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Cardinal symptom is usually steady, sudden-onset abdominal pain radiating to the back.

Associated with nausea and vomiting. A history of cholelithiasis or alcohol intake is often present.

Typical signs include epigastric tenderness, fever, and tachycardia.

Elevated serum amylase and lipase concentration supports, but is not pathognomonic for, the diagnosis of acute pancreatitis.

Initial treatment includes resuscitation with intravenous fluids and correction of electrolyte abnormalities, analgesia, and tight glucose control.

Treatment of severe acute pancreatitis includes support of end organ failure, most commonly of respiratory, renal, and circulatory systems.
**Acute pancreatitis**

**Basics**

**Definition**
A disorder of the exocrine pancreas, and is associated with acinar cell injury with local and systemic inflammatory responses.[1] The severity of the disease ranges from mild pancreatic oedema with full recuperation to severe systemic inflammatory response with pancreatic/peri-pancreatic necrosis, multiple organ failure, and death.

**Epidemiology**
Acute pancreatitis is a potentially lethal disease that is increasing in incidence. Incidence varies from 4.5 to 79.8 per 100,000 per year in different countries. This variation is due to different diagnostic criteria, geographical factors, and changes over time.[7] A 10-fold increase in its incidence from 1960 to 1980, with a mortality rate from 1% to 9%, was noted.[8] Approximately 275,000 patients are admitted to hospitals in the US each year with acute pancreatitis.[9] The mortality rate is influenced by the severity of the disease, and several prognostic factors have been investigated and described. In contrast to the milder form of the disease, which has a mortality rate of 1%, the mortality associated with severe acute pancreatitis is 10% with sterile and 25% with infected pancreatic necrosis.[1] Gallstone pancreatitis is more common in white women >60 years of age, especially among patients with microlithiasis. Alcoholic pancreatitis is seen more frequently in men.[10]

**Aetiology**
Several aetiological factors have been described for acute pancreatitis, but in 10% to 20% of cases an aetiological factor cannot be identified.[10] These cases are then considered idiopathic. The presence of microlithiasis or biliary sludge accounts for 80% of idiopathic pancreatitis. In the US, gallstones followed by alcohol intake are responsible for 80% to 90% of cases of acute pancreatitis.[11] The most common cause worldwide is alcohol consumption.

Other causes include:

- Hypertriglyceridaemia
- Hypercalcaemia
- Pancreatic malignancy
- Post-endoscopic retrograde cholangiopancreatography (ERCP) (2% to 3%)
- Trauma
- Infections (mumps, mycoplasma, Epstein-Barr virus, *Ascaris lumbricoides*, HIV-related co-infections)
- Drugs (e.g., furosemide, didanosine, oestrogens, azathioprine, thiazide diuretics, sulfonamides, tetracyclines, sulindac, mercaptopurine, valproic acid, L-asparaginase)[12][13]
- Autoimmune conditions (collagen vascular diseases)
- Pancreas divisum
- Intraductal papillary mucinous neoplasm
- Sphincter of Oddi dysfunction
- Heredity[4][7]
- Autoimmune (immunoglobulin G4-related) sclerosing acute pancreatitis.
Pathophysiology

The exact mechanism by which pancreatitis occurs is unknown, although there is evidence to suggest that abnormal intracellular calcium accumulation is an important step in the molecular pathophysiology of acute pancreatitis development. Increased calcium transients potentiate co-localisation of zymogen and lysosome granules and ultimately lead to premature enzymatic activation.[14]

Ethanol-induced pancreatitis has different pathophysiological mechanisms. Studies have described that ethanol is a direct toxic insult to the acinar cell, causing inflammation and membrane destruction. Other mechanisms include sphincter of Oddi dysfunction, induction of hypertriglyceridaemia, or formation of free oxygen radicals.[15] Some studies have demonstrated that ethanol causes an increase in ductal pressures secondary to protein deposition within the pancreatic duct, favouring retrograde flow and intra-pancreatic enzymatic activation.[1]

Classification

Atlanta classification[2]

The revised classification of acute pancreatitis identifies an early and a late phase of the disease. Severity is classified as mild, moderate, or severe.[2]

- Mild acute pancreatitis: the most common form, has no organ failure or local or systemic complications, and usually resolves in the first week.
- Moderately severe acute pancreatitis: presence of transient organ failure (resolves within 48 hours), and/or local complications or exacerbation of comorbid disease.
- Severe acute pancreatitis: persistent organ failure (>48 hours). Local complications are peri-pancreatic fluid collections, pancreatic and peri-pancreatic necrosis (sterile or infected), pseudocyst, and walled-off necrosis (sterile or infected).

Balthazar classification

This is a classification based on the extent of pancreatic inflammation and the presence or absence of fluid collections or gas suggestive of necrosis on CT with IV contrast.[3]

- A: Normal
- B: Focal or diffuse gland enlargement; small intra-pancreatic fluid collection
- C: Any of the above plus peri-pancreatic inflammatory changes and <30% gland necrosis
- D: Any of the above plus single extra-pancreatic fluid collection and 30% to 50% gland necrosis
- E: Any of the above plus extensive extra-pancreatic fluid collection, pancreatic abscess, and >50% gland necrosis.

General pathological classification

Surgical textbooks often distinguish between oedematous and haemorrhagic pancreatitis, based on pathological/histological features:

- Oedematous pancreatitis: pancreatic parenchyma and surrounding retroperitoneal structures are engorged with interstitial fluid and infiltration of inflammatory cells[4] [5]
• Haemorrhagic pancreatitis: bleeding into the parenchyma and surrounding retroperitoneal structures with extensive pancreatic necrosis.[4] [5]
Secondary prevention

The most important aspect of prevention is patient education. Eating a balanced, low-fat diet, maintaining adequate triacylglyceride control, and decreasing the amount of alcohol intake, preferably to zero, are a few dietary and behavioural measures that may decrease the incidence of acute pancreatitis. Data now highlight the substantial correlation between cigarette smoking and recurrent acute pancreatitis. Therefore, patients should be strongly encouraged to maintain complete abstinence from cigarettes (and other tobacco use).

Effectively addressing gallstone disease by any means available (such as cholecystectomy, endoscopic retrograde cholangiopancreatography [ERCP], ursodeoxycholic acid), may decrease the ductal obstruction risk and hence the risk of pancreatitis. In patients with hypertriglyceridaemia, statin use has been associated with a decreased risk of developing pancreatitis.[129] Other risk factors may be controlled through patient education and medicine dose adjustments.[26] [130] Probiotics, antioxidants and immune nutrition have no role in the prevention of acute pancreatitis.[131] [132] [133]

Several studies have addressed the use of pharmacological treatment (e.g., somatostatin analogues such as octreotide, gabexate, ulinastatin),[134] [135] adequate patient selection, and stent placements during ERCP to prevent pancreatic injury.[136] [137] [138] [139] [140] [141] [142] [143] [144] [145] [146] [147] The use of somatostatin analogues has been linked to a better protection against ERCP-induced pancreatitis than gabexate (a serine protease inhibitor) in some studies, but two meta-analyses yielded different conclusions.[148] [149] Meta-analyses have demonstrated ulinastatin (a urinary trypsin inhibitor) to have a preventive role in ERCP-induced pancreatitis. Further studies are needed to determine which agent is most efficacious in the prevention of ERCP-induced pancreatitis.[150] [151] [152] Gabexate and ulinastatin are not commercially available in all countries. Indometacin has been shown to be an effective agent with which to decrease the rate of post-ERCP pancreatitis. Stents are an option for endoscopists with experience in the field, but the manipulation to obtain biliary access (rather than patient characteristics or endoscopist experience) is the main factor in the development of ERCP-induced pancreatitis.[26] [27] [28] [153] The use of a guidewire bile duct cannulation technique during ERCP has been shown to decrease the incidence of post-ERCP pancreatitis in comparison with the standard contrast injection cannulation.[154] [155] [156]

Those with idiopathic chronic pancreatitis, recurrent acute pancreatitis, or a family history of pancreatitis should be considered for genetic testing, especially in the setting of pancreatic cancer. The clinical relevance and the therapeutic consequences of the gene mutations leading to pancreatitis are still controversial, and genetic testing is recommended when a patient with idiopathic pancreatitis is under 25 years of age at diagnosis or when one or more family members have either pancreatitis or pancreatic cancer. Genetic analysis of asymptomatic family members should only be offered after adequate genetic counselling, and antenatal diagnosis is not recommended.[157]
Case history

Case history #1

A 53-year-old man presents to the emergency department complaining of severe mid-epigastric abdominal pain that radiates to the back. The pain improves when the patient leans forwards or assumes the fetal position and worsens with deep inspiration and movement. He also complains of nausea, vomiting, and anorexia, and gives a history of heavy alcoholic intake this past week. He is tachycardic, tachypnoeic, and febrile with hypotension. He is slightly agitated and confused. He is diaphoretic with decreased breath sounds over the base of the left lung.

Case history #2

A 47-year-old overweight woman is admitted with generalised abdominal pain. She has been unable to eat or drink due to nausea and vomiting. She states the pain started in the right upper quadrant, similar to previous episodes that she had been to the emergency department with over the past few months. An ultrasound obtained on her last visit to the emergency department revealed gallstones with no inflammation of the gallbladder, and she was told that she should see a surgeon. She looks jaundiced and in distress. She has point tenderness under her ribs on the right, which is worsened with deep palpation. No mass is palpable.

Other presentations

Pancreatitis can mimic an acute surgical abdomen with rigid abdomen and peritoneal signs. It may also be uncovered in critically ill patients as a cause of ARDS.[6]

Step-by-step diagnostic approach

The diagnosis of pancreatitis is always one of exclusion, so it must be included with any complaint of severe abdominal pain. History and examination can be indicative of acute pancreatitis; however, 2 out of the following 3 criteria must be met for its diagnosis:[37]

- Clinical story (upper abdominal pain)
- Elevated serum amylase or lipase (>3 upper limit of normal)
- Imaging study (CT, MRI, ultrasound) consistent with acute pancreatitis.

