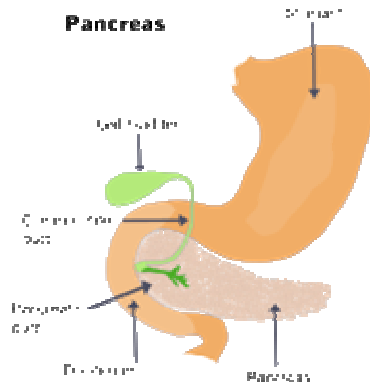


# Pancreatitis-- Acute

## Acute pancreatitis

*Classification and external resources*



[Pancreas](#)

*Acute pancreatitis* is a sudden inflammation of the pancreas. Depending on its severity, it can have severe complications and high mortality despite treatment. While mild cases are often successfully treated with conservative measures, such as oral or IV fluid rehydration; severe cases may require admission to the ICU or even surgery (often requiring more than one intervention) to deal with complications of the disease process.

*Symptoms and signs*

The most common symptoms and signs include:

- Severe epigastric pain radiating to the back
- Nausea, vomiting, diarrhea and loss of appetite
- Fever/chills
- Hemodynamic instability, including shock

Signs which are less common, and indicate severe disease, include:

- Grey-Turner's sign (hemorrhagic discoloration of the flanks)
- Cullen's sign (hemorrhagic discoloration of the umbilicus)

Other conditions to consider are:

- Pancreatic pseudocyst
- Pancreatic dysfunction (diabetes mellitus; malabsorption due to exocrine failure)
- Pancreatic cancer

Although these are common symptoms, they are not always present. Simple abdominal pain may be the sole symptom.

### *Causes*

#### *Most common causes*

A common mnemonic for the causes of pancreatitis spells “I get smashed”, an allusion to heavy drinking (one of the many causes):

I - idiopathic. Thought to be hypertensive sphincter or microlithiasis.

G - Gallstone. Gallstones that travel down the common bile duct and which subsequently get stuck in the Ampulla of Vater can cause obstruction in the outflow of pancreatic juices from the pancreas into the duodenum. The backflow of these digestive juices causes lyses (dissolving) of pancreatic cells and subsequent pancreatitis.

E - Ethanol (alcohol)

T - Trauma

S - Steroids

M - Mumps (para-myxovirus) and other viruses (Epstein-Barr virus, Cytomegalovirus)

A - Autoimmune disease (Polyarteritis nodosa, Systemic lupus erythematosus)

S - Scorpion sting (e.g. *Tityus trinitatis*), and also snake bites

H - Hypercalcemia, hyperlipidemia/hypertriglyceridemia and hypothermia

E - ERCP (Endoscopic Retrograde Cholangio-Pancreatography - a procedure that combines endoscopy and fluoroscopy)

D - drugs (SAND - steroids & sulfonamides, azathioprine, NSAIDS, diuretics such as furosemide and thiazides, and didanosine) and duodenal ulcers.

This mnemonic is also arranged according to the frequency of its causes. Thus: Gallstone pancreatitis is more common than pancreatitis caused by alcohol, trauma, or steroids.

#### *Less common causes*

- pancreas divisum
- long common duct
- carcinoma of the head of pancreas, and other cancer
- ascaris blocking pancreatic outflow
- chinese liver fluke
- ischemia from bypass surgery
- fatty necrosis
- pregnancy
- infections other than mumps, including varicella zoster
- Repeated marathon running.
- cystic fibrosis
- Valproic acid
- Anorexia or bulimia
- Treating Diabetics with Exenatide (Byetta)

#### *Causes by demographic*

The most common causes of pancreatitis are as follows:

- Western countries - chronic alcoholism and gallstones accounting for more than 85% of all cases
- Eastern countries - gallstones
- Children - trauma
- Adolescents and young adults - mumps

#### *Pathogenesis*

The exocrine pancreas produces a variety of enzymes, such as proteases, lipases, and saccharidases. These enzymes contribute to food digestion by breaking down food tissues. In acute pancreatitis, the worst offender among these enzymes may well be the protease trypsinogen which converts to the active trypsin which is most responsible for auto-digestion of the pancreas which causes the pain and complications of pancreatitis.

