ABC of diseases of liver, pancreas, and biliary system

Acute pancreatitis

I J Beckingham, P C Bornman

Acute pancreatitis is relatively common, with an annual incidence of 10-20/million population. In more than 80% of patients the disease is associated with alcohol or gall stones, although the ratio of these two causes has a wide geographical variation. Gallstone disease predominates in most UK centres by more than 2:1.

Pathogenesis and pathological processes

Apart from mechanical factors such as the passage of gall stones through the ampulla of Vater or cannulation at endoscopic retrograde cholangiopancreatography, little is known about how the disease process begins. What follows is also unclear, but proteolytic enzymes are thought to be activated while still within the pancreatic cells, setting off a local and systemic inflammatory cell response.

The process is self limiting in most cases and pathologically correlates with oedematous interstitial pancreatitis. In 15-20% of cases the process runs a fulminating course, most commonly within the first week. This is characterised by pancreatic necrosis and associated cytokine activation resulting in multiple organ dysfunction syndrome. The necrotic process mainly affects the peripancreatic tissue (mostly fat) and may spread extensively along the retroperitoneal space behind the colon and into the small bowel mesentery. The necrotic tissue can become infected, probably by translocation of bacteria from the gut.

Clinical presentation

Acute pancreatitis should always be considered in the differential diagnosis of patients with acute abdomen. The clinical presentation may vary considerably and is influenced by the aetiological factor, age, other associated illnesses, the stage of the disease, and the severity of the attack.

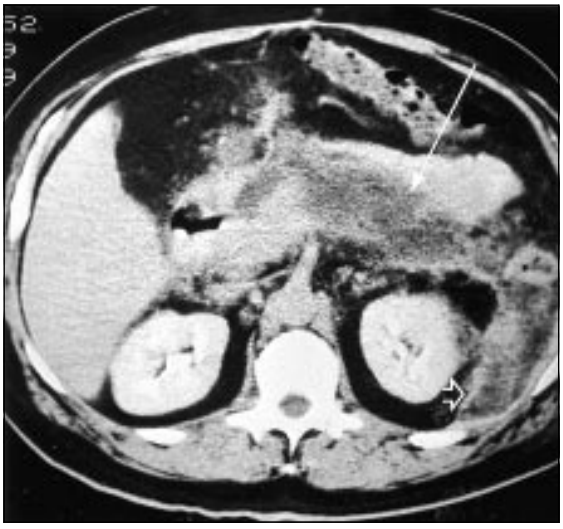
In alcohol induced pancreatitis symptoms usually begin 6-12 hours after an episode of binge drinking. Gall stones should be suspected in patients over 50 years of age (especially women), those who do not drink alcohol, and when the attack begins after a large meal. In patients with an alcohol history and proved gall stones it can be difficult to distinguish between the two causes. A serum alanine transaminase activity greater than three times above normal usually indicates that gall stones are the cause.

Patients usually have pain in the epigastrium that typically radiates through to the back. It is often associated with nausea and vomiting. Severe attacks often mimic other abdominal catastrophes such as perforated or ischaemic bowel and ruptured aortic aneurysm. Abdominal distension with or without a vague palpable epigastric mass is common in severe attacks. More rarely, patients develop discoloration in the lumbar regions and periumbilical area because of associated bleeding in the retroperitoneal space.

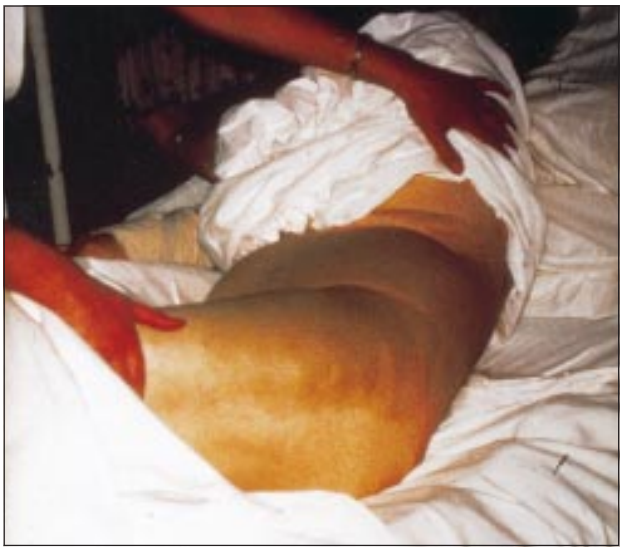
Acute pancreatitis may develop after cardiac or abdominal operations—for example, gastrectomy or biliary surgery—and the onset may be insidious with unexplained cardiorespiratory failure, fever, and ileus associated with minimal abdominal signs.