History

A detailed history is imperative to narrow the large number of differentials of abdominal pain. Metabolic, nutritional, and procedural aetiologies of pancreatitis should be considered during history-taking.[1] [5] [12] A detailed family history is important to rule out collagen vascular diseases, cancer, or hereditary pancreatitis. Any medicine, particularly new medicines, and indications for their use should be reviewed, because many medications can have pancreatic injury as an adverse effect. Age and sex are important demographic variables, because the 2 most common causes of acute pancreatitis differ. Gallstone pancreatitis is seen most commonly in patients with gallbladder disease - the 5 “Fs”: fat, forty, female,
Acute pancreatitis

Diagnosis

Acute pancreatitis is seen more frequently in men, generally younger than those with gallstone pancreatitis. Patients usually manifest after an average of 4 to 8 years of alcohol intake, and bingeing behaviour increases the risk of acute pancreatitis.

Patients may present with agitation and confusion, and in severe distress. They may give a history of anorexia, nausea, and vomiting with poor oral intake. The most common symptom is severe mid-epigastric pain that radiates to the back (sometimes band distribution, often straight through middle back; many patients describe it as being stabbed with a knife), worsens with movement, and is alleviated when assuming the fetal position (bent over, with spine, hips, and knees flexed).[5][12] Gallstone pancreatitis may be more acute in onset than alcoholic pancreatitis, which may be preceded with a few days of mild epigastric discomfort. Use of a standardised protocol improves diagnostic accuracy.[38]

Physical examination

Signs of hypovolaemia (decreased skin turgor, dry mucous membranes, hypotension) are usually found. Patients may appear diaphoretic, tachycardic, and tachypnoeic. The pulse acutely is thin and thready, consistent with intravascular volume depletion. Fever may indicate a complicated pancreatitis or may simply represent cytokine release as part of the inflammatory process. Decreased breath sounds may be detected if there is a pleural effusion (more common on the left side); this is seen in up to 50% of patients with acute pancreatitis.[6] The abdominal examination may reveal a tender and distended abdomen with diminished bowel sounds (if an ileus has developed) and voluntary guarding to palpation of the upper abdomen. There may be a mild rigidity without re-bound tenderness. Clinical signs of hypocalcaemia are rare but may be evident, such as facial muscle spasm when facial nerve is tapped (Chvostek's sign) and carpopedal spasm when blood pressure cuff is applied (Trousseau's sign). Complicated haemorrhagic pancreatitis is very rare and may exhibit ecchymotic discoloration of several areas, including the periumbilical skin (Cullen's sign), over both flanks (Grey-Turner's sign) or over the inguinal ligament (Fox's sign), and may be seen as soon as presentation or 24 to 48 hours after the onset.[7][8]

Laboratory work-up

Any patient with an acute abdomen should have an FBC with differential and a blood chemistry including renal, liver, and pancreatic function tests. Mild leukocytosis with left shift and elevated haematocrit as a result of dehydration or low haematocrit as a result of haemorrhage can be seen. The development of haemoconcentration is associated with an increased risk of developing necrotising pancreatitis.[39] As a result of dehydration there may be some degree of pre-renal azotaemia, manifested by elevated creatinine and urea. In the absence of choledocholithiasis, liver function tests are usually normal, but a slight increase in alkaline phosphatase and bilirubin may be seen.

Elevated levels of serum amylase or lipase (>3 upper limit of normal) support, but are not pathognomonic for, the diagnosis of acute pancreatitis. At standard threshold levels serum amylase and serum lipase have similar sensitivities and specificities.[40] However, about one quarter of people with acute pancreatitis fail to be diagnosed as having acute pancreatitis with serum amylase and serum lipase tests. It is therefore important to have a low threshold for admitting and treating patients whose symptoms are suggestive of acute pancreatitis, even if these tests are normal.[40] About 1 in 10 patients without acute pancreatitis may be wrongly diagnosed as having acute pancreatitis with these tests. It is important to consider other conditions that may require urgent surgery even if these tests are abnormal.[40] The diagnostic performance of these tests decreases with time, and additional investigations should be performed if there is suspicion of acute pancreatitis.[40]
It is important to monitor arterial oxygenation, because patients may be hypoxaemic, requiring supplemental oxygen. During initial management, arterial blood gases should be considered every 12 hours for the first 3 days to assess both oxygenation and acid-base status.[5]

Early and serial C-reactive protein (CRP) testing is used in acute pancreatitis as an indicator of severity and progression of inflammation.[41]

If sepsis is suspected in patients with pancreatic necrosis, a percutaneous needle aspiration may be performed to rule out bacterial colonisation, although there are reports to suggest that fine needle aspiration is not routinely performed in infected necrotising pancreatitis.[42]

**Imaging**

Radiographic studies are not used for diagnosis of acute pancreatitis, but may determine possible causative factors and exclude other diagnoses.

A CXR may show pleural effusion and basal atelectasis, and a sentinel loop (isolated dilatation of a segment of gut) may be seen in a KUB. Plain abdominal x-ray may reveal a sentinel loop adjacent to the pancreas, gas distending the right colon that abruptly stops in the mid- or left transverse colon (cut-off sign), or calcifications.

Magnetic resonance cholangiopancreatography (MRCP), endoscopic retrograde cholangiopancreatography (ERCP), trans-abdominal ultrasound, and endoscopic ultrasound (EUS) are usually indicated in patients with elevated liver function tests suggestive of bile duct obstruction, to exclude strictures, neoplasms, or stones.[8] [43]

Ultrasound is considered to be the preferred initial study if biliary aetiology is suspected. It is inexpensive, easy to perform at the bedside, and allows examination of the gallbladder and bile duct system. Its sensitivity in detecting pancreatitis is 62% to 95%. It is limited by obesity and bowel gas, and is operator-dependent.

The advantage of the ERCP is that it has the added benefit of treating certain aetiological conditions (e.g., by stone removal, stent placement, or sphincterotomy), but it has been largely superseded as a diagnostic modality by MRCP and ultrasound.

MRCP is generally used in patients with renal insufficiency, in whom the use of CT with IV contrast is discouraged. CT is the best initial modality for staging acute pancreatitis and detecting complications; however, for serial examinations, MRCP is gaining favour due to better imaging of biliary and pancreatic stones, as well as better characterisation of solid versus cystic lesions.[44] MRCP may be useful early in the course to exclude obstructing common bile duct stones in patients with biliary acute pancreatitis.[45]

Patients who show signs of systemic inflammatory response or sepsis, or who do not improve, should have a CT scan to rule out peri-pancreatic collections, necrosis, and abscess. Areas of non-perfusion indicate infected pancreatic necrosis. Of note, a CT scan is not recommended early in the course of the disease.

**Emerging tests**

Urinary trypsinogen-2 is now considered a better serological screening test than amylase but is not yet used clinically; sensitivity of 94% and specificity of 95%. [8] [46] [47] [48] Interleukins IL-6 and IL-8 are
inflammatory mediators that have been described as predictive serum markers for development of severe acute pancreatitis.[49]

[VIDEO: Venepuncture and phlebotomy animated demonstration ]

[VIDEO: Radial artery puncture animated demonstration ]

[VIDEO: Femoral artery puncture animated demonstration ]

Risk factors

**Strong**

**middle-aged women**

- Women between 50 and 70 years of age are more likely to have gallbladder disease and may present with pancreatitis at later age than men with alcoholic pancreatitis (40 to 55 years of age).

**young- to middle-aged men**

- Mostly associated with high alcohol intake.

**gallstones**

- Gallstone pancreatitis accounts for 45% to 50% of acute pancreatitis in the US.[15] It is seen more frequently in older women and those with history of gallstone disease. Impaction of a stone within the common bile duct causes reflux of biliohepatic secretions and intra-pancreatic enzymatic activation. Stones may cause inflammation and oedema of the ducts, causing some degree of flow restriction and backflow of activated enzymes into the pancreas.[15]

**alcohol**

- Ethanol causes 40% to 45% of all cases of acute pancreatitis and is the most common cause of acute pancreatitis in men. A dose-related destruction to the pancreatic parenchyma has been described. This form of pancreatitis is more commonly seen in men than in women and is usually seen after periods of binge drinking. There is no threshold for the development of acute pancreatitis. The average amount of alcohol intake in patients with acute pancreatitis is 150 to 175 g per day.[8] [15]

**hypertriglyceridaemia**

- It has been suggested that the pancreatic lipase can produce toxic fatty acids that are secreted into the pancreatic micro-circulation, leading to endothelial injury and ischaemic insult to the acinar cell.[12] Many patients with acute pancreatitis demonstrate an acute increase in circulating triglycerides in the range of 5 or 6mmol/L (a few hundred mg/dL). However, patients with true hypertriglyceridaemia-induced acute pancreatitis manifest a substantial increase in circulating triglycerides, commonly over 22 or 23mmol/L (2000mg/dL).[16]

**use of causative drugs**

- Azathioprine: mechanisms suggested for drug-induced pancreatitis include pancreatic duct constriction; immunosuppression; cytotoxic, osmotic, pressure, or metabolic effects; arteriolar thrombosis; direct cellular toxicity; and hepatic involvement.[13]
- Thiazide diuretics: thought to cause pancreatitis by affecting the acinar cells.[13]
• Furosemide: causes pancreatitis by an undefined immunological pathway.[13] [19]
• Other drugs known to cause pancreatitis include: sulfonamides, tetracyclines, oestrogens, didanosine, sulindac, mercaptopurine, valproic acid, and L-asparaginase.[13]

endoscopic retrograde cholangiopancreatography (ERCP)

• The use of contrast during ERCP has been linked to pancreatic inflammation. The incidence of ERCP-induced pancreatitis is 2% to 3%, and some studies have shown some risk reduction with the use of non-steroidal anti-inflammatory agents,[20] [21] [22] [23] pancreatic stents, guide wires,[24] [25] and octreotide infusion. The risk of ERCP-induced pancreatitis is slightly increased in young females, in patients with impacted stones or oedema of the ampulla or bile duct, and during technically demanding procedures.[26] [27] [28]

trauma

• Traumatic pancreatitis can be caused by therapeutic or diagnostic procedures or during external trauma. Blunt trauma is the most common cause of pancreatic injury and can be associated with parenchymal inflammation and hyperamylasaemia. Given that the pancreas is a retroperitoneal organ, trauma is not a common aetiological factor but its incidence may be under-reported, because patients may not have a clear clinical manifestation.[12]

systemic lupus erythematosus

• This is quite rare and the exact mechanisms are not well understood.[29] [30]

Sjogren’s syndrome

• This is quite rare and the exact mechanisms are not well understood.[29] [30]