### *Histopathology*

The acute pancreatitis (acute hemorrhagic pancreatic necrosis) is characterized by acute inflammation and necrosis of pancreas parenchyma, focal enzymic necrosis of pancreatic fat and vessel necrosis - hemorrhage. These are produced by intra-pancreatic activation of pancreatic enzymes. Lipase activation produces the necrosis of fat tissue in pancreatic interstitium and peri-pancreatic spaces. Necrotic fat cells appear as shadows, contours of cells, lacking the nucleus, pink, finely granular cytoplasm. It is possible to find calcium precipitates (hematoxylinophilic). Digestion of vascular walls results in thrombosis and hemorrhage. Inflammatory infiltrate is rich in neutrophils.

### *Investigations and diagnosis*

- Blood Investigations - Full blood count, Renal function tests, Liver Function, serum calcium, serum amylase and lipase, Arterial blood gas
- Imaging - Chest X-rays (for exclusion of perforated viscus), Abdominal X-rays (for detection of 'sentinel loop' dilated duodenum sign, and gallstones which are radio opaque in 10%) and CT abdomen

### *Amylase and lipase*

- Elevated serum amylase and lipase levels, in combination with severe abdominal pain, often trigger the initial diagnosis of acute pancreatitis.
- Serum lipase rises 4 to 8 hours from the onset of symptoms and normalizes within 7 to 14 days after treatment.

- Serum amylase may be normal (in 10% of cases) for cases of acute or chronic pancreatitis (depleted acinar cell mass) and hypertriglyceridemia.
- Reasons for false positive elevated serum amylase include salivary gland disease (elevated salivary amylase) and macroamylasemia.
- If the lipase level is about 2.5 to 3 times that of Amylase, it is an indication of pancreatitis due to Alcohol.

Regarding selection on these tests, two practice guidelines state:

It is usually not necessary to measure both serum amylase and lipase. Serum lipase may be preferable because it remains normal in some non-pancreatic conditions that increase serum amylase including macroamylasemia, parotitis, and some carcinomas. In general, serum lipase is thought to be more sensitive and specific than serum amylase in the diagnosis of acute pancreatitis.

Although amylase is widely available and provides acceptable accuracy of diagnosis, where lipase is available it is preferred for the diagnosis of acute pancreatitis (recommendation grade A).

In one large study, there were no patients with pancreatitis who had an elevated amylase with a normal lipase. Another study found that the amylase could add diagnostic value to the lipase, but only if the results of the two tests were combined with a discriminant function equation.

### *Computed tomography*

Regarding the need for computed tomography, practice guidelines state:

2006: “Many patients with acute pancreatitis do not require a CT scan at admission or at any time during the hospitalization. For example, a CT scan is usually not essential in patients with recurrent mild pancreatitis caused by alcohol. A reasonable indication for a CT scan at admission (but not necessarily a CT with IV contrast) is to distinguish acute pancreatitis from another serious intra-abdominal condition, such as a perforated ulcer.”

2005: “Patients with persisting organ failure, signs of sepsis, or deterioration in clinical status 6–10 days after admission will require CT (recommendation grade B).”

CT abdomen should not be performed before the 1st 48 hours of onset of symptoms as early CT (<48 h) may result in equivocal or normal findings.

CT Findings can be classified into the following categories for easy recall:

- Intra-pancreatic - diffuse or segmental enlargement, edema, gas bubbles, pancreatic pseudocysts and phlegmons/abscesses (which present 4 to 6 wks after initial onset)
- Peri-pancreatic / extra-pancreatic - irregular pancreatic outline, obliterated peri-pancreatic fat, retroperitoneal edema, fluid in the lesser sac, fluid in the left anterior para-renal space
- Loco-regional – Gerota’s fascia sign (thickening of inflamed Gerota’s fascia, which becomes visible), pancreatic ascites, pleural effusion (seen on basal cuts of the pleural cavity), adynamic ileus, etc.

