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Andrew Kingsnorth and Derek O'Reilly

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Acute pancreatitis
Andrew Kingsnorth, Derek O'Reilly

Acute pancreatitis is a potentially lethal disease that is increasing in incidence. The high mortality associated with acute pancreatitis has improved as a result of a greater understanding of the natural history of acute pancreatitis and recent advances in critical care. Optimal management requires a greater willingness to consider the diagnosis of acute pancreatitis, stratification of severity, and adequate fluid resuscitation. Here, we review who gets acute pancreatitis and how to deal with those patients in whom the cause remains unclear. We also examine the current controversies in acute pancreatitis: how to deliver nutritional support, what role exists for antibiotic prophylaxis, when to do a computed tomography scan, and the role of early endoscopic retrograde cholangiopancreatography (ERCP).

Is acute pancreatitis becoming more common?
Incidence rates vary from 5.4 per 100 000 population per year to 79.8 per 100 000 per year. Variation is due to different diagnostic criteria, geographical factors, and changes over time. One constant, however, is an apparent increase in the incidence of acute pancreatitis in the past 40 years. For example, the incidence in Scotland has risen from 9.4 per 100 000 per year in 1968-80 to 41.9 per 100 000 per year in 1995.1 This rise in incidence may be due to improved diagnostic capability during this period but may also reflect a true increase due to a greater prevalence of risk factors such as increased alcohol consumption.

How does acute pancreatitis present?
Abdominal pain, usually located in the epigastrium, is the cardinal symptom of acute pancreatitis. It typically increases in severity over a few hours before reaching a plateau that may last for several days. Continuance of the pain beyond this time is associated with the development of local complications, such as acute fluid collections, pseudocysts, and necrosis. Nausea and vomiting are associated symptoms. Abdominal signs may vary from mild tenderness to generalised peritonitis. Blue-grey discoloration of the flanks, due to exudation of fluid stained by pancreatic necrosis into the subcutaneous tissue, is known as Grey-Turner’s sign. Similar discoloration in the periumbilical area is known as Cullen’s sign.

Systemic inflammation may occur, producing respiratory failure and cardiovascular failure. The resulting hypoxia and hypotension may lead to both a decreased level of consciousness and acute renal failure. Metabolic complications (hypocalcaemia, hypomagnesaemia, hyperglycaemia) and haematological complications (disseminated intravascular coagulopathy) may occur. Fever on presentation may represent cytokine mediated systemic inflammation, or acute cholangitis if biliary obstruction is present. Fever

Summary points
Early identification of the severity of an episode determines allocation of critical care beds, early endoscopic retrograde cholangiopancreatography, computed tomography scanning, and nutritional support

Early enteral nutrition is an important mode of acute treatment

The first double blind trial of antibiotic prophylaxis in acute pancreatitis did not show a benefit for development of infected pancreatic necrosis

Patients with acute severe biliary pancreatitis should have early endoscopic retrograde cholangiopancreatography and endoscopic sphincterotomy within 72 hours of symptom onset

Patients with gallstone pancreatitis should have cholecystectomy, ideally during the same admission

Diagnosis of infected necrosis is an indication for radiological or surgical intervention

Sources and selection criteria
• We searched Medline with the key word "acute pancreatitis"
• We searched personal archives of references and the reference lists of articles
• We also reviewed recent guidelines on the management of acute pancreatitis and several relevant Cochrane reviews
due to bacterial infection of pancreatic necrosis usually does not occur until the second or third week.

Painless acute pancreatitis is a recognised entity and occurs in cases of shock of unknown origin, during the postoperative period, in renal transplant and peritoneal dialysis patients, and in diabetic ketoacidosis.

What is the initial management?
The main goal of initial management is adequate fluid resuscitation. Rapid transfusion of crystalloid fluid or colloid is needed to correct the plasma volume deficit. A urinary catheter ensures that output is accurately measured. Central venous monitoring may be needed in acute severe pancreatitis. Supplemental oxygen should be provided to maintain normal arterial oxygen saturation. All patients with severe acute pancreatitis should be managed in a high dependency unit or intensive therapy unit.

Adequate treatment of pain usually requires opiate analgesia. Despite the widespread belief that morphine exacerbates pancreatitis by stimulating the sphincter of Oddi, no definitive human study supports this view. A nasogastric tube is not useful routinely but may be helpful if protracted vomiting occurs in the presence of a radiologically demonstrated ileus.

How is it diagnosed?
Typical clinical features together with a high plasma concentration of pancreatic enzymes are the basis of diagnosis for most cases. Although serum amylase analysis is widely available, concentrations decline quickly over two to three days. Diagnosis should therefore rely not on arbitrary limits of values three or four times greater than normal but on values interpreted in light of the onset of abdominal pain. Furthermore, because hyperamylasaemia is found in several non-pancreatic diseases (visceral perforation, small bowel obstruction and ischaema, leaking aortic aneurysm, ectopic pregnancy), its specificity for acute pancreatitis is around 88%. Various tumours also secrete amylase. Lipase has a superior sensitivity and specificity for acute pancreatitis and, where available, is preferable to serum amylase for the diagnosis of acute pancreatitis.

