Acute Pancreatitis
Acute pancreatitis is the most terrible of all the calamities that occur in connection to the abdominal viscera. The suddenness of its onset, the illimitable agony which accompanies it, and the mortality attendant upon it, render it the most formidable of catastrophes.

B. Moynihan, 1925
Epidemiology

- Mean age of initial attack in 60s
- Fatalities are now less than 5% (down from 15-20%).
- **Severe** acute pancreatitis (AP) occurs in 10-20% and up to 25% die.
Pathophysiology

- Pathogenesis due to inappropriate activation of trypsinogen to trypsin, autodigestion of the pancreatic tissue with the result of pancreatic and fat necrosis and a necrotizing vasculitis.
- Active pancreatic enzyme is released in to the bloodstream and the inflammatory cascade is activated resulting in systemic inflammatory response syndrome (SIRS). This marks the **early phase** of pancreatitis (the first 7-14days).
Course

- The first phase is characterized by organ dysfunction and failure, usually not associated with infection.

- The second phase which begins after around 7-14 days is characterized by the septic complications that accompany a devitalized necrotic pancreas.

- Infection of the necrotic pancreas occurs in 8-12% of the patients with AP and in 30-40% of patients with necrotizing pancreatitis (>30% necrotic).
Findings

- Abdominal Pain
  - Upper abdomen
  - Sudden in occurrence and without a prodrome.
  - Classically dull, boring, worse when supine
  - Often radiating, bandlike to the lower thoracic region of the back
- Physical signs such as Gray-Turner’s (flank echymosis) or Cullen’s (periumbilical echymosis) are only found in 3% (mortality 37%)
Cullen’s Sign

![Image of Cullen's Sign](image-url)
Grey Turner’s Sign
Diagnosis

- Pancreatic enzymes are released into circulation during an acute attack.
- Levels peak early and decline over 3-4 days.
- Amylase and Lipase – interpret levels taking into consideration *when the pain* began as the levels drop over time. In general look for levels around 2-3 times normal.
Etiology

- Most common causes are:
  - Gallstones (more common in women)
  - Alcohol (more common in men)
  - Idiopathic (same in both)
    - Probably due to occult microlithiasis.
Gallstones

- Increased serum ALT up to 3 times normal is indicative of gallstone pancreatitis.
- Normal LFTs do **not** exclude gallstone pancreatitis (15-20% of patients with biliary AP have normal enzymes).
- If a Biliary etiology is suspected first investigation should be an ultrasound of the abdomen which can demonstrate a dilated biliary tree and look for stones or other pathology.
- If the ultrasound is normal and the suspicion is high then an MRCP or endoscopic ultrasound can be done to look for microlithiasis or other causes of duct obstruction.
- **Urgent** ERCP if **cholangitis** present (24h), if suspected stones then **early** ERCP (within 72h)+
Alcohol

- Acinar cell is the main target damaged by alcohol.
- No accepted explanation for why some patients are predisposed to alcoholic pancreatitis.
Other

- **Drug-induced** – 2%. Normally mild. Azathioprine, sulfonamides, tetracycline, valproic acid, didanosine, methylldopa, estrogens, lasix, 6-MP, pentamidine, steroids, octreotide.
- **Post-ERCP** – around 5%. Risks include female gender, a peri-ampulary diverticulum, and procedure related factors (time to cannulate...)
- **Trauma** – abdominal trauma causes a rise in amylase and lipase in 17% of cases and acute pancreatitis in 5%. More often due to penetrating injury.
- Infections - <1%, tend to be milder than biliary and alcohol induced AP. Viral most common (EBV, coxsackie, VZV, measles).
- **Hypercalcemia** - <1% of cases, due to TPN, vitamin D excessive dose, familial hypocalciuric hypercalcemia.
- **Hypertriglyceridermia** – usually not until TG reach 1000mg/dL, measure as soon as possible after hospitalization because fasting and IV fluid resuscitation drop TG quickly. Can be due to uncontrolled DM, alcohol, obesity.
- **Developmental pancreatic** – pancreas divisum, sphincter of Oddi dysfunction
- **Tumor** – 14% of patients with pancreatic tumors present with pancreatitis
- **Postoperative** – maybe due to transient hypotension or pancreatic trauma. Has a higher complication rate than other etiologies.
- **Autoimmune** - extremely rare cause of AP. Radiologic and histologic diagnosis with an elevated IgG4 level. Occurs in young patients with IBD, primary sclerosing cholangitis, primary biliary cirrhosis and Sjogren’s syndrome. Therapy is steroids.
Prediction of Severity

- Majority of patients have mild AP, it is difficult to identify patients who are at risk of developing severe disease on admission to the hospital.
- Clinical examination not specific.
- Plasma levels of the pancreatic enzymes have no role in predicting severity.
### Predictors of severity