### *Magnetic resonance imaging*

While computed tomography is considered the gold standard in diagnostic imaging for acute pancreatitis, magnetic resonance imaging (MRI) has become increasingly valuable as a tool for the visualization of the pancreas, particularly of pancreatic fluid collections and necrotized debris. Additional utility of MRI includes its indication for imaging of patients with an allergy to CT’s contrast material, and an overall greater sensitivity to hemorrhage, vascular complications, pseudo-aneurysms, and venous thrombosis.

Another advantage of MRI is its utilization of magnetic resonance cholangio-pancreatography (MRCP) sequences. MRCP provides useful information regarding the etiology of acute pancreatitis, i.e., the presence of tiny biliary stones (choledocholithiasis or cholelithiasis) and duct anomalies.

Clinical trials indicate that MRCP can be as effective a diagnostic tool for acute pancreatitis with biliary etiology as endoscopic retrograde cholangio-pancreatography, but with the benefits of being less invasive and causing fewer complications.

### ***Classification by severity***

#### *Progression of pathophysiology*

Acute pancreatitis can be further divided into mild and severe pancreatitis. Mostly the Atlanta classification (1992) is used. In severe pancreatitis serious amount of necrosis determine the further clinical outcome. About 20% of the acute pancreatitis is severe with a mortality of about 20%. This is an important classification as severe pancreatitis will need intensive care therapy whereas mild pancreatitis can be treated on the common ward.

Necrosis will be followed by a systemic inflammatory response syndrome (SIRS) and will determine the immediate clinical course. The further clinical course is then determined by bacterial infection. SIRS is the cause of bacterial (Gram negative) translocation from the patient's colon.

There are several ways to help distinguish between these two forms. One is the above mentioned Ranson Score.

#### *Prognostic indices*

In predicting the prognosis, there are several scoring indices that have been used as predictors of survival. Two such scoring systems are the Ranson and APACHE II (Acute Physiology, Age and Chronic Health Evaluation) indices. Most, but not all studies report that the Apache score may be more accurate. In the negative study of the Apache II, the Apache II 24 hr score was used rather than the 48 hour score.

In addition, all patients in the study received an ultrasound twice which may have influenced allocation of co-interventions. Regardless, only the Apache II can be fully calculated upon admission. As the Apache II is

more cumbersome to calculate, presumably patients whose only laboratory abnormality is an elevated lipase or amylase do not need prognostication with the Apache II; however, this approach is not studied.

Practice guidelines state:

2006: “The two tests that are most helpful at admission in distinguishing mild from severe acute pancreatitis are APACHE-II score and serum hematocrit. It is recommended that APACHE-II scores be generated during the first 3 days of hospitalization and thereafter as needed to help in this distinction. It is also recommended that serum hematocrit be obtained at admission, 12 h after admission, and 24 h after admission to help gauge adequacy of fluid resuscitation.”

2005: “Immediate assessment should include clinical evaluation, particularly of any cardiovascular, respiratory, and renal compromise, body mass index, chest x ray, and APACHE II score”.

### *Ranson criterion*

Ranson criterion is a clinical prediction rule for predicting the severity of acute pancreatitis. It was introduced in 1974.

### *At admission*

- age in years > 55 years
- white blood cell count > 16000 cells/mm<sup>3</sup>
- blood glucose > 11 mmol/L (> 200 mg/dL)
- serum AST > 250 IU/L
- serum LDH > 350 IU/L

### *At 48 hours*

- Calcium (serum calcium < 2.0 mmol/L (< 8.0 mg/dL)
- Hematocrit fall > 10%



- Oxygen (hypoxemia  $PO_2 < 60$  mmHg)
- BUN increased by 1.8 or more mmol/L (5 or more mg/dL) after IV fluid hydration
- Base deficit (negative base excess)  $> 4$  mEq/L
- Sequestration of fluids  $> 6$  L

The criterion for point assignment is that a certain breakpoint be met at anytime during that 48 hour period, so that in some situations it can be calculated shortly after admission. It is applicable to both gallstone and alcoholic pancreatitis.

