Acute Pancreatitis

This is acute inflammation of the pancreas, releasing exocrine enzymes that cause autodigestion of the organ. There may be involvement of local tissues and distant organs.

It should not be confused with chronic pancreatitis. See separate Chronic Pancreatitis article.

Epidemiology

- The incidence of acute pancreatitis in the UK ranges from 150 to 420 cases per million population and is currently rising.[1]
- There is considerable geographical variation. The incidence in the UK and the Netherlands is relatively low compared to Scandinavian countries and the USA.[2]
- A Croatian study reported a mean age of 60 with roughly equal gender distribution.[2] However, the condition has been reported in children: the causes are more varied than in adults and include drugs, traumas, infections, multisystem disorders and biliary anomalies.[3]

Aetiology

Gallbladder disease and excess alcohol consumption account for most cases and typically cause periductal necrosis.

- Gallstones cause pancreatitis by blocking the bile duct, causing back pressure in the main pancreatic duct.
- Perilobular necrosis is less common and usually found in those with hypothermia and gross hypotension.
- Haemorrhagic, necrotic black discolouration is only found in the most severe cases.

Studies suggest that in countries with high prevalence the main cause is alcohol, whilst in low-prevalence countries it is mainly related to biliary disease.[4]

Less common causes include:

- **Injury** - post-endoscopic retrograde cholangiopancreatography (ERCP), blunt trauma.
- **Viral** - Coxsackie B, hepatitis and mumps (prodromal diarrhoea is indicative).
- **Metabolic** - hyperlipoproteinaemia, hyperparathyroidism, hypothermia, uraemia, anorexia.
- **Drugs** - thiazides, valproate, azathioprine, L-asparaginase, corticosteroids (all rare).
- **Malignancy** - peri-ampullary tumour, pancreatic carcinoma, metastases to the pancreas.
- **Ischaemia** - visceral thromboembolism, abdominal vascular surgery, cardiopulmonary bypass.
- **Inflammatory bowel disease** - one UK study found a seven-fold increase in acute pancreatitis in patients with inflammatory bowel disease taking mesalazine, although it is not known whether this was due to the disease, the drug or a combination of both.[6]
- **Other rarities** - alpha-1-antitrypsin deficiency, sclerosing cholangitis, duodenal re-duplication, annular pancreas, vasculitis.
Presentation

Symptoms
Take careful history, including alcohol consumption and prodromal symptoms.

- Most commonly, this presents as severe upper abdominal pain of sudden onset with vomiting.
- Pain is focused in the left upper quadrant of the epigastrium and penetrates to the back. Occasionally, it encircles the abdomen.
- Pain tends to decrease steadily over 72 hours.

Signs
- Take the patient's temperature to exclude hypothermia; mild pyrexia is more common.
- Look for evidence of hyperlipidaemia.
- Probable tachycardia with the patient unwell and dehydrated.
- Jaundice may be present in patients with common bile duct stones or, to a lesser degree, in those with alcohol-induced disease, compression of the lower bile duct, or hepatitis.
- Epigastric or generalised abdominal tenderness, often with rigidity.
- Bowel sounds are usually present in the early phase. Paralytic ileus, causing absent bowel sounds can last for >4 days and is a useful marker of disease severity.
- In severe cases: gross hypotension, pyrexia, tachypnoea, acute ascites, pleural effusions, body wall staining around the umbilicus (Cullen's sign) or flanks (Grey Turner's sign).
- Hypoxaemia is characteristic of acute pancreatitis.