Weak hypercalcaemia

• Causal mechanisms are still not completely understood. Animal studies have showed that calcium has a direct toxic effect on the pancreatic acinar cell. Other proposed pathophysiological mechanisms include accumulation of zymogen granules in the cytoplasm, cytoplasmic vacuolisation, focal acinar depolarisation, acinar necrosis, increased amylase secretion,[17] [18] and formation of calcified stones intraductally.[12]

mumps

• Thought to cause pancreatitis by infecting the acinar cells.[19] [13]

coxsackievirus

• Thought to cause pancreatitis by infecting the acinar cells.[19] [13]

Mycoplasma pneumoniae

• Thought to cause pancreatitis by infecting the acinar cells.[19] [13]

pancreas divisum

• During organogenesis, the pancreas derives from the foregut after the fusion of the larger dorsal bud and the smaller ventral bud. The smaller accessory duct of Santorini drains the pancreatic structures that derive from the dorsal bud (upper half of the head, neck, body, and tail), whereas the larger duct of Wirsung drains the ventral bud (lower part of the head and uncinate process). Failure of the rotation
Acute pancreatitis

Diagnosis

of the ventral bud prevents fusion of both ducts, making the drainage of the dorsal bud derivate insufficient, which can lead to acute pancreatitis.[15] The role of endoscopic sphincterotomy of the minor papilla and stenting of the dorsal duct may decrease the recurrence of pancreatitis but its role for pain control has not been demonstrated.[31]

pancreatic cancer

• The most common primary malignancy of the pancreas is the adenocarcinoma. Cancer has been implicated as a potential risk factor for the development of pancreatitis if it causes duct obstruction. It has been reported that 1% to 2% of acute pancreatitis may be attributed to peri-ampullary tumours.[12]

sphincter of Oddi dysfunction

• Oddi’s dysfunction can be primary (idiopathic) or secondary (trauma during ERCP), and can lead to obstruction of bile and retrograde flow into the pancreatic parenchyma, causing inflammation.[32]

FHx of pancreatitis

• Patients with the familial form of pancreatitis present with abdominal pain early in childhood. The genetic defect appears to be transmitted as a non-X-linked dominant with variable penetrance and progress to chronic pancreatitis. Other conditions may be associated, such as diabetes mellitus or aminoaciduria.[5] Hereditary pancreatitis accounts for 1% of all cases, and several mutations have been described as possible inducers of the disease. The strongest correlations are with the cationic trypsinogen gene (PRSS1) on chromosome 7q35 and SPINK1 and CRTF gene mutations.[33][34][35] PRSS1 and CTRC (chymotrypsin C) mutations are strongly associated with early-onset pancreatitis.[36]

History & examination factors

Key diagnostic factors

presence of risk factors (common)

• Key risk factors include: middle-aged women, young- to middle-aged men, gallstones, alcohol, hypertriglyceridaemia, use of known causative medications, endoscopic retrograde cholangiopancreatography (ERCP) procedure, HIV/AIDS, SLE, and Sjogren's syndrome.

nausea (common)

• Nausea is one of the most common presenting symptoms and is seen in 70% to 80% of cases.[8]

vomiting (common)

• Emesis can lead to dehydration, electrolyte abnormalities, and hypokalaemic metabolic alkalosis.[8]

anorexia (common)

• Decreased appetite secondary to nausea, pain, and general malaise is commonly seen during an acute attack of acute pancreatitis.[8]

abdominal pain (common)

• Mid-epigastric pain that radiates to the back is characteristic of the disease.

tachycardia (common)
Acute pancreatitis

**Diagnosis**

- As a result of hypovolaemia.[1]

**Other diagnostic factors**

**Grey-Turner's sign (uncommon)**
- Bilateral flank blue discoloration indicating haemorrhagic pancreatitis.[5]

**Cullen's sign (uncommon)**
- Peri-umbilical blue discoloration indicating haemorrhagic pancreatitis.[5]

**Fox's sign (uncommon)**
- Ecchymosis over the inguinal ligament area.[5]

**Chvostek's sign (uncommon)**
- Facial muscle spasm when facial nerve is tapped.

**Hypotension (uncommon)**
- As a result of increased insensible fluid losses, third spacing, and emesis.[1]

**Abdominal distension (uncommon)**
- Develop localised ileus.[1]

**Diagnostic tests**

**1st test to order**

<table>
<thead>
<tr>
<th>Test</th>
<th>Result</th>
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<tbody>
<tr>
<td>serum lipase</td>
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<td>• About one quarter of people with acute pancreatitis fail to be diagnosed as having acute pancreatitis with serum amylase and serum lipase tests. It is therefore important to have a low threshold for admitting and treating patients whose symptoms are suggestive of acute pancreatitis, even if these tests are normal.[40]</td>
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| 3 times the upper limit of the normal range |                                              |
| AST/ALT                  | • Low sensitivity and specificity for pancreatitis.                                           |
|                          | if >3 times the upper normal limit, predicts gallstone disease as aetiology in 95% of cases  |
| FBC and differential     | • Mild leukocytosis with left shift and elevated haematocrit as a result of dehydration or low haematocrit as a result of haemorrhage can be seen. The development of haemoconcentration has been associated to predict the risk of developing necrotising pancreatitis. |
|                          | leukocytosis                                                                                 |
| C-reactive protein (CRP) | • Early and serial CRP testing is used in acute pancreatitis as an indicator of severity and progression of inflammation. |
|                          | if >200 units/L, is associated with pancreatic necrosis                                       |
| haematocrit              | • Indicator of severity and prognosis.                                                        |
|                          | if >44% on admission, is a predictor of pancreatic necrosis                                   |
| arterial blood gas       | • It is important to monitor the arterial oxygenation, because patients may be hypoxaemic, requiring supplemental oxygen. During the initial management, consider arterial blood gases every 12 hours for the first 3 days to assess both oxygenation and acid-base status. |
|                          | hypoxaemia and disturbances in acid-base balance                                             |
| abdominal plain film     | • Abnormal in two-thirds of patients.                                                          |
|                          | may find a sentinel loop (isolated dilatation of a segment of gut) adjacent to the pancreas, gas distending the right colon that abruptly stops in the mid- or left transverse colon (cut-off sign), or calcifications |
| CXR                      | • Radiographic studies are not used for diagnosis of acute pancreatitis, but may determine possible causative factors and exclude other diagnoses. |
|                          | may show atelectasis and pleural effusion (especially in the left side)                     |
### Acute Pancreatitis

#### Diagnosis

<table>
<thead>
<tr>
<th>Test</th>
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<tbody>
<tr>
<td>transabdominal ultrasound</td>
<td>• Preferred study if biliary aetiology suspected.</td>
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<tr>
<td></td>
<td>• Sensitivity in detecting gallstones in the setting of pancreatitis is 62% to 95%. Is non-invasive, easy to perform at the bedside, and inexpensive. Limited by obesity, bowel gas, and is operator-dependent. Useful when biliary causes are suspected. With a sensitivity and specificity of 95%, endoscopic ultrasound (EUS) has been demonstrated to have a decreased complication rate compared with ERCP.[50]</td>
</tr>
<tr>
<td>ratio of serum lipase:amylase</td>
<td>• Low sensitivity. Favours alcoholic pancreatitis.[46]</td>
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<td>&gt;5</td>
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**Other tests to consider**

<table>
<thead>
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<tbody>
<tr>
<td>abdominal CT scan</td>
<td>• A CT scan of the abdomen is not indicated in the first 48 hours from the diagnosis. CT scan with IV contrast is the most sensitive and specific study for confirming diagnosis of pancreatitis. Has a sensitivity of 90% and specificity of 100%. It is used when clinical and biochemical findings are equivocal. Ranson score of &gt;3 or APACHE II score of &gt;8 to detect and stage complications, and when patients have persisting organ failure, show signs of sepsis, or present with clinical deterioration or do not improve after 48 to 72 hours of treatment. Signs of complicated pancreatitis are usually seen 3 days after the onset of abdominal pain.</td>
</tr>
<tr>
<td>magnetic resonance cholangiopancreatography (MRCP)</td>
<td>• MRCP has the advantage of not requiring IV contrast or radiation, although intravenous gadolinium enhances images as compared with non-contrast MRI. In addition, MRCP allows better visualisation of common bile duct stones and the pancreatic duct. It can more readily distinguish solid from cystic in dealing with peri-pancreatic collections.[44]</td>
</tr>
<tr>
<td>endoscopic retrograde cholangiopancreatography (ERCP)</td>
<td>• ERCP has a limited use as a diagnostic tool in acute attacks of acute pancreatitis and has been mostly replaced by ultrasound and MRCP. Indications are preoperative evaluation to verify duct condition in patients with traumatic pancreatitis, in patients with severe pancreatitis and suspected biliary obstruction (allows sphincterotomy, stone removal, stent placement, tissue diagnosis) that do not improve after 24 hours of conservative management, and as work-up for idiopathic pancreatitis. Studies have shown a reduction of morbidity and mortality in patients with early ERCP (&lt;24 hours) and obstructing common bile duct stones;[5] [8] [10] however, early ERCP is not indicated in biliary acute pancreatitis in the absence of common bile duct obstruction.[45]</td>
</tr>
<tr>
<td></td>
<td>findings may include diffuse or segmental enlargement of the pancreas with irregular contour and obliteration of the peri-pancreatic fat, necrosis, or pseudocysts</td>
</tr>
<tr>
<td></td>
<td>findings may include stones, diffuse or segmental enlargement of the pancreas with irregular contour and obliteration of the peri-pancreatic fat, necrosis, or pseudocysts</td>
</tr>
<tr>
<td></td>
<td>identifies stones and allows their retrieval during the same intervention; can identify duct filling defects and strictures</td>
</tr>
</tbody>
</table>
**Acute pancreatitis**

**Diagnosis**

<table>
<thead>
<tr>
<th>Test</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>fine needle aspiration</td>
<td>identification of causative organism if bacterial colonisation</td>
</tr>
<tr>
<td>• If sepsis is suspected in patients with pancreatic necrosis, a percutaneous needle aspiration can be performed to rule out bacterial colonisation.</td>
<td></td>
</tr>
</tbody>
</table>

