Management of Pancreatic Necrosis
Definition

- Lack of enhancement of the gland with liquefaction and loss of normal glandular texture of a portion or the entire pancreatic gland
- Severe injury with occlusions and thrombosis of the pancreatic microcirculation
- Does not necessarily imply infection
History

- 1882 – W.A. Balser postulates the presence of fatty necrosis in acute pancreatitis
  - *Ueber Fettenneckrose, eine zuweilen tödliche Krankheit des Menschen*
- 1889 – R.H. Fitz suggests that extent of necrosis is sole determinant of survival
  - Argues against surgical intervention
- N. Senn vigorously disputes this conclusion
  - A century of controversy is born
Embryology

- Develops from dorsal and ventral pancreatic buds that arise from the caudal part of the foregut
  - Dorsal bud appears during 4th week opposite the hepatic diverticulum
  - Ventral bud appears during the 5th week
  - Duodenum rotates clockwise, carrying ventral bud along
  - Fusion occurs during 7th week
  - Acinar and islet cells arise from foregut endoderm
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Anatomy

- Soft, oblong gland, 12-15 cm long, lying transversely in the retroperitoneal space
- Lies at L2/L3 level
- Divided into head, body, and tail
- Stomach anteriorly, duodenum to the right, spleen to the left
- Main pancreatic duct (of Wirsung) has 20-30 lobular tributaries; in 10% the accessory duct (of Santorini) serves as the main route of pancreatic secretion
Anatomy

- **Blood supply**
  - Derived from celiac trunk and superior mesenteric artery
  - Head supplied by superior and inferior pancreaticoduodenal arteries
  - Body and tail supplied by transverse pancreatic artery
Statistics

- 185,000 new cases of acute pancreatitis per year in the US\(^1\)
- Alcohol is frequently said to be a close second to gallstones as an etiologic factor
- Necrosis present in 20 to 30 percent of cases
- Associated with morbidity of 82% and mortality of 23%

\(^1\) Baron T, Morgan D. Acute Necrotizing Pancreatitis. NEJM. 1999 May 6;340(18):1412-17
Etiology: Alcohol

- Pancreatitis is a consequence of chronic alcohol abuse; usually 6 to 10 years
- Daily consumption averages 100-150 g/day; 10% of heavy drinkers develop pancreatitis
- Associated with HLA antigen types B40, Aw23, Aw24 and B13, blood groups O and Le
- May cause spasm or inflammation of sphincter of Oddi
- May decrease solubility of intraductal proteins, promoting stone formation
- Decrease in pancreatic blood flow and alterations of lipid metabolism may contribute as well

Etiology: Alcohol

- Both oxidative and nonoxidative metabolism of ethanol occurs in pancreatic acinar cells
- Acetaldehyde directly toxic to pancreas
- Also inhibits secretion
- Alters redox state of cell
- Increased oxidative stress

Wilson JS, Apte MV. Role of alcohol metabolism in alcoholic pancreatitis. Pancreas. 27(4):311-315
Etiology: Alcohol

- FAEEs shown to induce pancreatic injury in vivo and in vitro
- Activate trypsinogen
- Destabilize lysosomes
- Both acetaldehyde and FAEEs affect cytokine expression
- Signaling molecules may provide therapeutic target
Prognostic indicators

- Ranson’s criteria:
  - As defined by Ranson\(^1\), <3 positive signs predicted mortality of 0.9% and >6 positive signs predicted mortality of 100%
  - More useful at extremes of severity
  - Based on alcoholic pancreatitis; relevance to gallstone pancreatitis questionable\(^2\)
  - Only allows for prediction after 48 hours

- Glasgow criteria:
  - No better\(^3\)

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**Present on Admission:**
- Age greater than 55 years
- WBC greater than 16,000/ul
- Blood glucose greater than 200 mg/dl
- Serum LDH greater than 350 I.U./L
- SGOT (AST) greater than 250 I.U./L

**Developing During the First 48 Hours:**
- Hematocrit fall greater than 10%
- BUN increase greater than 8 mg/dl
- Serum calcium less than 8 mg/dl
- Arterial oxygen saturation less than 60 mm Hg
- Base deficit greater than 4 meq/L
- Estimated fluid sequestration greater than 6 L

