Disease of the Pancreas

Resources

1. Practice Guidelines in Acute Pancreatitis
   Banks PA, Freeman ML and the Practice Parameters Committee of the ACG Am J of Gastroenterol 2006;101:2379-2400

2. Sleisenger & Fordtran’s Gastrointestinal and Liver Disease, 8th ed. Section VII The Pancreas
Topics

- Acute Pancreatitis
- Chronic Pancreatitis
- Pancreatic insufficiency
- Autoimmune Pancreatitis
- Hereditary Pancreatitis
- Cystic Neoplasms
Diagnosis of Acute Pancreatitis requires two of the following:

1. Abdominal pain characteristic of acute pancreatitis
2. Serum amylase and/or lipase > 3 times the upper limit of normal
3. Characteristic findings of acute pancreatitis on CT scan
Differential Diagnosis

- Mesenteric ischemia or infarction
- Perforated gastric or duodenal ulcer
- Biliary disease
- Dissecting AAA
- Bowel obstruction
- Inferior wall myocardial infarction
Acute Pancreatitis

Etiologies

- Autoimmune
- Drug-induced
- Iatrogenic
- IBD-related
- Infectious
- Inherited
- Metabolic
- Neoplastic
- Structural
- Toxic
- Traumatic
- Vascular

Other

Alcoholic

Biliary

Idiopathic
Drug Induced Pancreatitis Sorted by Incidence

**Common**
- asparaginase
- azathioprine
- 6-mercaptopurine
- didanosine (DDI)
- pentamidine
- valproate

**Uncommon**
- ACE inhibitors
- acetaminophen
- 5-amino ASA
- furosemide
- sulfasalazine
- thiazides

**Rare**
- carbamazepine
- corticosteroids
- estrogens
- minocycline
- nitrofurantoin
- tetracycline
ACUTE PANCREATITIS

Intracellular Injury

- Blockage of secretion
- Fusion of lysosomes and zymogens
- Activation of enzymes
- Intracellular injury

Lumen
Zymogen
Lysosome
Condensing Vacuole
Golgi Complex
HER
Local Effects of Enzymes

- Inflammation
- Third space losses
- Fat necrosis
- Pancreatic and peripancreatic necrosis
## Causes of Increased Serum Enzymes

<table>
<thead>
<tr>
<th>Condition</th>
<th>Amylase</th>
<th>Lipase</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pancreatitidis</td>
<td>↑</td>
<td>↑</td>
</tr>
<tr>
<td>Parotitis</td>
<td>↑</td>
<td>Normal</td>
</tr>
<tr>
<td>Biliary stone</td>
<td>↑</td>
<td>↑</td>
</tr>
<tr>
<td>Intestinal injury</td>
<td>↑</td>
<td>↑</td>
</tr>
<tr>
<td>Tubo-ovarian disease</td>
<td>↑</td>
<td>Normal</td>
</tr>
<tr>
<td>Renal failure</td>
<td>↑</td>
<td>↑</td>
</tr>
<tr>
<td>Macroamylasemia</td>
<td>↑</td>
<td>Normal</td>
</tr>
</tbody>
</table>
Acute Pancreatitis

Time Course of Enzyme Elevations

Serum levels of pancreatic enzymes in acute pancreatitis

- Lipase
- Amylase

Fold increase over normal

Hours after onset

0 6 12 24 48 72 96
Causes of mortality

**Acute Pancreatitis**

**DEATH**

**Early (< one week)**
- Systemic inflammatory response syndrome (SIRS)
- Multi-organ failure

**Late (> one week)**
- Multiorgan failure
- Pancreatic infections/sepsis
**Table 2. Systemic Inflammatory Response Syndrome (SIRS)**

Defined by Two or More of the Following Criteria:

- Pulse > 90 beats/min
- Respiratory rate > 20/min or PCO$_2$ < 32 mmHg
- Rectal temperature < 36°C or > 38°C
- White blood count < 4,000 or > 12,000/mm$^3$
Table 4. Organ Failure as Defined by Atlanta Symposium

<table>
<thead>
<tr>
<th>Condition</th>
<th>Criterion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Shock</td>
<td>Systolic pressure &lt; 90 mmHg</td>
</tr>
<tr>
<td></td>
<td>PaO₂ ≤ 60 mmHg</td>
</tr>
<tr>
<td>Creatinine</td>
<td>&gt; 2.0 mg/L after rehydration</td>
</tr>
<tr>
<td>Gastrointestinal bleeding</td>
<td>&gt; 500 cc/24 h</td>
</tr>
</tbody>
</table>
Table 3. Severe Acute Pancreatitis as Defined by Atlanta Symposium