How can disease severity be predicted?
Early identification of the severity of an episode is important because it facilitates the appropriate allocation of critical care beds, ERCP, computed tomography scanning, and nutritional support. At initial assessment, clinical assessment, body mass index over 30, pleural effusion, and an APACHE II score greater than 8 all predict a severe attack. Other scoring systems, such as the Ranson and Glasgow scores, cannot be completed until 48 hours after the onset of symptoms. A cut-off value for C reactive protein of 150 mg/l at 48 hours predicts a severe attack. Activation peptides of pancreatic enzymes show promise in providing prognostic information, but clinically useful assays are not yet widely available.

What causes acute pancreatitis?
Gallstones continue to be the most common cause of acute pancreatitis in most series. Occult gallstones (microlithiasis or biliary sludge) cause acute pancreatitis too, so every effort should be made to diagnose these to reduce the incidence of recurrent pancreatitis. Alcohol is the second most common cause, but an episode requiring admission to hospital may represent an exacerbation of chronic pancreatitis rather than true recurrent acute pancreatitis. Other causes include hypertriglyceridaemia, hyperparathyroidism, pancreatic malignancy, ERCP, trauma, infectious agents (increasingly associated with HIV infection), drugs (box 1), autoimmune, and heredity. Suspected but controversial causes include pancreas divisum (which arises from a failure of the dorsal and ventral ducts to fuse in embryo so that most of the pancreatic juice flows through the minor pancreatic duct and papilla) and sphincter of Oddi dysfunction.

How should idiopathic acute pancreatitis be investigated?
A thorough history and physical examination, liver function tests, and biliary ultrasonography will indicate the correct cause in most cases. Where this is not the case, follow-up investigations, during the recovery phase, should include fasting plasma lipids and calcium, viral antibody titres, and repeat biliary ultrasonography. Further investigations are appropriate for recurrent idiopathic acute pancreatitis. Exclusion of pancreatic cancer, microlithiasis, chronic pancreatitis, and pancreas divisum are facilitated by computed tomography, endoscopic ultrasonography, and magnetic resonance cholangiopancreatography, depending on local availability and expertise. ERCP may be needed to detect microlithiasis by bile

Box 1: Drugs that cause acute pancreatitis, for which at least one positive rechallenge has been documented
- a-methyldopa
- 5-aminosalicylate
- Azathioprine
- Cimetidine
- Cytosine arabinoside
- Dexamethasone
- Ethinylestradiol
- Frusemide (furosemide)
- Isoniazid
- Mercaptopurine
- Metronidazole
- Norethindrone
- Pentamidine
- Procaainamide
- Stilbogluconate
- Sulfamethazine
- Sulfamethoxazole
- Sulindac
- Tetracycline
- Trimethoprim
- Valproic acid
Clinical review

sampling, and sphincter of Oddi manometry for the
detection of sphincter of Oddi dysfunction. 16 Sphincter
of Oddi manometry is restricted to a few specialised
centres because of the fivefold increase in post-ERCP
pancreatitis in these patients compared with those who
have endoscopic sphincterotomy for other indica-
tions. 11 The only gene for which genetic testing is currently
recommended is the cationic trypsinogen gene
(PRSS1). 18 Box 2 gives a summary of patients for whom
genetic testing is recommended.

When is a computed tomography scan
indicated?

Plain radiographs contribute little to the diagnosis of
acute pancreatitis but may give clues to the cause (cal-
cified gallstones and pancreatic calcification on
abdominal radiograph), detect prognostic signs (pleu-
ral effusion on chest radiograph), or show complica-
tions (localised ileus on abdominal radiograph or adult
respiratory distress syndrome on chest radiograph).
The value of ultrasonography lies in its ability to show
gallstones and dilated bile ducts, and it is recom-
mended as the initial investigation in all patients with
acute pancreatitis.

Computed tomography scanning is occasionally
needed for diagnosis, when clinical and biochemical
findings are equivocal and the possibility exists of an
alternative abdominal emergency that would require a
laparotomy. The main indication for computed
tomography scanning is to detect and stage complica-
tions of acute severe pancreatitis, especially pancreatic
necrosis. The full extent of pancreatic necrosis cannot
be appreciated until at least three days after the onset
of symptoms. Patients with persisting organ failure,
signs of sepsis, or clinical deterioration occurring after
an initial improvement should have computed
tomography. This should be done according to
a pancreas protocol, and all patients should receive
oral and intravenous contrast. Follow-up scans are
needed if the clinical status fails to improve or
deteriorates. 1

When and how should nutritional
support be implemented?