Causes of acute pancreatitis

- Gallstones } 80%
- Alcohol }
- Idiopathic: 10%
- Endoscopic retrograde cholangiopancreatography or sphincterectomy: 5%
- Miscellaneous: 5%
  Hyperlipidaemia
  Trauma
  Hyperparathyroidism
  Viral (mumps, Epstein-Barr virus, cytomegalovirus, coxsackievirus)
  Drug induced (thiazide diuretics, angiotensin converting enzyme inhibitors, oestrogens, corticosteroids, azathioprine)
  Anatomical (pancreas divisum, annular pancreas)
  Parasites (*Ascaris lumbricoides*)



Computed tomogram showing extensive pancreatic necrosis (arrow) spreading into perinephric fat (open arrow head)



Discoloration of flank in patient with acute pancreatitis (Grey-Turner's sign)

Diagnosis

Pancreatitis is diagnosed on the basis of a combination of appropriate clinical features and a serum amylase activity over three times above normal (>330 U/l). Lower activities do not rule out the diagnosis as serum amylase activity may reduce or normalise within the first 24-48 hours. Measurement of urinary amylase activity, which remains high for longer periods, may be helpful in this situation.

Although amylase activity may be raised in several other conditions with similar clinical signs (notably perforated peptic ulcer and ischaemic bowel), the increase is rarely more than three times above normal. Serum lipase measurement has a higher sensitivity and specificity, and now that simpler methods of measurement are available it is likely to become the preferred diagnostic test.

Clinical course

Whatever the underlying cause of pancreatitis, the clinical course is usually similar. The disease process is self limiting in 80% of cases, but in severe cases, there are usually three phases: local inflammation and necrosis, a systemic inflammatory response leading to multiple organ dysfunction syndrome during the first two weeks, and, finally, local complications such as the development of a pseudocyst or infection in the pancreatic and peripancreatic necrotic tissue.

Assessment of severity

Early identification of patients with a severe attack is important as they require urgent admission to a high dependency or intensive care unit. Initial predictors of a severe attack include first attack of alcohol induced pancreatitis, obesity, haemodynamic instability, and severe abdominal signs (severe tenderness and haemorrhage of the abdominal wall).

Several scoring systems have been developed to predict patients with mild or severe pancreatitis. The most widely used in the United Kingdom is the modified Glasgow system (Imrie), which has a sensitivity of 68% and a specificity of 84%. Other commonly used systems are Ranson's and the acute physiological and chronic health evaluation (APACHE II). Changes in C reactive protein concentration and APACHE II scores correlate well with the ongoing disease process.

Radiology

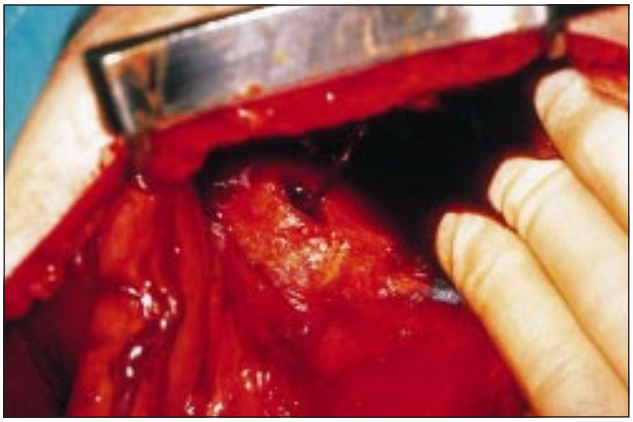
Chest and abdominal radiography are rarely diagnostic but are useful to exclude other acute abdominal conditions such as a perforated peptic ulcer. Abdominal ultrasonography is indicated at an early stage to identify gall stones and exclude biliary dilatation. The pancreas is visible in only 30-50% of patients because of the presence of bowel gas and obesity. When visible it appears oedematous and may be associated with fluid collections. Small gall stones may be missed during an acute episode, and if no cause is found patients should have repeat ultrasonography six to eight weeks after the attack.