Investigations[6]

- Serum amylase three or more times normal is the traditional way of diagnosing acute pancreatitis. However, lipase levels are more sensitive and more specific.[1, 7]
- FBC, U&EB, glucose and C-reactive protein (CRP) indicate prognosis:[7]
  - Raised bilirubin and/or serum aminotransferase suggest gallstones.
  - Hypocalcaemia is relatively common.
- Plain erect (if possible) abdominal X-ray:
  - This excludes some other causes (eg, intestinal obstruction and perforation) and may show calcification.
  - CXR may show elevation of one hemidiaphragm, infiltrates ± acute respiratory distress syndrome (ARDS) or pleural effusions in severe cases.
- CT scan with contrast enhancement may be diagnostic where clinical and biochemical results are equivocal on admission. However, in stable patients with mild symptoms it should not be performed for the sole purpose of assessing severity on admission:
  - The CT severity index (CTSI), derived by Balthazar et al, has become widely used for description of CT findings in acute pancreatitis. A modified index has been developed which is considered to be simpler to use and more accurate.[8]
  - Contrast-enhanced CT scanning can identify pancreatic swelling, fluid collection and change in density of gland. Such criteria can have prognostic value and predict the need for surgery.
- Ultrasound:
  - The pancreas is poorly visualised in 25-50% of cases.
  - Ultrasound can show a swollen pancreas, dilated common bile duct and free peritoneal fluid.
  - It is useful to detect the presence of gallstones.
  - Endoscopic ultrasound is a safe minimally invasive technique which is more accurate than transabdominal ultrasound and can accurately detect bile duct stones and other causes of recurrent acute pancreatitis.
MRI may reveal acute abdominal wall oedema which may be a supplementary indicator of severity.\cite{9}
Peritoneal aspiration of free fluid without bacterial contamination is a risk factor for mortality.\cite{10}
Laparoscopy can reveal diagnosis where suspicion is high but tests are inconclusive.\cite{11}

Differential diagnosis

Other causes of raised amylase
- Renal failure.
- Ectopic pregnancy.
- Diabetic ketoacidosis.
- Perforated duodenal ulcer.
- Mesenteric ischaemia/infarction (but will show bacterial contamination of peritoneal aspirate).

Other causes of similar pain
- Small bowel perforation/obstruction.
- Ruptured or dissecting aortic aneurysm.
- Atypical myocardial infarction.

Associated diseases
- Gallstones
- Alcoholism
- Hyperlipidaemia
- Hypothermia

Severity and prognostic assessment
- Scoring systems increase accuracy of prognosis.
- Use of the Glasgow Prognostic Score/Ranson’s Criteria/Acute Physiology and Chronic Health Evaluation II (APACHE II) Score can indicate prognosis, particularly if combined with measurement of CRP >150 mg/L.

<table>
<thead>
<tr>
<th>Pancreatitis Prognostic Scores</th>
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<tbody>
<tr>
<td><strong>Glasgow Prognostic Score</strong></td>
</tr>
<tr>
<td>Age &gt;55 years</td>
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<tr>
<td>WBC &gt;15 x 10⁹/L</td>
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<tr>
<td>Urea &gt;16 mmol/L</td>
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<tr>
<td>Glucose &gt;10 mmol/L</td>
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<tr>
<td>pO₂ &lt;8 kPa (60 mm Hg)</td>
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<tr>
<td>Albumin &lt;32 g/L</td>
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<tr>
<td>Calcium &lt;2 mmol/L</td>
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<tr>
<td>LDH &gt;600 units/L</td>
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<tr>
<td>AST/ALT &gt;200 units</td>
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<tr>
<td><strong>Ranson’s Criteria</strong></td>
</tr>
<tr>
<td>Present on admission:</td>
</tr>
<tr>
<td>Age &gt;55 years</td>
</tr>
<tr>
<td>WBC &gt;15 x 10⁹/L</td>
</tr>
<tr>
<td>Glucose &gt;10 mmol/L</td>
</tr>
<tr>
<td>Serum AST &gt;250 IU/L</td>
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<tr>
<td>Serum LDH &gt;350 IU/L</td>
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<tr>
<td>Developing during the first 48 hours:</td>
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<tr>
<td>Haematocrit fall &gt;10%</td>
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<tr>
<td>Urea increase ≥5 mg/dL (equivalent to ≥1.8 mmol/L)</td>
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<tr>
<td>Serum Ca &lt;2.0 mmol/L</td>
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<tr>
<td>Hypoxaemia - arterial pO₂ &lt;60 mm Hg</td>
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<tr>
<td>Base deficit &gt;4 meq/L</td>
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<tr>
<td>Estimated fluid sequestration &gt;6 L</td>
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In either scoring system, the presence of three or more criteria indicates severe pancreatitis, which is associated with a higher mortality.

