Acute pancreatitis is a disease with a variety of symptoms. In patients in whom the disease takes a more severe course, stabilization is mandatory, often in a high dependency unit or intensive care unit. When the pancreatitis is of biliary origin and cholangitis and cholestatic changes are proven or suspected, an endoscopic cholangiopancreatography is indicated. Aggressive organ support and continuation of the prophylactic antibiotics are the mainstay of treatment. When infected necrosis has been proven by CT-guided fine needle biopsy, surgical necroctomy and debridement with drainage are necessary. Enteral feeding is superior to parenteral feeding even in situations of severe pancreatitis. Further investigation into the role of selective digestive tract decontamination, by controlled randomized trials, is needed. Curr Opin Crit Care 2000, 6:271–275 © 2000 Lippincott Williams & Wilkins, Inc.

Department of Surgery and Intensive Care, University Hospital, Maastricht, the Netherlands

Correspondence to Marion B. M. van der Kolk, MD, Department of Surgery and Intensive Care, PO Box 5800, 6202 AZ Maastricht, the Netherlands; e-mail: bmvanderkolk@hotmail.com

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Abbreviations

APACHE Acute Physiology and Chronic Health Evaluation
ERCP endoscopic retrograde cholangiopancreatography
ICU intensive care unit
SDD selective digestive tract decontamination

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Acute pancreatitis manifests a great variety of symptoms and can take different courses. The spectrum ranges from a rather mild disease with minor symptoms (treated by starvation, after which pain and abdominal signs disappear within a few days), to a life-threatening entity with rapid progression to pancreatic necrosis, multiple organ failure, and complications. As a result of this clinical spectrum of symptoms, treatment of acute pancreatitis has been in debate for the last 10 years. Infection of pancreatic necrosis has a major impact on prognosis, morbidity, and mortality. Patients with pancreatic necrosis are treated in an intensive care unit (ICU), often undergoing surgery. Mortality, although improving, remains high. Different scoring systems are used to predict outcome and to prevent patients from being under- and overtreated [1,2]. Factors such as age, timing of surgery, and comorbidity are also important determinants of prognosis [3]. This review article highlights some current do’s and don’ts in the treatment of acute necrotizing pancreatitis.

Pathophysiology and incidence of acute necrotizing pancreatitis

The pathogenesis of pancreatitis is related to microcirculatory changes and premature activation of pancreatic protease, resulting in mobilization of various cascades of complement, coagulation, and fibrinolysis. Inflammatory mediators are thought to be important in the development of systemic symptoms in acute necrotizing pancreatitis. The induction of autodigestion of pancreatic tissue can start the systemic inflammatory response syndrome as the primary clinical phase of pancreatitis and multiple organ failure, and death can occur at the end of this intriguing spectrum. Eighty percent of patients with acute pancreatitis have a mild course of the disease and can be treated on a general ward. Symptoms disappear, and the patient is able to leave the hospital without any need for surgical intervention. Twenty percent of patients develop pancreatic necrosis and many of these patients need treatment in the ICU. Extensive necrosis (up to >50%) is associated with systemic complications; in cases of infected necrosis, surgical intervention is necessary [4,5,6,7]. This last group of patients comprises only 5% of patients with acute pancreatitis; however, 80% of the mortality in acute pancreatitis is related to infected necrosis. The tremendous efforts performed on the ICU for patients with infected pancreatic necrosis is well rewarded by the excellent performance status of 75% of the survivors [6,8].
**Prognostic scoring systems**

Identifying which case of acute pancreatitis will progress into multiple organ failure and complications is still difficult. Although scoring systems have been developed for groups in randomized trials, clinicians often discuss the interpretation of an individual patient’s signs and symptoms, resulting in an interobserver variability in the staging of the patient [9]. The Ranson score, modified by the Glasgow group, was the initial scoring system used in trials for acute pancreatitis; the severity of acute pancreatitis is estimated on admission and during the first 24 hours, using the Imrie score (Table 1). According to this system, the presence of three positive criteria indicates severe acute pancreatitis. The problem with this scoring system is the timing of admission to the hospital. Not all patients consult a physician or surgeon during the first days of symptoms. The Acute Physiology and Chronic Health Evaluation (APACHE) II and III scores are more accurate in specificity and sensitivity, although interobserver variability is also seen with the APACHE scoring systems, especially when it comes to chronic health points [2]. A second problem is that the APACHE II scoring system often starts in the ICU, often after resuscitation has already started. This influences the outcome of the prediction. An APACHE II score of more than 7 is taken as an indication of severe acute pancreatitis, but only 40% of these patients have a severe outcome [9].