<table>
<thead>
<tr>
<th>Early Prognostic Signs</th>
<th>Organ Failure</th>
<th>Local Complications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ranson signs ≥ 3</td>
<td>and/or</td>
<td>Necrosis</td>
</tr>
<tr>
<td>APACHE-II score ≥ 8</td>
<td></td>
<td>Abscess</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Pseudocyst</td>
</tr>
</tbody>
</table>
Ranson’s Criteria of Severity

At admission
- Age >55 years
- WBC >16,000/mm³
- Glucose >200 mg/dl
- LDH >350 IU/L
- AST >250 U/L

During initial 48 hours
- Hct decrease of >10
- BUN increase of >5 mg/dl
- Ca²⁺ <8 mg/dl
- PaO₂ <60 mm Hg
- Base deficit >4 mEq/L
- Fluid sequestration >6 L
Apache II

- Temperature
- Mean arterial pressure
- Heart Rate
- Respiratory rate
- Oxygen delivery
- PO2
- Arterial pH
- Serum sodium
- Serum potassium
- Serum creatinine
- Hematocrit
- White cell count
Danger Signals: First Few Hours

- Encephalopathy
- Hypoxemia
- Tachycardia > 130/min
- Hypotension < 90 mmHg
- Hct > 50
- Oliguria < 50 ml/hr
- Azotemia
Definitions

• Interstitial pancreatitis
  – Focal or diffuse enlargement of the pancreas with enhancement of the parenchyma that is either homogeneous or slightly heterogeneous in response to IV contrast

• Pancreatic necrosis
  – Diffuse or focal areas of nonviable pancreatic parenchyma that is typically associated with peripancreatic fat necrosis. CT criteria for necrosis include focal or diffuse well marginated zones of non-enhanced pancreatic parenchyma greater than 3 cm in size or greater that 30% of the pancreas
Facts

- 85% of patients with pancreatitis have interstitial pancreatitis
- 15% of patients have necrotizing pancreatitis, 33% of those have infected necrosis.
- 10% of patients with interstitial pancreatitis have organ failure
- Median prevalence of organ failure in necrotizing pancreatitis is 54%
Severity

- Pancreatic necrosis and organ failure are the two most important markers of severity.
- Contrast enhanced CT on the second or third day after admission is the best way to distinguish interstitial from necrotizing pancreatitis.
Acute Pancreatitis: Necrosis

Progression

Day 1  Day 3

Pancreas

Pancreatic necrosis
Organized Necrosis

- Sterile necrosis that organizes into an encapsulated structure
Box 1. CT grading system of Balthazar [1]

Grade A, normal pancreas consistent with mild pancreatitis
Grade B, focal or diffuse enlargement of the gland, including contour irregularities and inhomogeneous attenuation but without peripancreatic inflammation
Grade C, abnormalities seen in grade B plus peripancreatic inflammation
Grade D, grade C plus associated single fluid collection
Grade E, grade C plus two or more peripancreatic fluid collections or gas in the pancreas or retroperitoneum
Risk Factors of Severity at Admission

1. Age older than 55
2. Organ failure at admission, and pleural effusion and/or infiltrates
3. Obesity
## Hematocrit and Severity of Acute Pancreatitis

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Incidence of Necrosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Admission hematocrit &gt;44% OR fails to fall over first 24 hours</td>
<td>50%</td>
</tr>
<tr>
<td>Neither present</td>
<td>4%</td>
</tr>
</tbody>
</table>
ACUTE PANCREATITIS

Grey-Turner Sign
Antibiotics

• Not recommended prophylactically in necrotizing pancreatitis
Acute Pancreatitis: Management

**Resuscitation**

- **Severe** (Early indications of severity are positive and CRP >150)
  - Contrast enhanced CT scan
  - Prominent necrosis

- **Minimal or no necrosis**
  - Antibiotics for 1-2 weeks (?)

- **Supportive care** (No early indicators of severity and CRP <150 mg/ml)

**Clinical assessment of severity**

- **Minimal or no necrosis**
  - Supportive care

**Suspicion of pancreatic infection**

- **Contrast enhanced CT scan**
  - Prominent necrosis
  - Antibiotics for 1-2 weeks (?)
  - Continued fever, organ failure, infection

**CT-guided aspiration**

- **Infected**
  - Debride

- **Sterile**
  - Supportive care

**Management Algorithm for Acute Pancreatitis**

- **Mild to moderate**
  - Improvement
  - Continue antibiotics for total of 3 wks.

- **Severe** (Early indications of severity are positive and CRP >150)
  - Improvement
  - Continue antibiotics for total of 3 wks.