In patients in whom a diagnosis of pancreatitis is uncertain, early computed tomography is useful to look for pancreatic and peripancreatic oedema and fluid collections. This avoids inappropriate diagnostic laparotomy. Patients who are thought to have severe pancreatitis or in whom treatment is failing to resolve symptoms should have contrast enhanced computed tomography after 72 hours to look for pancreatic necrosis.

Differential diagnosis of acute pancreatitis

Mild attack
- Biliary colic or acute cholecystitis
- Complicated peptic ulcer disease
- Acute liver conditions
- Incomplete bowel obstruction
- Renal disease
- Lung disease (for example, pneumonia or pleurisy)

Severe attack
- Perforated or ischaemic bowel
- Ruptured aortic aneurysm
- Myocardial infarction

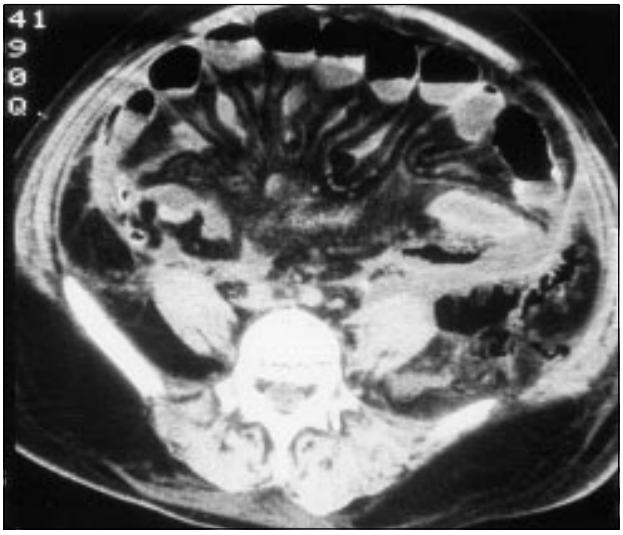


Removal of amylase-rich pericardial fluid from patient with acute pancreatitis

Modified Glasgow criteria

- Age >55 years
- White cell count $>15\times10^9$/l
- Blood glucose >10 mmol/l
- Urea >16 mmol/l
- Arterial oxygen partial pressure <8.0 kPa
- Albumin <32 g/l
- Calcium < 2.0 mmol/l
- Lactate dehydrogenase >600 U/l

Severe disease is present if ≥3 factors detected within 48 hours



Computed tomogram showing extensive mesenteric oedema caused by retroperitoneal fluid due to acute pancreatitis

Treatment of acute attacks

Mild pancreatitis

Treatment of mild pancreatitis is supportive. Patients require hospital admission, where they should receive intravenous crystalloid fluids and appropriate analgesia and should stop all oral intake. Most patients will require opiate analgesia, and although this may cause spasm of the sphincter of Oddi, there is no evidence that this affects the outcome of the disease. A nasogastric tube may be helpful if vomiting is severe. Antibiotics are of no benefit in the absence of coexisting infections. Investigations are limited to the initial blood tests and ultrasonography when gall stones are suspected. Most patients will recover in 48-72 hours, and fluids can be restarted once abdominal pain and tenderness are resolving.

Severe pancreatitis

Patients with severe pancreatitis should be admitted to a high dependency or intensive care unit for close monitoring. Adequate resuscitation of hypovolaemic shock (which is often underestimated) remains the cornerstone of management, and patients often require surprisingly large volumes of fluids over the first 24-48 hours. Resuscitation is mainly with crystalloids, but colloids may be required to restore circulating volume. Progress is monitored by ensuring that urine output is adequate (>30 ml/h). Measurement of central venous or pulmonary arterial pressure may be required, particularly in patients with cardiorespiratory compromise. Patients who develop adult respiratory distress syndrome and renal failure require ventilation and dialysis.

The role of prophylactic antibiotics in severe pancreatitis remains unclear, but recent randomised trials have shown a marginal benefit with antibiotics that have good penetration into pancreatic tissue (such as high dose cefuroxime and imipenem).