For many years conventional teaching said that oral or
enteral feeding might be harmful in acute pancreatitis;
feeding was thought to stimulate exocrine pancreatic
secretion and accelerate the autodigestive process.
Today, early enteral nutrition is considered an
important mode of acute treatment, 11 and it is
supported by several trials. Most studies show that,
compared with parenteral feeding, enteral feeding is
cheaper, safer, and associated with fewer septic compli-
cations and improved clinical outcome.12 Nutritional
support is essential in patients with severe disease. The
enteral route should be attempted in all patients, but
when this is not tolerated additional or total parenteral
nutrition may be needed. Box 3 outlines recom-
mended nutrient requirements. Although the use of
glutamine supplementation, “immunonutrition,” and
probiotics are conceptually sound, they are not
supported by large scale studies.13

The nasojejunal route for enteral feeding is
usually recommended but this has been challenged by
a recent randomised study of early nasogastric ver-
sus nasojejunal feeding in acute severe pancreatitis.
This study of 50 consecutive patients found no
significant differences between the groups for the
endpoints of APACHE II score, C reactive protein, or
predicted acute severe pancreatitis received intrave-
rous ciprofloxacin plus metronidazole or placebo, but
no benefit was found for antibiotic prophylaxis with
respect to developing infected pancreatic necrosis.
The authors thus advocate a policy of antibiotic treat-
ment “on demand” if any of the following occur: newly
developed sepsis or sepsis inflammatory response
syndrome, failure of two or more organ systems,
patients in this category. symptom onset, is now generally recommended for and endoscopic sphincterotomy, within 72 hours of pancreatitis. rates of readmission to hospital with recurrent definitely clear gallstones results in unacceptable detected by intraoperative cholangiography. Failure to options for the further management of bile duct stones exploration or postoperative ERCP are both valid graphy, ideally during the same admission. Bile duct have cholecystectomy with intraoperative cholangio-

How should gallstones be managed?

Widespread agreement exists that patients with acute pancreatitis and concomitant obstructive jaundice, cholangitis, or a dilated common bile duct should have early ERCP. The role of early ERCP in patients without evidence of biliary obstruction is more controversial. However, a Cochrane review of three randomised controlled trials showed a significant reduction in the complications of pancreatitis for patients with acute severe gallstone pancreatitis who had ERCP compared with those who had conservative management.3 ERCP and endoscopic sphincterotomy, within 72 hours of symptom onset, is now generally recommended for patients in this category.2 5

Patients with mild gallstone pancreatitis should have cholecystectomy with intraoperative cholangiography, ideally during the same admission. Bile duct exploration or postoperative ERCP are both valid options for the further management of bile duct stones detected by intraoperative cholangiography. Failure to definitively clear gallstones results in unacceptable rates of readmission to hospital with recurrent pancreatitis.2 5 For patients with severe gallstone pancreatitis, cholecystectomy may be delayed until systemic complications have resolved. For those unfit to undergo cholecystectomy, endoscopic sphincterotomy alone is considered sufficient treatment.2

proven infection, or an increase in serum C reactive protein in combination with other evidence supporting the possibility of infection. Although no consensus has yet been reached, this study does take us closer to the goal of a more specific use of antibiotics in acute pancreatitis.

If antibiotic prophylaxis is used, patients with pancreatic necrosis proved by computed tomography should receive agents active against enteric organisms (cefuroxime, imipenem, or ofloxacin with metronida-zole) for one to two weeks.5

How should pancreatic necrosis be managed?

Differentiation between sterile and infected necrosis is essential for patients with greater than 30% necrosis on computed tomography and persistent symptoms or those with any degree of necrosis and signs of sep-sis. This is achieved by fine needle aspiration for bacteriology of pancreatic or peripancreatic necrosis or the presence of retroperitoneal gas on computed tomography.5 7 Patients with sterile necrosis should usually continue to be managed conservatively. The diagnosis of infected necrosis is an indication for radiological or surgical intervention.

Although good outcomes have been reported in patients with infected pancreatic necrosis managed by radiologically placed percutaneous drains, standard treatment remains surgical necrosectomy (figure).7 Techniques for necrosectomy include necrosectomy combined with open packing, planned staged relaparotomies with repeated lavage, closed continuous lavage of the lesser sac and retroperitoneum, and closed packing.7 Mortality rates are similar with all techniques, and the absence of randomised trials means that the choice can be based on local expertise.

Additional educational resources

• British Society of Gastroenterology. UK guidelines for the management of acute pancreatitis—www.bsg.org.uk (guidelines index)


• Pancreas Web—www.pancreasweb.com (resources include email alerts, consensus papers, and congress calendar)

• Journal of the Pancreas—www.joplink.net (the first electronic journal of pancreatology)

Information for patients

• University of Liverpool. Acute pancreatitis—www.liv.ac.uk/surgery/acute1.html (detailed information for patients, written by J P Neoptolemos)

• Pancreas.org—www.pancreasorg/patients/patients_ap.html (written by D C Whitcomb, this site provides information on acute and hereditary pancreatitis)
Novel minimal access approaches to necrosectomy have been described, and particularly encouraging results have been achieved by a retroperitoneoscopic approach combined with postoperative continuous irrigation. Whatever the approach, a successful technique is one that adheres to the principles of organ preservation, minimisation of intraoperative haemorrhage, and maximisation of postoperative removal of debris and exudates.

Contributors: AK and DOR identified the recent key developments in acute pancreatitis, determined the priorities for inclusion, and concoted this review.

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