An APACHE II score of 8 or more is severe.\cite{12}

The Atlanta Classification - revised in 2012 - allows comparison of these scoring systems and of clinical trials.\cite{13}
- The Classification identifies two phases - early (within the first two weeks) and late (thereafter).
- Severity of disease is classified into three levels: mild (no complications), moderately severe (complications lasting for less than two days, local complications and/or recurrence of co-existing disease) and severe (organ failure lasting for more than two days).
- Local complications are usually detected by CT and may include peripancreatic fluid collection, pseudocysts and necrosis.
- Clinically apparent organ failure includes pulmonary, circulatory or renal insufficiency.
There has been criticism of current scoring systems as being unwieldy and difficult to interpret. Procalcitonin (PCT) and Bedside Index for Severity in Acute Pancreatitis (BISAP) have been mooted as possible candidates in the search for a more simplified approach. Studies have shown that low PCT levels are associated with better outcomes in acute pancreatitis. A meta-analysis showed that compared with Ranson's Criteria and the APACHE II Score, the BISAP Score showed higher specificity and lower sensitivity for mortality and severe acute pancreatitis. Further prospective studies are warranted.

Management

Mild cases

- Manage on a general ward.
- Pain relief with pethidine or buprenorphine ± intravenous (IV) benzodiazepines. Morphine is relatively contra-indicated because of possible spastic effect on the sphincter of Oddi. Non-steroidal drugs may be effective during the recovery phase.
- IV fluids with nil by mouth.
- Nasogastric tube only for severe vomiting.
- Antibiotics for specific infections.
- No other treatment is necessary; no CT scan is necessary.
- When pain and other symptoms have resolved and blood tests are normal, oral fluids and then solids, can be resumed. If gallstones are the cause then consider common bile duct clearance and cholecystectomy after recovery, preferably during original admission.

Severe case

- Treat in ITU or a high dependency unit.
- Where there is evidence of significant pancreatic necrosis, IV antibiotics should be given, preferably following percutaneous aspiration of peritoneal fluid for culture. The role of routine prophylactic antibiotics for severe cases is less clear. A Cochrane review found evidence that imipenem (a beta-lactam) when used as monotherapy may reduce the incidence of superinfection of necrotic tissue, if given for 10-14 days in cases with CT-proven necrosis. However, the studies used differing agents and aetiology/use of surgical debridement may have influenced results; so, more research is needed to answer this question definitively.
- Feed with enteral nutrition (EN) via a nasogastric tube placed beyond the ligament of Treitz, provided there is no ileus (this ligament connects the duodenum to the diaphragm and feeding here is less likely to stimulate the pancreas). A Cochrane review found that EN significantly reduced mortality, multiple organ failure, systemic infections and the need for operative interventions and was associated with shorter hospital stays.
- A Cochrane review supports early ERCP for patients with co-existing cholangitis or biliary obstruction.
- Surgery is only required where there is infection and necrosis. Open surgical debridement is being largely replaced by newer minimally invasive techniques such as transgastric endoscopy and video-assisted translumbar retroperitoneal necrosectomy followed by closed lavage of infected pancreatic necrosis. Refinement of techniques may lead to exclusive use of drainage procedures, without the need for necrosectomy.
- Percutaneous catheter drainage with saline irrigation can sometimes avoid surgery.
- Hyperbaric oxygen therapy - administration of 100% oxygen at a pressure of 2.5 atmospheres for 90 minutes twice-daily for five days has been shown to improve APACHE II and CTSI grading scores. Hyperbaric oxygen treatment acted by normalising the pancreatic microvasculature.
- The poly(ADP-ribose) polymerase (PARP) enzyme system responsible for the control of cellular processes, such as DNA repair, mitochondrial functions and programmed cell death, is involved in the pathological processes causing cellular damage in acute pancreatitis. One study reported the successful combination of a PARP inhibitor - 3-aminobenzamide (3-AB) - in combination with hyperbaric oxygen in the management of acute pancreatitis.
- Human adipose-derived stromal/stem cells may provide a valuable tool for cell-based therapy.