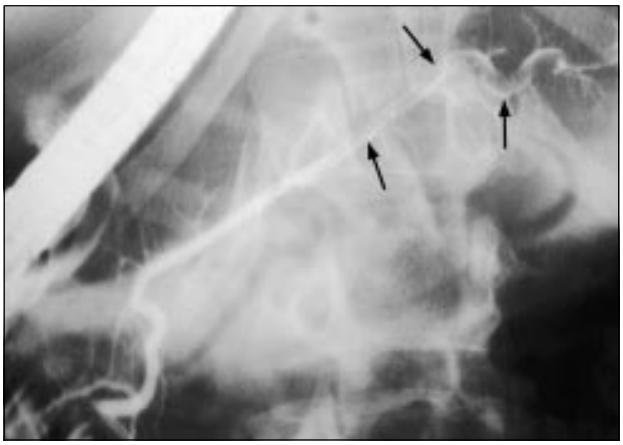
Patients with severe gallstone pancreatitis and biliary sepsis or obstruction benefit from endoscopic retrograde cholangiopancreatography and removal of stones from the common bile duct within the first 48 hours of admission. However, the benefit of sphincterotomy is equivocal in patients without biliary obstruction.

Despite intensive search, no effective drug has been developed to prevent the development of severe pancreatitis. Several new drugs including antagonists of platelet activating factor (Lexipafant) and free radical scavengers that may limit propagation of the cytokine cascade hold theoretical promise, but initial clinical trials have been disappointing.

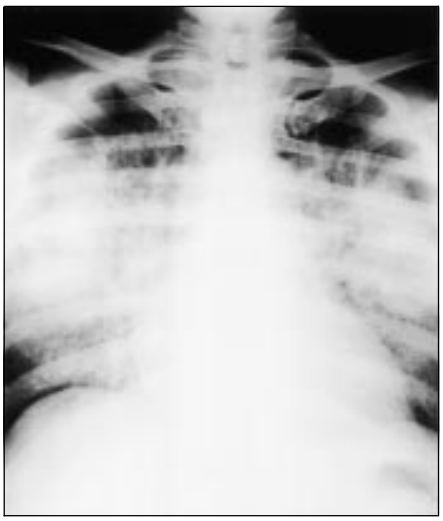
Patients who deteriorate despite maximum support pose a difficult management problem. The possibility of infection in the necrotic process should be considered, particularly when deterioration occurs after the first week. Infection can usually be confirmed by computed tomography guided fine needle aspiration. Patients with infected pancreatic necrosis have a 70% mortality and require surgical debridement (necrectomy). The role of necrectomy in patients without infection is unclear . Several new approaches are being investigated, including the use of minimally invasive necrectomy and lavage and the use of enteral rather than parenteral nutrition, which may reduce gut permeability and bacterial translocation and limit infection in the necrotic pancreas.

Prognosis

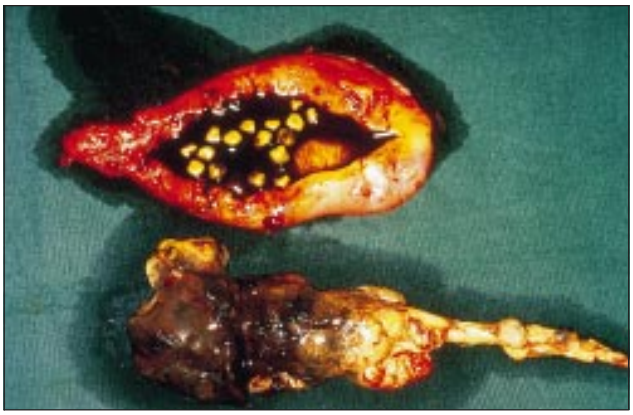
The overall mortality of patients with acute pancreatitis is 10-15% and has not changed in the past 20 years. The mortality of mild pancreatitis is below 5% compared with 20-25% in severe pancreatitis.



Ascaris lumbricoides in pancreatic duct: a rare cause of acute pancreatitis



Chest radiograph of patient with adult respiratory distress syndrome as a complication of acute pancreatitis



Gall bladder and severe necrotic pancreas (necrectomy specimen) removed from patient with acute pancreatitis induced by gall stones

Long term management

Patients with gall stones are best treated by laparoscopic cholecystectomy. This should ideally be done within the same hospital admission after the acute episode has settled to prevent recurrent attacks, which may be fatal. In high risk patients who are considered unfit for surgery, an endoscopic sphincterotomy will prevent most recurrent attacks.

Newer investigative techniques, including bile sampling and analysis and endoscopic ultrasonography, are showing that many patients with "idiopathic" pancreatitis have biliary microlithiasis due to cholesterol crystals, biliary sludge, or small stones that are missed by routine abdominal ultrasonography. Early results confirm that laparoscopic cholecystectomy is curative in most of these cases.