Alternatively, pancreatitis can be diagnosed by meeting any of the following:

*APACHE II score*

Apache score of  $\geq 8$  Organ failure Substantial pancreatic necrosis (at least 30% glandular necrosis according to contrast-enhanced CT)

Interpretation If the score  $\geq 3$ , severe pancreatitis likely. If the score  $< 3$ , severe pancreatitis is unlikely

Or

Score 0 to 2 : 2% mortality Score 3 to 4 : 15% mortality Score 5 to 6 : 40% mortality Score 7 to 8 : 100% mortality

Mnemonic for memorizing Ranson's criteria at admission: 'GA LAW' (glucose, age, LDH, AST, WBC count) At 48 hours: 'C Hobbs' (calcium, hematocrit, O<sub>2</sub>, BUN, Base deficit, sequestration (of fluid) greater than 6 L.

*APACHE*

Acute Physiology and Chronic Health Evaluation score  $> 8$  points predicts 11% to 18% mortality

- Hemorrhagic peritoneal fluid

- Obesity
- Indicators of organ failure
- Hypotension (SBP <90 mmHG) or tachycardia > 130 beat/min
- PO<sub>2</sub> <60 mmHg
- Oliguria (<50 mL/h) or increasing BUN and creatinine
- Serum calcium < 1.90 mmol/L (<8.0 mg/dL) or serum albumin <33 g/L (<3.2.g/dL)>

### *Balthazar scoring*

Developed in the early 1990s by Emil J. Balthazar et al.,<sup>[15]</sup> the Computed Tomography Severity Index (CTSI) is a grading system used to determine the severity of acute pancreatitis. The numerical CTSI has a maximum of ten points, and is the sum of the Balthazar grade points and pancreatic necrosis grade points:

### Balthazar Grade

<i>Balthazar Grade</i>	<i>Appearance on CT</i>	<i>CT Grade Points</i>
Grade A	Normal CT	0 points
Grade B	Focal or diffuse enlargement of the pancreas	1 point
Grade C	Pancreatic gland abnormalities and peri-pancreatic inflammation	2 points
Grade D	Fluid collection in a single location	3 points
Grade E	Two or more fluid collections and / or gas bubbles in or adjacent to pancreas	4 points

### Necrosis Score

#### **Necrosis Percentage Points**

No necrosis	0 points
0 to 30% necrosis	2 points
30 to 50% necrosis	4 points
Over 50% necrosis	6 points

CTSI's staging of acute pancreatitis severity has been shown by a number of studies to provide more accurate assessment than APACHE II, Ranson, and C-reactive protein (CRP) level. However, a few studies indicate that CTSI is not significantly associated with the prognosis of hospitalization in patients with pancreatic necrosis, nor is it an accurate predictor of AP severity.

### *Treatment*

#### *Pain control*

Originally it was thought that analgesia should not be provided by morphine because it may cause spasm of the sphincter of Oddi and worsen the pain, so the drug of choice was meperidine. However, due to lack of efficacy and risk of toxicity of meperidine, more recent studies have found morphine the analgesic of choice. Meperidine may still be used by some practitioners in more minor cases, or where morphine is contraindicated.

#### *Bowel rest*

In the management of acute pancreatitis, the treatment is to stop feeding the patient, giving him or her nothing by mouth, giving intravenous fluids to prevent dehydration, and sufficient pain control. As the pancreas is stimulated to secrete enzymes by the presence of food in the stomach, having no food pass through the system allows the pancreas to rest. Approximately 20% of patients have a relapse of pain during acute pancreatitis. Approximately 75% of relapses occur within 48 hours of oral re-feeding.

The incidence of relapse after oral re-feeding may be reduced by post-pyloric enteral rather than parenteral feeding prior to oral re-feeding. IMRIE scoring is also useful.

### *Nutritional support*

Recently, there has been a shift in the management paradigm from TPN (total parenteral nutrition) to early, post-pyloric enteral feeding (in which a feeding tube is endoscopically or radio-graphically introduced to the third portion of the duodenum). The advantage of enteral feeding is that it is more physiological, prevents gut mucosal atrophy, and is free from the side effects of TPN (such as fungemia). The additional advantages of post-pyloric feeding are the inverse relationship of pancreatic exocrine secretions and distance of nutrient delivery from the pylorus, as well as reduced risk of aspiration.