**Initial treatment of acute necrotizing pancreatitis in the intensive care unit**

The first intervention in the treatment of acute pancreatitis is ending oral intake, rehydration, and prevention of renal and respiratory insufficiency. In situations of hemodynamic instability and oliguria, not stabilizing after fluid resuscitation, central venous catheter, or Swan-Ganz monitoring can give useful information about the condition of the patient. Interventions like fluid supplementation with crystalloids and/or colloids or inotropes can be tailored to the patient. The patient with a severe attack of acute pancreatitis is best monitored in the ICU or a high dependency unit. We must be aware of the fact that acute pancreatitis can lead to paralytic ileus and capillary leak syndrome. In both situations large amounts of crystalloids and colloids are necessary in the stabilization period. The use of inotropes or vasoconstrictors can be needed in periods of distributive shock with a low systemic resistance because of vasodilatation.

**Antibiotics**

Early studies of the use of antibiotics in acute necrotizing pancreatitis were negative because in many situations there was not always infected pancreatic necrosis, and inappropriate antibiotics were used.

Because mortality of acute necrotizing pancreatitis is associated with infected necrosis, the use of antibiotics has been the subject of debate for many years, and still is. In experimental pancreatic necrosis, infection occurs due to translocation from the colon, to the retroperitoneum or to a localized abscess. Studies of the effectiveness of antibiotic treatment in preventing infected necrosis in cases of acute necrotizing pancreatitis have not given sufficient evidence of reduced mortality [11••,12]. A controlled clinical trial in biliary pancreatitis and the use of imipenem resulted in less pancreatic infection, but no significant reduction in multiorgan failure or mortality [13]. A multicenter trial from the same group, comparing pefloxacin with imipenem, gave evidence of the superiority of imipenem. However, the experimental penetration of antibiotics in pancreatic necrosis was superior for pefloxacin versus imipenem, so these results were rather surprising [14]. The Finland study using cefuroxim as antibiotic prophylaxis in acute necrotizing pancreatitis did show less infected necrosis, a reduction in mortality, and fewer indications for surgery [15]. The reason most clinicians start with imipenem in the treatment of severe acute pancreatitis, despite these poor results in clinical trials, is that infected necrosis substantially increases mortality. The broad spectrum of imipenem will treat most potential infections, but with selection pressure for fungal infections. Gram stains of CT-guided needle aspirations will not show bacterial growth when patients are treated with imipenem, but the leukocyte count in the aspirate will be the differentiator for infection. When a high leukocyte count is found in the Gram stain of the CT-guided aspirate of the pancreas necrosis, the necrosis is infected and surgical intervention is needed.
Selective decontamination of the gut in acute necrotizing pancreatitis

Good animal experimental work on selective gut decontamination showed evidence that bacterial translocation causes infected necrosis [16].

The concept of selective digestive tract decontamination (SDD) of the gut by using oral nonabsorbable antibiotics together with 4 days of systemic treatment with cefotaxim was based on the idea that infection could be prevented by modulating colonization in the digestive tract, thus reducing the incidence of respiratory infections [17]. Meta-analysis of SDD suggests a positive effect, with reduction of mortality in the critically ill patient [15]. One prospective randomized trial was associated with a positive outcome in acute necrotizing pancreatitis [18]. The reduction in gram-negative pancreatic infections led to a reduction of mortality. When SDD failed to eliminate all gram-negative bacteria from the digestive tract, there was a higher risk of development of infections and mortality [18]. For the general ICU, the use of SDD remains very controversial, but a recent evidence-based review of the literature states that SDD improves outcome in acute necrotizing pancreatitis, based on the only controlled trial of SDD [11••].

