Antibiotic Prophylaxis of Pancreatic Infection in Patients with Necrotizing Pancreatitis: Rationale, Evidence, and Recommendations

Issac Moyshenyat, MD, Ephraim Mandell, MD, and Scott Tenner, MD, MPH

Introduction
Although more often a mild disease, acute pancreatitis can manifest an unpredictable course with a myriad of complications [1]. The initial management of patients with acute pancreatitis requires close monitoring, aggressive intravenous hydration, and control of pain [2••]. Following the initial management of a patient with acute pancreatitis, the course can be complicated by organ failure or the development of pancreatic necrosis. Although many patients with acute pancreatitis manifest early signs of systemic inflammation with fever, tachycardia, and leukocytosis, these symptoms rarely require antibiotics. Even in patients with gallstone pancreatitis, the common bile duct stones typically pass with little need of antibiotics or endoscopic intervention.

Later in the course of the disease, infectious complications are the most common cause of morbidity and mortality in patients suffering from severe acute pancreatitis [3,4]. Approximately 25% of patients develop pancreatic necrosis. In these patients with severe disease that is complicated by necrosis, there is evidence that preventing infection of the pancreatic necrosis decreases morbidity and mortality [5]. Whereas sterile necrosis is often treated conservatively, surgical debridement is required when the necrosis becomes infected [6••]. Although surgery is necessary in patients with infected necrosis, surgical intervention for a variety of reasons increases the morbidity and mortality of the disease [7].

Prevention of infectious complications, such as infected necrosis, through the use of prophylactic antibiotics is controversial [8,9••,10]. Despite reviewing the same evidence, different authors and organizations have arrived at different conclusions. In their review for the Cochrane Database, Bassi et al. [9••] found evidence to justify the use of antibiotics in the prevention of infection in patients with necrotizing pancreatitis. Conversely, guidelines for the management of patients with severe acute pancreatitis recently published by the Society for Critical Care Medicine do not support the routine use of antibiotics in patients with necrotizing pancreatitis [10]. This review evaluates the evidence and provides a guide to the clinician caring for patients with acute pancreatitis complicated by pancreatic necrosis.

Necrotizing Pancreatitis
Most patients with acute pancreatitis have interstitial disease, characterized by edema of the parenchyma, loss of
the pancreatic border, peripancreatic stranding, and fluid collections. On a contrast-enhanced CT scan, interstitial pancreatitis is characterized by perfusion (enhancement) of the pancreas (Fig. 1). Pancreatic necrosis develops in only 15% to 20% of patients with acute pancreatitis and is characterized by non-enhancement of greater than 3 cm of the pancreatic parenchyma on CT (Fig. 2). Necrosis of the pancreas appears early in the course of the disease, usually within the first 48 hours. The pathogenesis is perpetuated by inadequate perfusion of the pancreas during the initial 48 hours of the disease [2••]. Several factors lead to the development of pancreatic ischemia and subsequent necrosis during the early stages of the disease, including the amount of inflammation during the inciting attack of pancreatitis, the individual’s reserve for maintaining perfusion of the pancreas, and the amount of intravascular repletion that occurs during the first hours of therapy. Genetic factors have been discovered that are involved in an individual’s response to injury and may contribute to the development of pancreatic necrosis (Whitcomb D, Personal communication).

Patients with sterile necrosis can appear ill with multisystem organ failure. However, with maximal supportive care, the natural history is less complicated than that of patients who develop infected necrosis. Patients with sterile necrosis appear to have a much better prognosis than patients with infected necrosis. Whereas sterile necrosis can be managed most often with conservative supportive care, infected necrosis warrants surgical intervention. The intervention of a surgeon performing a necrosectomy in a patient with infected necrosis, though necessary, increases the morbidity and mortality of the disease when compared with the conservative supportive care afforded the patient with sterile necrosis. Therefore, any method that can maintain the sterile necrotic parenchyma from becoming infected is of great importance.

The development of infected necrosis

The mechanism by which the necrotic pancreas becomes infected is unclear, but experimental and clinical data suggest that bacterial translocation from the colon is the source of the organisms that eventually result in infected necrosis. Animal models that allow the isolation of the colon by the placement of “foil” around the bowel have revealed a decreased incidence of infected necrosis compared with animals that had not had the colon isolated by foil. The bacterial flora of the colon may be more pathogenic during the attack of acute pancreatitis. The typical ileus seen during an attack of acute pancreatitis may lead to bacterial overgrowth due to stasis of colonic contents. Within a short period of time, there is intestinal colonization by pathogens that precede pancreatic infection. The inflammatory process leads to translocation of the bacterial flora from the colon directly to colonize the necrotic pancreatic bed. In time, as the inflammatory process recedes, the bacterial seeding of the necrotic pancreatic bed leads to the clinically apparent infection that characterizes infected necrosis [11,12].

Luiten et al. [13] used an interesting strategy to decrease morbidity and mortality in patients with acute pancreatitis focusing on the colon as the source of infection. One hundred two patients with severe acute pancreatitis were randomly assigned to undergo an intensive “sterilization” or decontamination regimen of the colon in an attempt to decrease the morbidity and mortality. The treatment group received an oral and rectal regimen of colistin, amphotericin, and norfloxacin. Compared with placebo patients, there was a significant reduction in pancreatic infection and mortality in subjects treated with “selective decontamination.” Although this study demonstrates the importance of the colon in the pathogenesis of infected necrosis, the method of