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Prognostic indicators

- **APACHE-II, APACHE-O:**
  - Can be calculated immediately and daily thereafter
  - Predicts 68% of severe attacks on admission vs. 34% by clinical assessment
  - As good as Ranson and Glasgow after 48 hours
  - May be the scoring system of choice

Prognostic indicators

- CT Severity Index
  - Based on extent of necrosis
  - High correlation with morbidity and mortality
  - Cannot distinguish between sterile and infected necrosis
  - IV contrast may have deleterious effects on pancreatic microcirculation

Medical Management

- Critical care
- Prophylactic antibiotics?
  - Infections occur in 30-40% of patients in who have over >30% necrosis
  - Infectious complications account for 80% of deaths from pancreatitis
  - Bacterial translocation from gut implicated; enteric Gram negative organisms most frequently isolated

2 Ammori BJ. Role of the gut in the course of severe acute pancreatitis. Pancreas 2003;26:122-9
## Medical management

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<tr>
<th>Reference</th>
<th>Year</th>
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Operative Indications

- Infected pancreatic necrosis is considered universally fatal without intervention\(^1\)
- Aggressive debridement on the basis of pancreatic necrosis alone was being advocated into the 1980s\(^2\)
- In 1991 Bradley and Allen\(^3\) established nonoperative management of sterile necrosis as preferred option
  - Studied 194 consecutive patients with acute pancreatitis. 38 (20\%) developed pancreatic necrosis. Of those, all 11 in whom the necrosis remained sterile were treated successfully without surgery

\(^1\) Banks PA. Infected necrosis: morbidity and therapeutic consequences. Hepatogastroenterology 1991;38:116-9
\(^2\) Rattner DW, Warshaw AL. Surgical intervention in acute pancreatitis. Crit Care Med 1988;16(1):89-95
Operative Indications

- Intractability?
  - Persistent systemic illness (>4 weeks) is frequently cited as an indication for debridement of sterile necrosis\(^1,2\)
  - Not a universally accepted indication\(^3\)

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Operative Indications

- Timing of surgery still debated
- Trend toward delayed operation
  - Mier et al. randomized 41 patients to either early (48 to 72 hours) or late (>12 days) necrosectomy. 58% mortality in early group vs. 27% mortality in late group
  - Benefits of delayed surgery attributed to better demarcation between viable and nonviable tissue

Operative management: Evolution

- Formal resection was standard treatment into the 1980s
  - Did not abort necrotic process
  - Excessive removal of healthy tissue
  - Abandoned due to high morbidity and mortality

Operative management: Evolution

- Necrosectomy is the current standard of care
  - Removal of devitalized pancreatic parenchyma and retroperitoneal fat
  - Conventional: debridement with Penrose drain
  - Modifications include continuous irrigation, mandatory re-exploration, and laparostomy

Interventional Radiology

- Role in diagnosis clearly established
  - Diagnosis of pancreatic infection almost always requires tissue sample
- Therapeutic role limited
  - Percutaneous drainage of solid necrotic material ineffective; liquefied necrosis more amenable
    - Freeny et al.: Management of 34 patients with infected necrosis; 47% cured by this modality alone
    - Echenique et al.: 20 patients with solid infected necrosis cured by catheter-based procedures. Mean 17 debridements per patient
  - Very labor intensive, requiring multiple CT scans, catheter exchanges, and bedside visits by the interventionalist

Laparoscopy

- Open necrosectomy associated with incisional hernia rate of 50% and enteric fistula rate of 20%
- Postulated advantages of laparoscopic approach are decreased recovery time, reduced patient pain, shorter ICU stay and shorter overall hospital stay
  - Gagner reported successful treatment of 6/8 patients with transperitoneal laparoscopy\(^1\)
  - Retroperitoneal approaches, often in conjunction with percutaneous catheter placement, have been described as well\(^2\)
- Feasibility has been demonstrated; safety and efficacy have not

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\(^2\) Kellogg TA, Horvath KD. Minimal-access approaches to complications of acute pancreatitis and benign neoplasms of the pancreas. Surg Endosc 200;17:1692-1704
Conclusions

- Recognition of patients with pancreatitis who have or are at high risk of developing necrosis is of paramount importance.
- Determining whether pancreatic necrosis is complicated by infection is pivotal.
- The subset of patients with infected necrosis is at high risk for morbidity and mortality; surgical debridement is the only established modality available to ameliorate the course of illness.