Complications

- **Pancreatic necrosis** - if infected, this trebles mortality risk:
  - Rising CRP suggests necrosis and is confirmed by dynamic CT.
  - Infection occurs in 30-70% of cases of necrosis (the risk can be reduced by gut decontamination).
  - Take special care of aseptic technique with invasive procedures.
  - Where the patient suddenly deteriorates or worsens with intensive support, use CT-guided fine-needle aspiration for culture and microscopy.

- **Infected necrosis** - is almost always fatal without intervention:
  - The standard is IV antibiotics and aggressive surgical pancreatic debridement (necrosectomy) involving drain placement. In many cases, this can be accomplished using minimally invasive techniques, even if necrosis is severe.

- **Acute fluid collections** - are common in patients with severe pancreatitis (occurring in 30-50%).
  - The majority will resolve spontaneously and, in an otherwise stable patient, they do not require treatment.
  - Unnecessary percutaneous procedures risk introducing infections.

- **Pancreatic abscess** - is a collection of pus adjacent to the pancreas, presenting several months after an attack:
  - It requires surgery.
• **Acute pseudo-cyst** - contains pancreatic juice in a wall of fibrous or granulation tissue:
  • it arises four weeks after attack.
  • It can rupture or haemorrhage.
  • It requires surgery.

• **Pancreatic ascites** - occurs when a pseudo-cyst collapses into the peritoneal cavity or major pancreatic duct breaks down and releases pancreatic juices into the peritoneal cavity:
  • Treat with IV feeding plus synthetic somatostatin or surgical excision of the segment of pancreas drained by the broken duct.

• **Acute cholecystitis** - complicates approximately 10% of patients with severe acute pancreatitis in the late stage.\[30\]

### Systemic complications

- **Respiratory**:
  - Pulmonary oedema
  - Pleural effusions
  - Consolidation
  - ARDS

- **Cardiovascular**:
  - Hypovolaemia
  - Shock

- **Disseminated intravascular coagulopathy (DIC)**.
- Renal dysfunction due to hypovolaemia, intravascular coagulation. Usually avoided by adequate fluid replacement plus/minus low-dose dopamine; however, acute tubular or cortical necrosis can follow.

- **Metabolic**:
  - Hypocalcaemia
  - Hypomagnesaemia
  - Hyperglycaemia

- **Gastrointestinal**:
  - Haemorrhage
  - Ileus

- **Weber-Christian disease**:
  - Subcutaneous fat necrosis - relapsing febrile nodular nonsuppurative panniculitis. Recurring crops of tender nodules in the skin and subcutaneous fat of the trunk, thighs and buttocks, which is more common in middle-aged women.
  - These often ulcerate and then scar on healing.
  - Difficult to treat - try prednisolone or immunosuppressives.

- **Splenic vein thrombosis**.

### Prognosis

- 80% of patients have mild disease and recover without complications.\[31\]
- An American study found that 22% of patients admitted with a first attack of pancreatitis subsequently had one or more attacks. However, progression to chronic pancreatitis occurred in only 6% of patients and this was normally against a background of recurrent attacks, alcohol or smoking.\[4\]
- 5% mortality in mild cases; up to 30% mortality in severe cases.
- Severe cases may be deficient in pancreatic enzymes for up to two years but only those with steatorrhoea and weight loss need treatment.
- Subtle glucose intolerance is common but diabetes is uncommon.

### Prevention

- Avoid alcohol.
- Treat gallstones in patients who present with acute pancreatitis.
- Plasmapheresis may help to reduce the incidence of acute pancreatitis in patients with severe hypertriglyceridaemia.

### Further reading & references

- **Pancreatitis; NICE Guidance (Sept 2018)**


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