**Emerging tests**

<table>
<thead>
<tr>
<th>Test</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>urinary trypsinogen-2</td>
<td>elevated</td>
</tr>
<tr>
<td>• Sensitivity of 94% and specificity of 95%. Now considered a better serological screening test than amylase.[8] [46] [47] [48]</td>
<td></td>
</tr>
<tr>
<td>serum IL-6</td>
<td>elevated</td>
</tr>
<tr>
<td>• Sensitivity of 81% to 88% and specificity of 75% to 85% for prediction of severe acute pancreatitis.[49]</td>
<td></td>
</tr>
<tr>
<td>serum IL-8</td>
<td>elevated</td>
</tr>
<tr>
<td>• Sensitivity of 65% to 70% and specificity of 69% to 91% for prediction of severe acute pancreatitis.[49]</td>
<td></td>
</tr>
</tbody>
</table>

**Differential diagnosis**

<table>
<thead>
<tr>
<th>Condition</th>
<th>Differentiating signs / symptoms</th>
<th>Differentiating tests</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peptic ulcer disease</td>
<td>• Longstanding epigastric pain, which does not generally radiate to the back; reflux; heartburn; and anorexia. Identifiable causes such as non-steroidal anti-inflammatory drug (NSAID) use, <em>Helicobacter pylori</em>, Zollinger-Ellison's syndrome may be present.</td>
<td>• May improve with proton pump inhibitors, lifestyle modifications, and <em>H pylori</em> treatment.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Normal lipase and amylase. Tonometry may show evidence of reflux.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Laboratory evaluation will show normal values of amylase and lipase. Endoscopic evaluation will be diagnostic after visualising erosions, erythema, or ulcers, and allows biopsies to be performed.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Perforated viscus</td>
<td>• Will present with acute abdomen, peritoneal signs, tachycardia, and sepsis. Generally the abdomen is rigid and tender in all 4 quadrants, with guarding.</td>
<td>Normal or elevated lipase. May have elevated amylase (usually less marked than that seen in acute pancreatitis).</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Plain x-rays show sub-diaphragmatic air.</td>
</tr>
<tr>
<td>Condition</td>
<td>Differentiating signs / symptoms</td>
<td>Differentiating tests</td>
</tr>
<tr>
<td>---------------------------</td>
<td>-------------------------------------------------------------------------------------------------</td>
<td>---------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Oesophageal spasm</td>
<td>• Dysphagia, odynophagia, weight loss, history of retrosternal pain. Physical examination may be normal.</td>
<td>• A swallow study may demonstrate a contracted and abnormal-appearing oesophagus with increased pressures on oesophageal manometry.</td>
</tr>
<tr>
<td>Intestinal obstruction</td>
<td>• History of abdominal surgeries (especially colon resection, caesarean sections, and aortic procedures).&lt;br&gt;• Hernias, usually with incarcerated bowel, in the physical examination.&lt;br&gt;• Presents with abdominal distension (depends on the level of obstruction), tympanism, decreased bowel sounds, anorexia, emesis (quality depends on location of obstruction), obstipation, or constipation.</td>
<td>• Normal lipase and amylase.&lt;br&gt;• Acute abdominal series will show ground glass appearance, air-fluid levels, distended bowel loops, absence of distal gas, pneumatosis.&lt;br&gt;• An abdomen/pelvic CT scan may be more diagnostic, and will show point of transition and potentially identify aetiology (such as volvulus, hernias, intussusception, masses).</td>
</tr>
<tr>
<td>Abdominal aorta aneurysm</td>
<td>• Cardiovascular risk factors: hyperlipidaemia, tobacco, diabetes mellitus, homocystinaemia.&lt;br&gt;• Acute tearing-like abdominal pain, pulsating abdominal mass, hypotension, and mottled lower extremities with decreased pulses and abdominal distension.</td>
<td>• High index of suspicion is necessary to make a rapid diagnosis and improve outcomes. In stable patients, where history and physical examination are equivocal, a CT angiography may be useful as a rapid way to make diagnosis.&lt;br&gt;• If too unstable for radiographic evaluation, patients usually go directly to surgery.</td>
</tr>
<tr>
<td>Cholangitis</td>
<td>• Charcot's triad (jaundice, right upper quadrant pain, and fever) present in 70% of patients, altered mental status, and hypotension indicate biliary sepsis, usually caused by gram-negative bacteria.&lt;br&gt;• Patient may have a history of gallstones, peri-ampullary neoplasms, or biliary manipulation such as endoscopic retrograde cholangiopancreatography (ERCP).</td>
<td>• Several clinical findings are present more frequently in cholangitis, such as fever (95%), right upper quadrant pain (90%), and jaundice (80%).&lt;br&gt;• Normal lipase and amylase.&lt;br&gt;• Blood cultures are usually positive, especially during episodes of chills, with <em>Escherichia coli</em> and <em>Klebsiella</em> as the most common micro-organisms isolated from infected bile.[13]</td>
</tr>
<tr>
<td>Condition</td>
<td>Differentiating signs / symptoms</td>
<td>Differentiating tests</td>
</tr>
<tr>
<td>--------------------</td>
<td>-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------</td>
<td>----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Choledocholithiasis</td>
<td>• Severe right upper quadrant pain of sudden onset, jaundice, acholia, choluria, and hx of choledolithiasis. May occlude the common bile duct and cause pancreatitis.</td>
<td>• Normal lipase and amylase.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Ultrasound will show gallstones, stones within the common bile duct with extra-hepatic and/or intra-hepatic duct dilatation.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Chemistry will show biochemical obstruction, with increased levels of total and direct bilirubin, alkaline phosphatase, gamma-GT, and a slight increase in ALT/AST but normal levels of pancreatic enzymes (especially lipase).</td>
</tr>
<tr>
<td>Cholecystitis</td>
<td>• Pain is generally triggered after a fatty meal and localised in the right upper quadrant. More common in overweight females between 40 and 50 years of age. Anorexia, nausea, and vomiting may be present. May show a positive Murphy's sign and low-grade fever.</td>
<td>• Normal lipase and amylase.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• A right upper quadrant ultrasound will show thickened gallbladder wall, stones with acoustic shadows, biliary sludge, peri-cholecystic fluid, and sonographic Murphy's sign, and allows evaluation of the duct system. Can suggest pancreatic head inflammation. May show mild leukocytosis and a very mild elevation of liver enzymes.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• A hepatobiliary iminodiacetic acid (HIDA) scan is diagnostic when there is no filling of the gallbladder or with delayed emptying of the radiotracer.</td>
</tr>
<tr>
<td>Viral gastroenteritis</td>
<td>• Generalised non-specific abdominal pain, anorexia, nausea, emesis, diarrhoea, and dehydration. Is usually a self-limiting viral infection but if fever is documented, bacterial and invasive organisms should be suspected. Consider in travellers and immunosuppressed patients.</td>
<td>• Normal lipase and amylase.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Important to obtain serum electrolytes and an FBC.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Hypokalaemia and alkalosis may be seen secondary to diarrhoea, vomiting, and dehydration.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Stool examination for microscopy, culture, osmolality, ova, parasites, <em>Clostridium difficile</em> toxin, and white blood cells may help in identifying the causative factor.</td>
</tr>
</tbody>
</table>
### Condition | Differentiating signs / symptoms | Differentiating tests
--- | --- | ---
Hepatitis | • Jaundice, right upper quadrant pain, anorexia, and general malaise. Choluria and acholuria may be seen. • Examination: tenderness to palpation over the right upper quadrant and enlarged liver. | • Normal lipase and amylase. • Elevated liver function tests are characteristic. AST/ALT in the range of the 1000 units/L is not rare. Serological titres can make diagnosis of aetiological cause. • Radiographic studies not important for its diagnosis.
Mesenteric ischaemia | • Patients are usually older, may have a history of atrial fibrillation and risk factors for peripheral vascular disease. • Hypercoagulable states may lead to bowel necrosis. Pain is usually out of proportion to the finding of the physical examination. | • High index of suspicion of diagnosis is necessary. Angiography and CT scan may be useful in diagnosis as well as lactic acid levels. • Normal lipase. May have elevated amylase (usually less marked than that seen in acute pancreatitis).
Myocardial infarction | • Pain is usually retrosternal with radiation to jaw, neck, and left upper extremity. Associated with shortness of breath, nausea, vomiting, and diaphoresis. Cardiovascular risk factors in the history. | • Elevated cardiac enzymes (creatine kinase or creatine phosphokinase, troponins), ECG changes, and clinical scenario make the diagnosis. • Normal lipase and amylase. Cardiac catheterisation, perfusion scans, and echocardiograms are useful during the work-up of cardiac ischaemia.

### Diagnostic criteria

**International Association of Pancreatology/American Pancreatic Association criteria (IAP/APA)**[37]

Two out of three of the following criteria must be met for the diagnosis of acute pancreatitis:

- Clinical (upper abdominal pain)
- Laboratory (serum amylase or lipase >3 upper limit of normal)
- Imaging (CT, MR, ultrasound) criteria.

**Ranson criteria (non-gallstone pancreatitis)**[12] [51]

Used for prediction of severe acute pancreatitis - not diagnosis.

Criteria on admission: age >55 years; glucose >11.1 mmols/L (200 mg/dL); WBC count >16 x 10^9/L (16 x 10^3/microlitre); serum AST (SGOT) >250 units/L; and serum LDH >350 units/L.
Acute pancreatitis

Criteria after 48 hours of admission: Hct fall >10%; estimated fluid sequestration >6 L; base deficit >4 mEq/L; blood urea nitrogen rise >1.8 mmols/L (5 mg/dL); serum calcium <2 mmols/L (8 mg/dL); PO2 <8 kPa (60 mmHg).

Number of criteria and approximate mortality (%):

- 0 to 2 = 0%
- 3 to 4 = 15%
- 5 to 6 = 50%
- >6 = 100%.

**Ranson criteria (gallstone-associated)**[12]

Used for prediction of severe acute pancreatitis - not diagnosis.

Criteria on admission: age >70 years; glucose >12.2 mmols/L (220 mg/dL); WBC count >18 x 10^9/L (18 x 10^3/ microlitre); serum AST (SGOT) >250 units/L; and serum LDH >400 units/L.

Criteria after 48 hours of admission: Hct fall >10%; estimated fluid sequestration >4 L; base deficit >5 mEq/L; blood urea nitrogen rise >0.7 mmols/L (2 mg/dL); serum calcium <2 mmols/L (8 mg/dL).

**Balthazar CT severity index**[52] [51]

Used for grading of severity - not diagnosis.

CT features and score:

- I Grade
  - Normal gland = 0
  - Focal/diffuse enlargement = 1
  - Peri-pancreatic inflammation = 2
  - Single pancreatic fluid collection = 3
  - Two or more fluid collections or abscess = 4.