Key points

- Acute pancreatitis is a common cause of severe acute abdominal pain and gall stones are the commonest cause in the United Kingdom
- Severity scoring should be used to identify patients at greatest risk of complications
- Treatment is mainly supportive
- Patients with acute gallstone pancreatitis require early laparoscopic cholecystectomy once the attack has settled
- Biliary microlithiasis is increasingly recognised as a cause of "idiopathic" pancreatitis
- Mortality for acute pancreatitis is 10% overall but rises to 70% in patients with infected severe pancreatitis

Further reading

Glazer G, Mann DV on behalf of working party of British Society of Gastroenterology. United Kingdom guidelines for the management of acute pancreatitis. *Gut* 1998;42(suppl 2)

A review of acute pancreatitis. *Eur J Gastroenterol Hepatol* 1997;9:1-120

Bradley EL. Complications of acute pancreatitis and their management. In: Trede M, Carter DC, Longmire WP, eds. *Surgery of the pancreas.* Edinburgh: Churchill Livingstone, 1997:245-62

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The ABC of diseases of liver, pancreas, and biliary system is edited by I J Beckingham, consultant hepatobiliary and laparoscopic surgeon, department of surgery, Queen's Medical Centre, Nottingham (Ian.Beckingham@nottingham.ac.uk). The series will be published as a book later this year.

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The silver lining

In August 1998 we celebrated our ruby wedding and took all our family—four children, four spouses, and nine grandchildren—for a holiday in Perthshire. Our happy celebration came to a tragic halt when our son in law, Richard, was knocked off his cycle by an 18 year old driver. Before we could reach him he had been airlifted to the neurosurgical unit at the Southern General Hospital in Glasgow. The senior registrar told us that Richard's intracranial pressure was incompatible with life. The scans showed that cerebral oedema had flattened the ventricles and the blood vessels.

Our daughter Catriona's fortitude and faith were amazing. Within minutes of hearing the sad news she was clear that she wanted Richard's organs donated for transplantation. The transplant coordinator worked hard, but timing was tricky. Although we knew that the intracranial pressure would continue to rise, no one could predict when Richard could be declared brain dead. Catriona wanted their four children, aged 6 to 12, to say goodbye, and she wanted to be with him until he went back to theatre.

On the anniversary of receiving a right lung transplant, Gerry wrote to Catriona expressing his profound thanks. Although still in his mid-50s and in the prime of his productive professional life, fibrosing alveolitis had left him severely disabled. Before the operation he was "too breathless to bend down and do up my shoelaces." He needed oxygen 24 hours a day. Now he is no longer tied to an oxygen cylinder and has resumed a full active life. His letter took several months to traverse the confidential transplantation network, but Catriona responded eagerly. Letters and family photos were exchanged.

Exactly two years after the transplantation the two families met and spent three days together. Catriona, her four children, and her parents travelled to Gerry's home in Derry (Londonderry). Both families were nervous as they knew little about each other. Because Gerry and Catriona are both positive people, the time together was a great success. We were united by a living lung that had rich memories of the past, gave vitality for the present, and hope for the future. The hospitality of Gerry's family was overwhelming. We shared the traumatic and stressful experiences of two years before and our hopes for the future. We ate, talked, laughed, and walked the beaches of Donegal together. Gerry even kicked a football around the garden with our grandson, Timothy.

From a humble background Gerry's dynamic character has built up a thriving construction business that is respected for its quality and personal nature. He uses and enthuses tradespeople from both sides of a divided community, giving jobs and hope. His vision includes the development and revitalisation of the neglected waterfront of the River Foyle. Remarkably our family has had the privilege of contributing to this vision. For us the meeting was a positive part of a slow healing process. From the dark cloud of our tragedy fell tears of sorrow, but now we have had the opportunity to glimpse the silver lining.

We hope that our experience will encourage other families to grasp the opportunity of organ donation at a time of tragedy. We also found that contact with the recipient and his family can help in the adjustment to bereavement and loss.

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We welcome articles of up to 600 words on topics such as *A memorable patient, A paper that changed my practice, My most unfortunate mistake,* or any other piece conveying instruction, pathos, or humour. If possible the article should be supplied on a disk. Permission is needed from the patient or a relative if an identifiable patient is referred to. We also welcome contributions for "Endpieces," consisting of quotations of up to 80 words (but most are considerably shorter) from any source, ancient or modern, which have appealed to the reader.