Disadvantages of a naso-enteric feeding tube include increased risk of sinusitis (especially if the tube remains in place greater than two weeks) and a still-present risk of accidentally intubating the bronchus even in intubated patients (contrary to popular belief, the endotracheal tube cuff alone is not always sufficient to prevent NG tube entry into the trachea).

### *Antibiotics*

A meta-analysis by the Cochrane Collaboration concluded that antibiotics help with a number needed to treat of 11 patients to reduce mortality. However, the one study in the meta-analysis that used a quinolone, and a subsequent randomized controlled trial that studied ciprofloxacin were both negative.

### *Carbapenems*

An early randomized controlled trial of imipenem 0.5 gram intravenously every eight hours for two weeks showed a reduction in pancreatic sepsis from 30% to 12%.

Another randomized controlled trial with patients who had at least 50% pancreatic necrosis found a benefit from imipenem compared to pefloxacin with a reduction in infected necrosis from 34% to 20%.

A subsequent randomized controlled trial that used meropenem 1 gram intravenously every 8 hours for 7 to 21 days stated no benefit; however, 28% of patients in the group subsequently required open antibiotic treatment vs. 46% in the placebo group. In addition, the control group had only 18% incidence of peripancreatic infections and less biliary pancreatitis than the treatment group (44% versus 24%).

The role of antibiotics is controversial. One recent expert opinion (prior to the last negative trial of meropenem) suggested the use of imipenem if CT scan showed more than 30% necrosis of the pancreas.

### *ERCP*

Early ERCP (endoscopic retrograde cholangiopancreatography), performed within 24 to 72 hours of presentation, is known to reduce morbidity and mortality. The indications for early ERCP are as follows:

- Clinical deterioration or lack of improvement after 24 hours
- Detection of common bile duct stones or dilated intra-hepatic or extrahepatic ducts on CT abdomen

The disadvantages of ERCP are as follows:

- ERCP precipitates pancreatitis, and can introduce infection to sterile pancreatitis
- The inherent risks of ERCP i.e. bleeding

It is worth noting that ERCP itself can be a cause of pancreatitis.

### *Surgery*

Surgery is indicated for (i) infected pancreatic necrosis and (ii) diagnostic uncertainty and (iii) complications. The most common cause of death in acute pancreatitis is secondary infection. Infection is diagnosed based on 2 criteria.

- Gas bubbles on CT scan (present in 20 to 50% of infected necrosis)

- Positive bacterial culture on FNA (fine needle aspiration, usually CT or US guided) of the pancreas.

Surgical options for infected necrosis include:

- Minimally invasive management - necrosectomy through small incision in skin (left flank) or stomach
- Conventional management - necrosectomy with simple drainage
- Closed management - necrosectomy with closed continuous postoperative lavage
- Open management - necrosectomy with planned staged reoperations at definite intervals (up to 20+ reoperations in some cases)

#### *Other measures*

- Pancreatic enzyme inhibitors are not proven to work.
- The use of octreotide has not been shown to improve outcome.

#### *Complications*

Complications can be systemic or locoregional.

- Systemic complications include ARDS, multiple organ dysfunction syndrome, DIC, hypocalcemia (from fat saponification), hyperglycemia and insulin dependent diabetes mellitus (from pancreatic insulin producing beta cell damage)
- Locoregional complications include pancreatic pseudocyst and phlegmon / abscess formation, splenic artery pseudoaneurysms, hemorrhage from erosions into splenic artery and vein, thrombosis of the splenic vein, superior mesenteric vein and portal veins (in descending order of frequency), duodenal obstruction, common bile duct obstruction, progression to chronic pancreatitis

#### *Epidemiology*

- Annual incidence in the U.S. is 18 per 100,000 population. In a European cross-sectional study, incidence of acute pancreatitis

increased from 12.4 to 15.9 per 100,000 annually from 1985 to 1995; however, mortality remained stable as a result of better outcomes. Another study showed a lower incidence of 9.8 per 100,000 but a similar worsening trend (increasing from 4.9 in 1963-74) over time.