- II Necrosis
  - None = 0
  - <30% = 2
  - 30% to 50% = 4
  - >50% = 6.

Morbidity and mortality by Balthazar scoring:

(score = morbidity [%]/mortality [%])

- 0 to 3 = 8%/3%
- 4 to 6 = 35%/6%
- 7 to 10 = 92%/17%. 

Glasgow prognostic criteria (Imrie's criteria)[53]

The Glasgow system is a simple prognostic system that uses age, and 7 laboratory values collected during the first 48 hours following admission for pancreatitis, to predict severe pancreatitis. It is applicable to both biliary and alcoholic pancreatitis.

A point is assigned if a certain breakpoint is met at any time during that 48-hour period.

The parameters and breakpoints are:

- Age >55 years = 1 point
- Serum albumin <32 g/L (3.2 g/dL) = 1 point
- Arterial PO2 on room air <8 kPa (60 mmHg) = 1 point
- Serum calcium <2 mmols/L (8 mg/dL) = 1 point
- Blood glucose >10.0 mmols/L (180 mg/dL) = 1 point
- Serum LDH >600 units/L = 1 point
- Serum urea nitrogen >16.1 mmols/L (45 mg/dL) = 1 point
- WBC count >15 x 10^9/L (15 x 10^3/microlitre) = 1 point.

The addition of the parameter points yields the Glasgow prognostic criteria. The score can range from 0 to 8. If the score is >2, the likelihood of severe pancreatitis is high. If the score is <3, severe pancreatitis is unlikely.

The extrapancreatic inflammation on computed tomography score[54] [55] [56]

The extrapancreatic inflammation on computed tomography (EPIC) score assesses the severity of acute pancreatitis based on extrapancreatic complications. The score ranges from 0 to 7 based on CT findings. Scores 0 to 3 are associated with 0% mortality; scores 4 to 7 are associated with 67% mortality.

Signs of extrapancreatic inflammation and score:

- Pleural effusion
  - None = 0
  - Unilateral = 1
  - Bilateral = 2.

- Ascites in any of these locations: perisplenic, periphepatic, interloop, pelvis
  - None = 0
  - One location = 1
  - More than one location = 2.

- Retroperitoneal inflammation
  - None = 0
Acute pancreatitis

Diagnosis

- Unilateral = 1
- Bilateral = 2.

- Mesenteric inflammation
  - Absent = 0
  - Present = 1.

Acute physiology and chronic health evaluation II (APACHE II) score[57]

The APACHE score is commonly used to establish illness severity in the ICU and predict the risk of death.

[VIDEO: APACHE II scoring system ]

There is a high risk of death if the score is 25 or above.
Step-by-step treatment approach

The main goal of initial treatment is to prevent complications of severe pancreatitis by reducing pancreatic secretory stimuli and correction of fluid and electrolyte abnormalities. Initially, the patients should be fluid resuscitated and kept nothing by mouth with bowel rest when nausea, vomiting, and abdominal pain are an issue.[5]

At diagnosis supportive care continues until pain is resolved and diet re-started. The majority of patients will improve within 3 to 7 days of conservative management. Patients with organ failure or with poor prognostic signs (Glasgow score >3, APACHE score >8, and Ranson score >3) should be admitted to the intensive care unit.[7][58]

Initial resuscitation

Resuscitation with intravenous (IV) fluids, analgesics, and antiemetics are the initial treatments even before diagnosis is made.

IV hydration with crystalloids is essential (Ringer’s lactate solution is recommended), and an effort to keep urinary output above 30 mL/hour is necessary to avoid potential kidney damage. Aggressive resuscitation (e.g., 1 litre bolus of crystalloid followed by a continuous infusion rate of 3 mL/kg/hour) is important within the first 24 hours.[59] The patient should be catheterised to monitor urinary output in severe cases of acute pancreatitis. The adequacy of fluid replacement is the single most important aspect of the medical management.[1][5][58][60][61][62]

Pain control is important when pain is present, and the most commonly used drugs are opioids, which relieve pain and have a very low risk profile[63] and confer no need for multi-modality therapy.[64] Fentanyl or morphine can be used, either for breakthrough pain or as patient-controlled analgesia (PCA). Ketorolac, a non-steroidal anti-inflammatory drug (NSAID), can be used in patients with intact renal function.

It is important to monitor the arterial oxygenation, because patients may be hypoxaemic, requiring supplemental oxygen. During the initial management, consider arterial blood gases every 12 hours for the first 3 days to assess both oxygenation and acid-base status.[5] Close monitoring and treatment of hyperglycaemia should follow the intensive treatment modes of other critically ill patients.[65]

Severe pancreatitis

In severe cases of pancreatitis, hypocalcaemia should be identified and treated because it may lead to cardiac dysrhythmias. Magnesium should be replaced if low levels are identified, commonly seen in alcoholic patients.

Blood glucose control and insulin administration to keep glucose <8.33 mmol/L (<150 mg/dL) has been associated with reductions in morbidity and mortality in critically ill patients. Insulin sliding scales, insulin drips, or long-acting insulin should be used in patients with hyperglycaemia that is difficult to treat.[66][67]

A Cochrane systematic review found very-low-quality evidence to suggest that pharmacological interventions (e.g., antibiotics, antioxidants, aprotinin, calcitonin, cinetidine, disodium edetate, glucagon, octreotide, probiotics, and activated protein C) do not decrease short-term mortality (3 months) when added to supportive care.[68] There was evidence that some treatments may be of benefit for particular
Acute pancreatitis

Treatment

The use of antibiotics in non-infected pancreatitis has fluctuated over the last decade, but is not currently routine practice as there is no clear evidence of benefit. Prophylactic antibiotics have not been shown to affect mortality, extrapancreatic infections, or the need for surgical intervention. A meta-analysis demonstrated no difference in the mortality rate between patients receiving antibiotics and those receiving a placebo for the treatment of severe acute pancreatitis. Other meta-analyses have found no difference in the reduction of morbidity, the incidence of infected pancreatic necrosis or non-pancreatic infection, or the need for surgery in patients receiving antibiotics. However, because these studies involved small populations, further investigations are needed to determine the effectiveness of antibiotics in selected episodes of severe pancreatitis. Some studies have shown some benefit in cases of severe necrotising pancreatitis; therefore, antibiotic use should be restricted to patients in whom there are signs, symptoms, and laboratory tests indicating that infection is present (e.g., fever, leukocytosis, organ failure, and positive cultures).

The main indication for necrosectomy is infection in severe necrotising pancreatitis. Somatostatin analogues may reduce perioperative complications, specifically the incidence of pancreatic fistula, but do not reduce perioperative mortality.

The management of pancreatic and peri-pancreatic collections has evolved over the past decade. Indications to intervene on pancreatic collections include:

- Infection (systemic signs of sepsis or evidence of gas in the collection on cross-sectional imaging)
- Clinical deterioration
- Symptomatic sterile necrosis (may include abdominal pain, anorexia, early satiety, nausea, vomiting, biliary obstruction, or persistent unwellness [i.e., malaise, fatigue, and low-grade fever]).

Some collections will reabsorb without intervention. Persistent collections that are asymptomatic may be observed.

General goals of intervention include:

- Debridement of solid necrotic material and drainage of pancreatic exocrine secretion
- Cholecystectomy in patients with biliary pancreatitis
- Enteral access (i.e., gastrostomy/jejunostomy feeding tubes) in patients with severe acute pancreatitis.

Pancreatic and peri-pancreatic collections are heterogeneous. The choice and progression of intervention depends on individual patient physiological condition and the anatomy of the collection. Interventions may include the following approaches: transgastric/transenteric (endoscopic or surgical), percutaneous, open surgical, or often some combination of these approaches.

In general, many patients are suitable for a ‘step-up’ approach, starting with a percutaneous drainage. Up to 30% of patients may be definitively managed by percutaneous drainage alone. In highly selected patients treated at experienced high-volume pancreatic centres, endoscopic debridement may be considered as a first approach.

Patients who do not respond to percutaneous drainage may require a ‘step-up’ approach to larger or different percutaneous drains (e.g., endoscopic transluminal), ‘sinus-tract’ necrosectomy, or surgical necrosectomy. The timing and choice of approach requires specialist consultation.
Nutrition

Whereas in mild pancreatitis enteral nutrition may be started once abdominal pain has subsided, in severe pancreatitis a period of nothing by mouth is required until the resuscitation is complete, usually during the first 24 to 48 hours after the onset of pancreatitis. Concerns are minimal but not absent, as premature resumption of diet may result in exacerbation of the disease.

In patients who are unable to resume oral intake, a feeding tube should be placed (trans-pyloric nasojejunostomy - i.e., beyond the ampulla of Vater is preferred, although many patients tolerate intragastric feedings). This allows enteral nutrition without stimulating the pancreas. A nasogastric feeding tube can be placed if tolerated by the patient. Enteral nutrition has been associated with lower complication and morbidity rates.

A systematic review of 11 randomised studies found limited evidence to suggest that early feeding (≤48 hours after hospitalisation; studies assessed oral, nasogastric, and nasojejunal routes) is not associated with an increased risk of adverse events compared with delayed feeding. For patients with mild to moderate pancreatitis, early feeding may reduce length of hospital stay.

Parenteral nutrition should be reserved for patients who do not tolerate enteral feeding or in whom an adequate infusion cannot be reached within 2 to 4 days. When compared with parenteral nutrition, enteral feeds are associated with better outcomes, less mortality, and better blood glucose control. They also protect the gut barrier by preventing intestinal atrophy, leading to less sepsis and fewer infectious complications. A randomised trial showed that an oral diet after 72 hours was just as effective in reducing the rate of infection or death in patients with acute pancreatitis when compared with early nasoenteric tube feeding. No specific enteral nutrition formulation has been proven to be better than another in patients with acute pancreatitis.

The recommended nutrient requirements in severe acute pancreatitis are as follows: energy 25 to 35 kcal/kg/day, protein 1.2 to 1.5 g/kg/day, carbohydrates 3 to 6 g/kg/day, and lipids 2 g/kg/day.

Alcohol-induced pancreatitis

Patients with alcohol-induced pancreatitis may need alcohol-withdrawal prophylaxis. Lorazepam, thiamine, folic acid, and multi-vitamins are generally used in this group of patients.