Indications for endoscopic retrograde cholangiopancreatography in acute biliary pancreatitis

Acute pancreatitis is associated with gallstones in the biliary tract in 40% of patients. In the majority of these patients the disease will take a mild course. In many situations where no biliary stones were found the origin of the pancreatitis was thought to be idiopathic; we now presume that microlithiasis plays a role in the pathophysiology. Endoscopic retrograde cholangiopancreatography (ERCP) is one of the cornerstones in the treatment of acute biliary pancreatitis, although indications are limited because of associated morbidity and the risk of exacerbation of the pancreatitis, duodenal perforation, and hemorrhage after papillotomy. According to authors of the randomized trial of the German Study Group on acute biliary pancreatitis [20,21], ERCP should be performed within 48 hours in situations of gallstone impaction in the common bile duct and/or cholangitis. Patients without these symptoms do not benefit from this procedure and are exposed to the complications and the risk of death. We must be aware of the fact that even experienced endoscopists could encounter difficulties during the ERCP of a patient in the ICU experiencing suboptimal conditions as hemodynamic instability and coagulopathy. In very special situations, a nasobiliary drain could be an option instead of a papillotomy.

Surgical treatment of acute necrotizing pancreatitis

The discussion of timing and indication for surgery in acute necrotizing pancreatitis continues. A CT scan with contrast is a prerequisite for diagnosing necrosis [22]. The major indication of surgical intervention in the treatment of acute necrotizing pancreatitis is infected necrosis; not much disagreement between surgeons exist in this situation. Some surgeons also open the abdomen because of peripancreatic fluid collections or because of clinical sepsis with worsening of the multiorgan failure. The diagnosis of infected necrosis is made by CT-guided fine needle aspiration of the pancreatic necrosis. When a Gram stain reveals infection, surgery is the next step in the treatment of acute pancreatitis. In situations in which the radiologist is not able to perform a CT- or ultrasound-guided fine needle aspirate, protamine could be of help in the differentiation of infected versus sterile necrosis [23]. The importance of the diagnosis of infected necrosis is related to the fact that mortality is strongly associated with infected necrosis. Mortality is also associated with the timing of surgery (within 2 weeks of admission, mortality is 100%, probably because of hemorrhage in a situation where obliteration of the end arteries was not total) [3]. Advanced age, comorbidity, and delay in transfer to a referral center also influence mortality [3,24].

Various procedures are used by surgeons in the surgical treatment of infected necrosis of the pancreas. Formerly, pancreatic resection was an option in the treatment of acute necrotizing pancreatitis. However, mortality was high, and the risk of resection of functional pancreas tissue resulting in diabetes mellitus is high. A second reason not to perform a resection is the fact that necrosis is seldom limited to the pancreas, and often the resection is much larger than needed. The treatment of infected pancreatic necrosis includes extensive debridement of necrotic tissue and continuous postoperative peritoneal lavage with 6–12 L of saline [1,4,7,25] through drains placed in the lesser sac or alternatively planned relaparotomy. Risks of both procedures are hemorrhage, formation of enteral and pancreatic fistulae, and colonic perforation. Although Beger et al. [4] prefer a large midline incision, the authors prefer a transverse upper abdominal incision, because it creates the possibility of making a compartment of the lesser sac, without disturbing the intestines during the necrosectomy procedures, and probably with fewer adhesions. The advantage of continuous peritoneal lavage is the fact that the abdomen is closed after the debridement. Often fibrin in the drains will be a burden during the lavage procedure. Electrolyte disturbances and hypothermia are also a serious complication of continuous peritoneal lavage. Planned relaparotomies do have a risk of bowel lesions and adhesions, and there is also the
difficulty of deciding on the indication and timing of the last laparotomy. Often patients will need a secondary closure of the abdomen months after the period of acute pancreatitis.

**Abdominal compartment syndrome and acute pancreatitis**

Abdominal compartment syndrome was recognized in the literature for the first time in 1982 [26]. Much has been written since, especially associated with trauma and abdominal aortic aneurysm surgery. We must be aware of the fact that acute pancreatitis can result in paralytic ileus and that abdominal pressure can be elevated above the level of 25 cm H₂O. Research during a period of high abdominal pressure showed a lower gastric pH, suggesting reduced splanchnic perfusion [27]. Sugerman [28•] stated that, as a result of this situation, multiple organ failure can develop. The authors advise that bladder pressure be measured in patients with paralytic ileus, oliguria, and high inspiratory pressures. In the situation of an elevated pressure, laparotomy is performed with the goal only of lessening the pressure; there should be no opening of the lesser sac or pancreatic exploration. The preferred incision should be an incision for a possible necrosectomy; lavage may be needed if during the treatment period infected pancreatic necrosis occurs.

