotic material and collections. Necrosectomy can be performed through a transperitoneal or a retroperitoneal approach. Most often several operations are necessary to remove all necrotic tissues. The choice of the surgical approach depends on the location of necrosis and collections. Retroperitoneal approach is best indicated when collections develop to the left. Some authors favor planned relaparotomies, others reoperate only if clinical, biological and radiological parameters lead to a suspicion of persisting infected collections and necrosis. Laparoscopic techniques are not yet widely used but allow a limited approach, thus avoiding large wound dehiscence and bowel fistulas.

Etiological treatment

It concerns mainly biliary pancreatitis and its modalities are based on the severity of pancreatitis.

In mild pancreatitis, most authors recommend biliary surgery during the same admission, after normalization of clinical and biological parameters. Laparoscopic cholecystectomy is associated with peroperative cholangiography which can show a common bile duct stone. When operation is performed within 48 hours of onset of pancreatitis, common bile duct stones are found in up to 75% of patients, falls to 45% between day 2 and 4 and to 5% between day 5 and 7 because of spontaneous duodenal migrations of stones.

In severe pancreatitis, early biliary surgery worsens the prognosis. It has been suggested that early ERCP (Endoscopic Retrograde Cholangio-Pancreatography) associated with ES (Endoscopic Sphincterotomy) may improve the evolution by decompressing the pancreatic duct obstructed by the migrating gallstone. Three prospective, randomized studies have been performed to assess the role of early ERCP and ES. Morbidity is decreased by this approach but there is no difference in mortality or percentage of infected necrosis. The only indication of urgent ERCP and ES is the presence of acute cholangitis.