Gallstone pancreatitis

Endoscopic ultrasound is an accurate test with which to evaluate the presence of common bile duct stones; however, it may be technically challenging in patients with severe acute pancreatitis due to duodenal deformity. In patients in whom the diagnosis of acute gallstone pancreatitis is obtained by ultrasound, imaging of the common bile duct is required. If the presence of stones in the common bile duct is confirmed, a cholecystectomy with common bile duct exploration (either surgical or postoperatively with endoscopic retrograde cholangiopancreatography [ERCP]) should be performed during the same hospitalisation. A longer delay, even of a few weeks, is associated with a high recurrence (80%) of acute pancreatitis and re-admission.

If the pancreatitis is severe, the inflammation should be allowed to subside before performing a cholecystectomy during the same admission. Cholecystectomy should be delayed in patients with severe/necrotising acute pancreatitis.
ERCP is not routinely performed in patients with biliary acute pancreatitis; however, it should be performed early in the course for patients with biliary acute pancreatitis who have cholangitis or are deteriorating in the first 48 hours despite maximum support, because there is a concern in these patients for an impacted common bile duct stone. Also, patients who are not candidates for general anaesthesia/surgery may have ERCP with sphincterotomy as ‘definitive’ treatment for acute pancreatitis. Recurrent pancreatitis may occur in 3% of patients treated in this fashion. ERCP is not indicated for mild or severe gallstone pancreatitis without cholangitis in the absence of common bile duct obstruction.[45]

**Pancreatitis found on laparotomy**

When a laparotomy is performed for diagnosis and mild to moderate pancreatitis is found, cholecystectomy with intra-operative cholangiogram should be performed but the pancreas should be left alone. For severe pancreatitis, the lesser sac should be opened and the pancreas fully inspected. Some surgeons place drains and irrigating catheter around the pancreas.[5]

[VIDEO: Central venous catheter insertion animated demonstration ]

[VIDEO: Peripheral venous cannulation animated demonstration ]

**Treatment details overview**

Consult your local pharmaceutical database for comprehensive drug information including contraindications, drug interactions, and alternative dosing. (see Disclaimer)

<table>
<thead>
<tr>
<th>Acute</th>
<th>(summary)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>all patients</strong></td>
<td></td>
</tr>
<tr>
<td>1st</td>
<td>initial resuscitation</td>
</tr>
<tr>
<td>plus</td>
<td>nutritional support</td>
</tr>
<tr>
<td><strong>adjunct</strong></td>
<td>analgesia</td>
</tr>
<tr>
<td><strong>adjunct</strong></td>
<td>antiemetic</td>
</tr>
<tr>
<td><strong>adjunct</strong></td>
<td>calcium replacement therapy</td>
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<tr>
<td><strong>adjunct</strong></td>
<td>magnesium replacement therapy</td>
</tr>
<tr>
<td><strong>adjunct</strong></td>
<td>insulin</td>
</tr>
<tr>
<td><strong>adjunct</strong></td>
<td>antibiotic therapy</td>
</tr>
<tr>
<td><strong>with gallstones: surgical candidates</strong></td>
<td>plus</td>
</tr>
<tr>
<td><strong>with gallstones: non-surgical candidates or deteriorating after first 48 hours of maximum support</strong></td>
<td>plus</td>
</tr>
<tr>
<td><strong>with alcohol-induced disease</strong></td>
<td>plus</td>
</tr>
<tr>
<td>Acute</td>
<td>( summary )</td>
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<tr>
<td>-------</td>
<td>-------------</td>
</tr>
<tr>
<td>with infected pancreatic necrosis</td>
<td>plus vitamin and mineral replacement</td>
</tr>
<tr>
<td></td>
<td>adjunct percutaneous catheter drainage</td>
</tr>
<tr>
<td></td>
<td>adjunct larger drain or sinus-tract necrosectomy or surgical necrosectomy</td>
</tr>
</tbody>
</table>
## Treatment options

### Acute

<table>
<thead>
<tr>
<th>all patients</th>
</tr>
</thead>
</table>

#### 1st initial resuscitation

- Intravenous (IV) hydration with crystalloids (Ringer’s lactate solution is recommended) is essential at a rate of 0.5 to 1 mL/kg/hour, and an effort to keep urinary output above 30 mL/hour is necessary to avoid potential kidney damage.[115]

- The adequacy of fluid replacement is the single most important aspect of the medical management.[1] [5] [58] [60] [61] [62]

- Aggressive resuscitation (e.g., 1 litre bolus of crystalloid followed by a continuous infusion rate of 3 mL/kg/hour) is important within the first 24 hours.[59]

- The patient should be catheterised to monitor urinary output in severe cases of acute pancreatitis.

- In hemorrhagic pancreatitis, blood transfusion may be necessary.

#### plus nutritional support

- Initially patients should be kept nothing by mouth. Oral intake is re-started when there is notable clinical improvement and nausea and abdominal pain has resolved. Premature resumption of diet may result in exacerbation of the disease.[66] [116] [117]

- In patients who are expected to have a prolonged nothing by mouth status, a transpyloric nasojejunal feeding tube should be placed, allowing enteral nutrition without stimulating the pancreas. A nasogastric feeding tube can be placed if tolerated by the patient.[88] [89] Enteral nutrition has been associated with lower complication and morbidity rates.[90] [91]

- A systematic review of 11 randomised studies found limited evidence to suggest that early feeding (≤48 hours after hospitalisation; studies assessed oral, nasogastric, and nasojejunal routes) is not associated with an increased risk of adverse events compared with delayed feeding.[92] For patients with mild to moderate pancreatitis, early feeding may reduce length of hospital stay.[92]
Acute pancreatitis

**TREATMENT**

**Acute**

» Parenteral nutrition should be reserved for patients who do not tolerate enteral feeding or in whom an adequate infusion cannot be reached within 2 to 4 days. A randomised trial showed that an oral diet after 72 hours was just as effective in reducing the rate of infection or death in patients with acute pancreatitis when compared with early nasoenteric tube feeding.[93] No specific enteral nutrition formulation has been proven to be better than another in patients with acute pancreatitis.[94]

» The regimen should provide 25 to 35 kcal/kg/day energy, 1.2 to 1.5 g/kg/day protein, 3 to 6 g/kg/day carbohydrates, and 2 g/kg/day lipids.[95][96][97]

**adjunct analgesia**

**Primary options**

» **morphine sulfate**: 1-5 mg intravenously every 4 hours when required

OR

» **fentanyl**: 50-100 micrograms intravenously, followed by 50 micrograms every 1-2 hours when required

OR

» **ketorolac**: 10 mg intravenously/intramuscularly initially, followed by 10-30 mg every 4-6 hours when required for 2 days, maximum 90 mg/day

» Pain control is important when pain is present, and the most commonly used drugs are the opioids, which relieve pain and have a very low risk profile[63] and confer no need for multi-modality therapy.[64] Fentanyl or morphine can be used, either for breakthrough pain or as patient-controlled analgesia. Monitor respiratory and CNS depression.[118] Ketorolac, a non-steroidal anti-inflammatory drug (NSAID), can be used in patients with intact renal function.

**adjunct antiemetic**

**Primary options**

» **ondansetron**: 2-4 mg intravenously every 4-6 hours when required

» Ondansetron is the most commonly used antiemetic.

**adjunct calcium replacement therapy**
### Acute Pancreatitis

#### Treatment

<table>
<thead>
<tr>
<th>Adjunct</th>
<th>Magnesium replacement therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Primary options</strong></td>
<td></td>
</tr>
<tr>
<td>» magnesium sulfate: 1-2 g intravenously every 6 hours on first day, followed by 60 mg/kg/day as an infusion, or see local specialist protocol for dosing guidelines</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Adjunct</th>
<th>Insulin</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Primary options</strong></td>
<td></td>
</tr>
<tr>
<td>» Blood glucose control and insulin administration to keep glucose &lt;8.33 mmol/L (&lt;150 mg/dL) has been associated with reductions in morbidity and mortality in critically ill patients. In less severe cases, regular insulin sliding scales can be used.[66]</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Adjunct</th>
<th>Antibiotic therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Primary options</strong></td>
<td></td>
</tr>
<tr>
<td>» imipenem/cilastatin: 500-1000 mg intravenously every 6 hours Dose refers to imipenem component only.</td>
<td></td>
</tr>
</tbody>
</table>

| Secondary options |  |
|-------------------|  |
| » ceftriaxone: 1-2 g intravenously every 12 hours OR |  |

| Secondary options |  |
|-------------------|  |
| » ampicillin: 500 mg intravenously every 6 hours |  |
Acute pancreatitis

Treatment

TREATMENT

- Acute OR

  - ciprofloxacin: 400 mg intravenously every 12 hours

- The use of antibiotics in non-infected pancreatitis has fluctuated over the last decade, but is not currently routine practice as there is no clear evidence of benefit.[69] Prophylactic antibiotics have not been shown to affect mortality, extrapancreatic infections, or the need for surgical intervention.[70]

- A meta-analysis demonstrated no difference in the mortality rate between patients receiving antibiotics and those receiving a placebo for the treatment of severe acute pancreatitis.[71] Other meta-analyses have found no difference in the reduction of morbidity, the incidence of infected pancreatic necrosis or non-pancreatic infection, or the need for surgery in patients receiving antibiotics.[72] [73] However, because these studies involved small populations, further investigations are needed to determine the effectiveness of antibiotics in selected episodes of severe pancreatitis.

- Some studies have shown some benefit in cases of severe necrotising pancreatitis,[74] [75] [76] [77] [78] [79] therefore, antibiotic use should be restricted to patients in whom there are signs, symptoms, and laboratory tests indicating that infection is present (e.g., fever, leukocytosis, organ failure, and positive cultures).[80] Imipenem is usually recommended first line because of its pancreatic penetration.

- There is no consensus in the literature to date of how long patients need to be on antibiotics. However, clinical improvement, with resolution of organ failure and improvement of systemic markers of inflammation, can be considered as reasonable indicators that antimicrobials can be stopped.