**Complications**

The risk of bleeding is highest in the first 2 weeks of pancreatic necrosis because obliteration of the end arteries is not yet fully achieved. Bleeding of the splenic artery or vein is still one of the major hazards of the necrosectomy and is best treated by ending of the procedure and packing of the area with gauze or a large balloon catheter. Fistulas are often seen in the splenic flexure of the colon, because, in this watershed area, the vascular supply can be at risk when necrosis of the mesentery also obliterates the smaller vessels. A colostomy or ileostomy is the treatment of choice; the wound contamination can be controlled and nursing of the wound is easier. Pseudocyst is one of the later complications, treated by surgical, endoscopic, or radiologic drainage procedures only in situations of bleeding, infection, or obstruction. Abscesses are often treated by CT- or ultrasound-guided drainage procedures.

**Feeding the patient with acute pancreatitis**

Traditionally, patients with acute pancreatitis are treated by starvation and intravenous fluid. If the symptoms do not resolve, a condition develops in which a patient with increased energy requirements enters into a catabolic state. The first step is often to start parenteral nutrition, because it is thought that enteral nutrition will stimulate pancreatic excretion. The literature has changed in recent years, and early enteral feeding is indicated for patients with severe acute pancreatitis [28,29]. A randomized prospective trial in patients with severe acute pancreatitis [31], comparing early parenteral feeding with early enteral feeding, showed that early enteral feeding was well tolerated and was of comparable efficacy. Enteral feeding was also associated with significantly fewer complications. Patients treated nonoperatively could be given an endoscopically placed nasojejunal feeding tube. The reason to start jejunal feeding instead of feeding in the horizontal part of the duodenum is based on the fact that cholecystokinin in part III of the duodenum can still stimulate the exocrine pancreas, [10••,32]. Because dislocation of the tube can lead to multiple endoscopic procedures, the authors advise that, in patients with infected pancreatic necrosis, the laparotomy for necrosectomy should also include placement of a gastrostomy and a jejunostomy feeding tube. The gastrostomy should be placed to prevent esophagus ulceration, always a risk after a long period with a nasogastric tube [1].

**Conclusions**

Treatment of the intriguing spectrum of problems related to acute pancreatitis is based on its diversity. The patient must first be rapidly and adequately resuscitated, with a focus on patients identified as severe by the Ranson or Imrie scores. When the patient is stable and choledocholithiasis is proven, or suspected, because of cholangitis or cholestatic changes, the first step should be an ERCP with a papillotomy. In patients in whom the disease take a more severe course, stabilization often must be achieved in a high dependency unit or ICU. When the patient deteriorates, a CT scan is indicated and when pancreatic necrosis is found, a CT- or ultrasound-guided fine needle aspirate should be taken. Antibiotics such as imipenem should be started when necrosis is found on the CT scan. When infection has been proven, surgical necrosectomy and debridement with drainage is indicated. Enteral feeding can start even in situations of severe acute pancreatitis by endoscopic placement of a nasojejunal tube. Paralytic ileus and an enteral fistula are reasons to withhold enteral feeding and start parenteral nutrition. In situations of oliguria or high inspiratory pressure, measurement of the pressure of the bladder could reveal an abdominal compartment syndrome. This could be a “second hit” in acute necrotizing pancreatitis, resulting in bacterial translocation and infected necrosis. The treatment of the abdominal compartment syndrome is opening of the abdomen and closure with a Bogota bag or vicryl mesh (Ethicon, Somerville, NJ) without opening of the lesser sac. For patients after surgery, or in whom surgery is not indicated, aggressive organ support and continuation of the prophylactic antibiotics are the mainstay of treatment. The potential role of SDD is worthy of further confirmation.
References and recommended reading

Papers of particular interest, published within the annual period of review, have been highlighted as:

** Of special interest
*** Of outstanding interest

29. This article summarizes what happens to various organ systems when elevated intra-abdominal pressure occurs. It emphasizes the importance of recognizing symptoms such as oliguria and high peak inspiratory pressure in the ICU, and discusses treatment by opening of the abdomen and staged closure.