Table 6

Suggested Cutoff Values for Proven Markers of Severity

<table>
<thead>
<tr>
<th>Predictor</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Obesity</td>
<td>BMI &gt; 30</td>
</tr>
<tr>
<td>Chest radiography</td>
<td>Left/bilateral effusion</td>
</tr>
<tr>
<td>APACHE II</td>
<td>≥6</td>
</tr>
<tr>
<td>APACHE O&lt;sup&gt;a&lt;/sup&gt;</td>
<td>≥6</td>
</tr>
<tr>
<td>CRP</td>
<td>&gt;150 mg/L</td>
</tr>
</tbody>
</table>

<sup>a</sup>APACHE II plus 1 point BMI 25–30, 2 points BMI > 30.
<table>
<thead>
<tr>
<th>Ranson’s criteria</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>At admission</strong></td>
<td></td>
</tr>
<tr>
<td>Age &gt;55 years</td>
<td></td>
</tr>
<tr>
<td>White blood cell count &gt; 16000 cells/mm</td>
<td></td>
</tr>
<tr>
<td>Blood glucose &gt;200mg/dL</td>
<td></td>
</tr>
<tr>
<td>Serum AST &gt;250IU/L</td>
<td></td>
</tr>
<tr>
<td>Serum LDH &gt; 350IU/L</td>
<td></td>
</tr>
<tr>
<td><strong>At 48hours</strong></td>
<td></td>
</tr>
<tr>
<td>Calcium &lt;8mg/dL</td>
<td></td>
</tr>
<tr>
<td>Hematocrit fall &gt;10%</td>
<td></td>
</tr>
<tr>
<td>Oxygen PO2 &lt;60mmHg</td>
<td></td>
</tr>
<tr>
<td>GUN increases by 5 or more mg/dL after hydration</td>
<td></td>
</tr>
<tr>
<td>Base deficit (24-HCO3) &gt;4mEq/L</td>
<td></td>
</tr>
<tr>
<td>Sequestration of fluid &gt;6L</td>
<td></td>
</tr>
</tbody>
</table>

Risk factors <3: 1% mortality, 3-4: 15% mortality, 5-6: 40% mortality, >7: 100% mortality
Severity of Pancreatitis

Ranson's criteria
APACHE 2
MODS
CT- scan based severity scales
Balthazar.

(e.g. no necrosis or fluid collections: interstitial or mild pancreatitis - mortality <1%, no necrosis but fluid collections: exudative pancreatitis mort <8%. Extensive necrosis: mortality >= 25%. )
Necrotic and Infected Pancreatitis

- Contrast-enhanced CT scan is the test of choice of the diagnosis of pancreatic necrosis.
  - Full extent of necrosis takes at least 4 days after onset of symptoms – the longer the delay before CT scan the less likely it is to underestimate.

- Secondary infection is the most common cause of death in severe pancreatitis*.
  - Mortality increases from 5-25% in patients with sterile necrosis up to 28% with infected necrosis.
  - Infection occurs in 10-50% of necrotic pancreatitis.

- FNA is the only reliable method of diagnosing infected necrosis other than surgery.

- Infection is usually due to enteric flora such as E. coli.

Necrotic and Infected Pancreatitis

- Prophylactic antibiotic therapy still debated.
- Trend towards improved survival and infection but not statistically significant on meta-analysis.
- Limit use to antibacterials.
- Antibiotics used should have good pancreatic penetration such as Imipenem.
- Beta lactams better than quinolones.
Therapy

1. Aggressive fluid resuscitation
2. Pain control
3. Oxygen
4. Early feeding
5. Watch for infectious complications
Aggressive fluid resuscitation

Aggressive fluid resuscitation within 24 hours improves organ failure rates and decreases hospital stay\textsuperscript{++} for those with severe volume depletion 500-1000mL each hour for several hours for those without signs of extracellular fluid loss 250-300/hour.

Reevaluate every 1-4 hours

Watch for Pulmonary Edema

Fluid needs of 5L or more are not uncommon

\textsuperscript{++}Clinical Gastroenterology and Hepatology 2008;6:1070-1076
Pain control

- Uncontrolled pain can cause hemodynamic instability.
- Pain control requires opiates such as Fentanyl, morphine.
- Can use PCA pump if patient is cooperative and alert.
Oxygen

Oxygen to keep sat above 95%

* Gut 2005;54;1-9
Feeding

- Severe pancreatitis is a very catabolic state.
- Feeding may aid in preserving gut barrier and function, attenuates inflammatory response**.
- Early post-pyloric feeding with NJ with elemental or semi-elemental feeds.
- Not really beneficial in mild pancreatitis.
- If unable to feed due to ileus for >5 days consider TPN*.

** Gut 1998, 42:431-435
* Gut 2005;54;1-9
Infectious complications

- Antibiotic use (preferably **imipenem**) in necrotic pancreatitis if there are signs of infection* such as positive cultures, leukocytosis, fever, organ failure.
- Prophylactic antibiotics are likely ineffective in reducing complications**
  - Especially true for patients with <30% necrosis
- Necrostomy if patient fails to improve after antibiotics and attempts at percutaneous drainage.
  - endoscopic US guided drainage
fin