- In patients in whom the diagnosis of acute gallstone pancreatitis is obtained by ultrasound, a cholecystectomy with common bile duct exploration (either surgical or postoperatively with endoscopic retrograde cholangiopancreatography [ERCP]) should be performed during the same hospitalisation for the acute attack, soon after the attack resolves. A longer delay, even a few weeks, is associated with a high recurrence (80%) of acute

- with gallstones: surgical candidates plus cholecystectomy
Acute pancreatitis and re-admission.[99] [100] [101] [102] [103]

» When a laparotomy is performed for diagnosis and mild to moderate pancreatitis is found, cholecystectomy with intra-operative cholangiogram should be performed but the pancreas should be left alone. For severe pancreatitis, the lesser sac should be opened and the pancreas fully inspected. Some surgeons place drains and irrigating catheter around the pancreas.[5]

with gallstones: non-surgical candidates or deteriorating after first 48 hours of maximum support plus endoscopic retrograde cholangiopancreatography (ERCP) with sphincterotomy

» ERCP is the standard of care in biliary acute pancreatitis patients who have cholangitis or are deteriorating in the first 48 hours despite maximum support (concerns for impacted common bile duct stone). ERCP is not indicated for mild or severe gallstone pancreatitis without cholangitis in the absence of common bile duct obstruction.[45]

» A meta-analysis of 4 randomised controlled trials of endoscopic sphincterotomy in patients with severe acute pancreatitis showed that sphincterotomy reduced complications and mortality. The role of ERCP in patients without biliary obstruction or cholangitis is unknown,[7] [8] [119] however, it is recommended that early ERCP should also be performed in these patients.[120]

» Patients who are not candidates for general anaesthesia/surgery (high American Society of Anesthesiologists [ASA] index, sepsis, or severe disease) may receive urgent ERCP with sphincterotomy.

with alcohol-induced disease plus benzodiazepine

Primary options

» lorazepam: 1-2 mg orally/intravenously/intramuscularly every 6-8 hours

» Patients with alcohol-induced pancreatitis may need alcohol-withdrawal prophylaxis. Lorazepam is generally used in this group of patients.[121]

plus vitamin and mineral replacement

Primary options

» thiamine: 100 mg orally/intravenously/intramuscularly once daily -and-
**Acute pancreatitis**

**Treatment**

- **folic acid**: 1 mg orally/intramuscularly once daily
- **cyanocobalamin**: 1000 micrograms intramuscularly/orally once daily for 1-2 weeks, followed by 1000 micrograms once every 1-3 months

The objective of replacement of thiamine in chronic alcoholism is to replenish the stores in patients. The treatment has to be continued until the patient can return to eating a well-balanced meal during hospitalisation.

Other water-soluble vitamins that are supplemented during hospital or emergency department course include folic acid and cyanocobalamin. Cyanocobalamin can be given orally except in states when absorption is impaired.

**with infected pancreatic necrosis**

**adjunct**

**percutaneous catheter drainage**

In general, many patients are suitable for the 'step-up' approach, starting with percutaneous drainage. Up to 30% of patients may be definitively managed by percutaneous drainage alone.[37] [82] In highly selected patients treated at experienced high-volume pancreatic centres, endoscopic debridement may be considered as a first approach.

Invasive intervention should be delayed where possible until at least 4 weeks after initial presentation of acute pancreatitis to allow the collection to become 'walled-off'.[37] [82]

**adjunct**

**larger drain or sinus-tract necrosectomy or surgical necrosectomy**

Patients who do not respond to percutaneous drainage may require a 'step-up' approach to larger or different percutaneous drains (e.g., endoscopic transluminal drainage), sinus-tract necrosectomy, or surgical necrosectomy.[37] [82]

The timing and choice of approach requires specialist consultation.

Invasive intervention should be delayed where possible until at least 4 weeks after initial presentation of acute pancreatitis to allow the collection to become 'walled-off'.[37] [82]
Emerging

Gastric antisecretory agents

H2 antagonists and proton pump inhibitors (PPI) may have a role in the treatment of acute pancreatitis by decreasing pancreatic stimulation; however, more research is needed.

CM4620

CM4620, a novel calcium release-activated calcium (CRAC) channel inhibitor for the treatment of acute pancreatitis, has received fast-track designation from the US Food and Drug Administration and orphan designation from the European Medicines Agency. CM4620 is expected to reduce cell damage and death in the pancreas, thereby minimising symptoms.
**Recommendations**

**Monitoring**

Long-term monitoring is not necessary. Patients usually resolve after their acute attack. If they modify their risk factors, another episode may not recur later in life. Lipids should be monitored in those with hypertriglyceridaemia. Smoking cessation is critical.

**Patient instructions**

Before discharge from hospital after an acute attack of acute pancreatitis, patients should be advised to modify lifestyle risk factors. For example, alcoholic patients need to stop drinking, especially bingeing behaviour, modify diet in order to control hypertriglyceridaemia, and use lipid-lowering medicines such as statins or niacin. Patients taking medicines that can cause pancreatitis (e.g., furosemide, didanosine, oestrogens, azathioprine, thiazide diuretics, sulfonamides, tetracyclines, sulindac, mercaptopurine, valproic acid, L-asparaginase) should be educated about the adverse effects and how to recognise an acute attack of pancreatitis.

Patients should be advised to eat small, low-fat meals of carbohydrates and proteins, with a gradual increase in quantity over a period of 3 to 6 days as tolerated.

**Complications**

<table>
<thead>
<tr>
<th>Complications</th>
<th>Timeframe</th>
<th>Likelihood</th>
</tr>
</thead>
<tbody>
<tr>
<td>acute renal failure</td>
<td>short term</td>
<td>high</td>
</tr>
<tr>
<td>Seen in patients with severe acute pancreatitis. May be caused by circulating toxins or rhabdomyolysis. Hypovolaemia and inflammatory mediators. Acute renal failure is a complication with poor outcome.[124]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>pancreatic abscess</td>
<td>short term</td>
<td>low</td>
</tr>
<tr>
<td>Occurs when the peri-pancreatic fluid collections become colonised and infected. Invariably fatal if not treated surgically. Follows secondary bacterial contamination of necrotic pancreatic tissue and haemorrhagic exudates. It is unknown whether prophylactic antibiotics given early in the course of the disease decrease the incidence of abscess. Generally patients present 2 to 4 weeks after the onset of pancreatitis, with fever, and clinically worsen. CT is diagnostic, showing a ring-enhancing fluid collection with gas. Its treatment is drainage (surgical versus percutaneous) and antibiotics to cover <em>E. coli</em>, <em>Bacteroides</em>, <em>Staphylococcus</em>, <em>Klebsiella</em>, <em>Proteus</em>, and <em>Candida albicans</em>.[5]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>necrotising pancreatitis</td>
<td>short term</td>
<td>low</td>
</tr>
<tr>
<td>Secondary to inadequate fluid resuscitation, vasoactive and toxic substances (phospholipases, endotoxins, activated trypsin, complement activation, thromboxane, and elastase).[4]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>pancreatic insufficiency</td>
<td>long term</td>
<td>low</td>
</tr>
<tr>
<td>Recurrent attacks may lead to exocrine pancreatic insufficiency more commonly than endocrine failure.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>chronic pancreatitis</td>
<td>long term</td>
<td>low</td>
</tr>
</tbody>
</table>
## Acute pancreatitis

### Complications

<table>
<thead>
<tr>
<th>Complication</th>
<th>Timeframe</th>
<th>Likelihood</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute pancreatitis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Recurrent attacks of acute pancreatitis may lead to chronic scarring, and, if the aetiological factor is not treated, may present with the classic characteristics of chronic pancreatitis: glucose intolerance, pancreatic insufficiency, and calcifications.</td>
<td>long term</td>
<td>low</td>
</tr>
<tr>
<td><strong>portal vein/splenic thrombosis</strong></td>
<td>long term</td>
<td>low</td>
</tr>
<tr>
<td>Ongoing pancreatic inflammation may cause irritation and inflammation of the portal vein and/or splenic vein, leading to portal hypertension. Suspect splenic vein thrombosis in patients with recurrent pancreatitis, splenomegaly, and bleeding from gastric varices.</td>
<td>variable</td>
<td>medium</td>
</tr>
<tr>
<td><strong>enteric fistulas</strong></td>
<td>variable</td>
<td>medium</td>
</tr>
<tr>
<td>Resulting from inflammation surrounding the pancreas and adjacent duodenum or transverse colon.</td>
<td>variable</td>
<td>medium</td>
</tr>
<tr>
<td><strong>intestinal obstruction</strong></td>
<td></td>
<td>low</td>
</tr>
<tr>
<td>Ileus may be frequently seen in pancreatitis, a result of dehydration, electrolyte abnormalities, or adjacent bowel inflammation. Intestinal obstruction can be seen later in the course of the disease, when a pseudocyst or abscess causes a mechanical compression of the bowel (generally duodenum or transverse colon).</td>
<td>variable</td>
<td>medium</td>
</tr>
<tr>
<td><strong>sepsis</strong></td>
<td>variable</td>
<td>medium</td>
</tr>
<tr>
<td>The gut mucosa plays a central role in the development of sepsis. Several descriptions about how the gut modulates the inflammatory response by priming neutrophils and secreting cytokines can be found in the literature.</td>
<td>variable</td>
<td>medium</td>
</tr>
<tr>
<td><strong>retroperitoneal bleeding</strong></td>
<td>variable</td>
<td>medium</td>
</tr>
<tr>
<td>From arterial pseudoaneurysm.</td>
<td>variable</td>
<td>medium</td>
</tr>
<tr>
<td><strong>infected pancreatic necrosis</strong></td>
<td>variable</td>
<td>medium</td>
</tr>
<tr>
<td>Infection is responsible for 80% of deaths. Gram-negative bacteria (Esterichia coli, Pseudomonas, Klebsiella, Proteus, Enterobacter) are more common than gram-positive micro-organisms. Previous studies describe a mortality rate of 50% to 80% in the absence of operative treatment and 10% to 40% among patients who receive debridement.</td>
<td>variable</td>
<td>medium</td>
</tr>
<tr>
<td><strong>acute lung injury/ARDS</strong></td>
<td>variable</td>
<td>medium</td>
</tr>
<tr>
<td>The production and excretion of inflammatory mediators (such as cytokines, prostaglandins, and thromboxanes) during pancreatitis may damage the alveolocapillary membrane, leading to destruction of pneumocytes and decrease in the amount of surfactant. This leads to airway destruction, increase in superficial tension, and inadequate oxygenation. Patients usually present with hypoxaemia, requiring higher levels of supplemental oxygen, with bilateral interstitial infiltrates, PaO2:FIO2 ratio &lt;300, and a normal pulmonary capillary wedge pressure. Patients may require mechanical ventilation during the course of their disease.</td>
<td>variable</td>
<td>medium</td>
</tr>
<tr>
<td><strong>disseminated intravascular coagulation</strong></td>
<td>variable</td>
<td>low</td>
</tr>
<tr>
<td>Complications</td>
<td>Timeframe</td>
<td>Likelihood</td>
</tr>
<tr>
<td>--------------------------</td>
<td>-----------</td>
<td>------------</td>
</tr>
<tr>
<td>Severe acute pancreatitis, especially if associated with necrosis, has been linked to liberation of cytokines and systemic inflammatory response, with activation of the complement, coagulation, and fibrinolytic cascades, leading to a state of coagulopathy and disseminated intravascular coagulation with elevated levels of split fibrin products and d-dimer with low fibrinogen.</td>
<td>variable</td>
<td>low</td>
</tr>
<tr>
<td>multiorgan failure</td>
<td>variable</td>
<td>low</td>
</tr>
<tr>
<td>The gut mucosa plays a central role in the development of multi-organ failure. Several descriptions about how the gut modulates the inflammatory response by priming neutrophils and secreting cytokines can be found in the literature.</td>
<td>variable</td>
<td>low</td>
</tr>
<tr>
<td>pseudocyst</td>
<td>variable</td>
<td>low</td>
</tr>
<tr>
<td>Pseudocysts are encapsulated collections of fluid with high enzyme concentrations. The walls are formed by inflammatory fibrosis of the peritoneal, mesenteric, and serosal membranes, which limits the spread of the pancreatic fluid. Pseudocysts have no epithelial lining. Pseudocyst diagnosis should be suspected when a patient fails to respond after 1 week of treatment or symptoms recur. Pain is the most common finding, followed by a palpable mass. CT scan is the diagnostic study of choice. Pseudocysts can be complicated with infection, rupture (in 5%), and haemorrhage. The principal indications for treatment are to improve symptoms and to prevent complications.</td>
<td>variable</td>
<td>low</td>
</tr>
<tr>
<td>Expectant management is important in the first 6 to 12 weeks of existence of cysts that have arisen during an acute attack of acute pancreatitis. The chance of spontaneous resolution is 40%. Thereafter, for cysts &gt;5 cm in size, treatment is usually recommended over conservative management.</td>
<td>variable</td>
<td>low</td>
</tr>
<tr>
<td>Treatment options include excision of the cyst, external drainage (surgical or percutaneous), or internal drainage (preferred method of treatment), which can be either a cystojejunostomy Roux-en-Y, cystogastrostomy, or cystoduodenostomy. Endoscopic transgastric and transduodenal drainage are gaining popularity as treatment options due to a reported decrease in complication and mortality rates.</td>
<td>variable</td>
<td>low</td>
</tr>
<tr>
<td>gastrointestinal bleeding</td>
<td>variable</td>
<td>low</td>
</tr>
<tr>
<td>From adjacent inflamed stomach or duodenum, ruptured pseudocyst, arterial pseudoaneurysm, or peptic ulcer.</td>
<td>variable</td>
<td>low</td>
</tr>
<tr>
<td>intraperitoneal bleeding</td>
<td>variable</td>
<td>low</td>
</tr>
<tr>
<td>From coeliac or splenic artery rupture or acute splenic vein thrombosis.</td>
<td>variable</td>
<td>low</td>
</tr>
<tr>
<td>pancreatic ascites</td>
<td>variable</td>
<td>low</td>
</tr>
<tr>
<td>Consists of accumulated pancreatic fluid in the peritoneal cavity. It is due to chronic leakage of a pseudocyst, but some cases may be due to duct disruption. Clinically manifested by weight loss and unresponsiveness of the ascites to diuretics. Initial treatment involves hyper-alimentation and somatostatin analogues. If no improvement is obtained in 2 to 3 weeks, endoscopic retrograde cholangiopancreatography (ERCP) and surgery should be considered.</td>
<td>variable</td>
<td>low</td>
</tr>
<tr>
<td>pancreatic effusion</td>
<td>variable</td>
<td>low</td>
</tr>
</tbody>
</table>
Complications | Timeframe | Likelihood
--- | --- | ---
Secondary to pancreatic fistula draining into the chest. The diagnosis is based on thoracentesis with fluid rich in amylase and a CT scan/retrograde pancreatogram that shows the fistula. Its treatment consists of drainage with a chest tube, somatostatin analogues, and total parenteral nutrition. If fistula persists, operative intervention with fistula resection or distal pancreatectomy should be performed.[5]

Prognosis

The majority of patients with acute pancreatitis will improve within 3 to 7 days of conservative management. The cause of pancreatitis should be identified, and a plan to prevent recurrence should be initiated before the patient is discharged from hospital. In gallstone pancreatitis, a cholecystectomy should be performed before discharge in mild cases and a few months after the discharge date in patients with severe symptoms. In patients who are not candidates for surgery, endoscopic retrograde cholangiopancreatography (ERCP) must be considered.

Long-term prognosis is based on the aetiological factor and patient compliance to lifestyle modifications. Acute pancreatitis generally resolves and leaves pancreatic function intact. May progress to recurrent acute pancreatitis or chronic pancreatitis, and the risk is higher among people who smoke, alcoholics, and men.[122]

The most commonly used prognostic scores are APACHE II, Ranson, Glasgow, Balthazar, and Atlanta.

[VIDEO: APACHE II scoring system ]

[1] [123]

[VIDEO: Pancreatitis Prognosis Criteria ]
# Diagnostic guidelines

## Europe

**Consensus guidelines on severe acute pancreatitis**

*Published by:* Italian Association for the Study of the Pancreas  
*Last published:* 2015

**Practical guidelines for acute pancreatitis**

*Published by:* Italian Association for the Study of the Pancreas  
*Last published:* 2010

**UK guidelines for the management of acute pancreatitis**

*Published by:* UK Working Party on Acute Pancreatitis  
*Last published:* 2005

## North America

**The role of endoscopy in the diagnosis and treatment of inflammatory pancreatic fluid collections**

*Published by:* American Society for Gastrointestinal Endoscopy  
*Last published:* 2016

**ACR appropriateness criteria: acute pancreatitis**

*Published by:* American College of Radiology  
*Last published:* 2013

**Management of acute pancreatitis**

*Published by:* American College of Gastroenterology  
*Last published:* 2013

## Asia

**Japanese guidelines for the management of acute pancreatitis**

*Published by:* Journal of Hepatobiliary Pancreatic Surgery  
*Last published:* 2015

## Treatment guidelines

## Europe

**Consensus guidelines on severe acute pancreatitis**

*Published by:* Italian Association for the Study of the Pancreas  
*Last published:* 2015

**Prophylaxis of post-ERCP pancreatitis**

*Published by:* European Society of Gastrointestinal Endoscopy  
*Last published:* 2014

**Practical guidelines for acute pancreatitis**

*Published by:* Italian Association for the Study of the Pancreas  
*Last published:* 2010

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### Europe

**UK guidelines for the management of acute pancreatitis**  
**Published by:** British Society of Gastroenterology: UK Working Party on Acute Pancreatitis  
**Last published:** 2005

### International

**IAP/APA evidence-based guidelines for the management of acute pancreatitis**  
**Published by:** International Association of Pancreatology; American Pancreatic Association  
**Last published:** 2013

**IAP guidelines for the surgical management of acute pancreatitis**  
**Published by:** International Association of Pancreatology  
**Last published:** 2002

### North America

**The role of endoscopy in the diagnosis and treatment of inflammatory pancreatic fluid collections**  
**Published by:** American Society for Gastrointestinal Endoscopy  
**Last published:** 2016

**The role of ERCP in benign diseases of the biliary tract**  
**Published by:** American Society for Gastrointestinal Endoscopy  
**Last published:** 2015

**Treatment of gallstone and gallbladder disease**  
**Published by:** Society for Surgery of the Alimentary Tract  
**Last published:** 2014

**Management of acute pancreatitis**  
**Published by:** American College of Gastroenterology  
**Last published:** 2013

**Treatment of acute pancreatitis**  
**Published by:** Society for Surgery of the Alimentary Tract  
**Last published:** 2004

### Asia

**Post-ERCP pancreatitis**  
**Published by:** Journal of Hepatobiliary Pancreatic Sciences  
**Last published:** 2009

**Fundamental and intensive care of acute pancreatitis**  
**Published by:** Journal of Hepatobiliary Pancreatic Sciences  
**Last published:** 2009

**Gallstone-induced acute pancreatitis**  
**Published by:** Journal of Hepatobiliary Pancreatic Sciences  
**Last published:** 2009
Asia

Treatment strategy for acute pancreatitis

Published by: Journal of Hepatobiliary Pancreatic Sciences  Last published: 2009
Key articles


References


20. Akbar A, Abu Dayyeh BK, Baron TH, et al. Rectal nonsteroidal anti-inflammatory drugs are superior to pancreatic duct stents in preventing pancreatitis after endoscopic retrograde
Acute pancreatitis


109. Abbott Northwestern Hospital Internal Medicine Residency. Internal jugular central venous line. 2015 [internet publication]. Full text


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Contact us
+ 44 (0) 207 111 1105
support@bmj.com

BMJ
BMA House
Tavistock Square
London
WC1H 9JR
UK
Contributors:

// Authors:

Nicholas J. Zyromski, MD
Associate Professor of Surgery
Department of Surgery, Indiana University, Indianapolis, IN
DISCLOSURES: NJZ is an author of a reference cited in this monograph.

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// Peer Reviewers:

Tamas A. Gonda, MD
Assistant Professor of Medicine
Attending Physician and Director of Research, Columbia University Medical Center, New York, NY
DISCLOSURES: TAG declares that he has no competing interests.

Alan Moss, MD
Harvard Medical Faculty Physician
Division of Gastroenterology, Beth Israel Deaconess Medical Center, Boston, MA
DISCLOSURES: AM declares that he has no competing interests.

Derek O’Reilly, MD
Consultant Hepatobiliary & Pancreatic Surgeon
Department of Surgery, North Manchester General Hospital, Manchester, UK
DISCLOSURES: DOR is an author of a reference cited in this monograph. He declares that he has no other competing interests.

Eric Frykberg, MD
Professor
Department of Surgery, Division General Surgery, Shands Jacksonville Medical Center, FL
DISCLOSURES: At the time of the peer review, Dr E. Frykberg declared no competing interests. We were made aware that Dr Frykberg is now deceased.