- **Minimal or no necrosis**
  - Supportive care

- **Infected**
  - Debride

- **Sterile**
  - Supportive care

- **Supportive care** (No early indicators of severity and CRP <150 mg/ml)
Acute Pancreatitis

Treatment

Supportive care

- Aggressive fluid and electrolyte replacement
- Monitoring
  - Vital signs
  - Urine output
  - $O_2$ saturation
  - Pain
- Analgesia, anti-emetics

Other treatments

- Acid suppression
- Antibiotics
- NG tube
- Nutritional support
- Urgent ERCP
Acute Pancreatitis

Nutritional Support

- Consider when protracted course is likely
- Enteral vs parenteral
  - Safety
  - ? Effect on outcome
- Monitor calcium and triglycerides
Acute Pancreatitis

Major Complications

Local
- Fluid collections
- Necrosis
- Infection
- Ascites
- Erosion into adjacent structures

Systemic
- Pulmonary
- Renal
- CNS
- Multiorgan failure

Metabolic
- Hypocalcemia
- Hyperglycemia

GI obstruction
- Hemorrhage
Progression to Pseudocyst
PSEUDOCYST

Needle Aspiration
Pancreatic Necrosis

- Non-perfusion
- Systemic complications
- Local complications
  - Hemorrhage
  - Infection

Pancreatic necrosis: an overview
Pancreatic Necrosis

Treatment Strategies

Sterile
- Medical therapy
- Debridement for persistent organ failure?

Infected
- Antibiotics
- Debridement
Necrosis: Sterile

Appearance of severe pancreatic necrosis
Non-infected vs infected necrosis diagnosed by needle aspiration and Gram-stain.
Signs of Infected Pancreatic Necrosis

- Increasing markers of inflammation (serum CRP, white blood cell count)
- Newly developed fever without extra pancreatic infection
- Signs of infection on CT (gas collection within areas of necrosis)
ACUTE PANCREATITIS: COMPLICATIONS

Abscess Drainage
Evaluation of Unexplained or Recurrent Pancreatitis

Negative history, lab tests, ultrasonogram, CT

ERCP

Abnormal

Gallstones
Pancreas divisum
Chronic pancreatitis
Ampullary stenosis
Pancreatic stricture
Annular pancreas
Choledochal cyst

Normal

No further tests
Consider biliary manometry

or MRCP
Chronic Pancreatitis

- Pain
- Calcification
- Pancreatic insufficiency
Etiologies of Chronic Pancreatitis

- Alcoholic
- Idiopathic
- Other

Cystic fibrosis
Hereditary pancreatitis
Hypertriglyceridemia
Autoimmune
Tropical
Chronic Pancreatitis

Course

% patients

Presentation 15 years

- Pain
- Calcification
- Malabsorption
- Diabetes

Tsiotos, 2002
Lankisch PG, Pancreatology 2001; 1:3
Chronic Pancreatitis

Steatorrhea

Mechanisms

- Decreased concentration of lipase and colipase
- ↓ Duodenal pH
  - Inactivation of pancreatic lipase pH<4.5
  - Precipitation of bile salts

Stool with excessive fat

Sudan stain

Fat droplet
Secretin Test

**Volume**
- Normal
- Pancreatitis

**Max [HCO₃⁻]**
- Normal
- Pancreatitis

Sensitive and specific
Unpleasant
Time consuming
Requires x-rays
Not readily available
Chronic Pancreatitis

Nutritional Management of Exocrine Insufficiency

Diet and exogenous enzymes
- Modify fat intake
- Medium chain triglycerides
- Enzyme replacement
  - Coated vs uncoated
  - Acid suppression

Vitamins, supplements
- Fat soluble
- Calcium
- Cyanocobalamin (B$_{12}$)
## Chronic Pancreatitis

### Pain Management

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Effectiveness</th>
</tr>
</thead>
<tbody>
<tr>
<td>No alcohol</td>
<td>Low to moderate</td>
</tr>
<tr>
<td>Analgesia</td>
<td>Moderate</td>
</tr>
<tr>
<td>Enzyme replacement</td>
<td>Low</td>
</tr>
<tr>
<td>Neurolytic therapy</td>
<td>Moderate short term</td>
</tr>
<tr>
<td>Pseudocyst drainage</td>
<td>High</td>
</tr>
<tr>
<td>Duct decompression</td>
<td>Moderate</td>
</tr>
<tr>
<td>Stone removal</td>
<td>Moderate</td>
</tr>
</tbody>
</table>
Chronic Pancreatitis

Use of Exogenous Enzymes for Pain

<table>
<thead>
<tr>
<th>Study</th>
<th>Preparation</th>
<th>Response</th>
</tr>
</thead>
<tbody>
<tr>
<td>Isaksson (1983)</td>
<td>uncoated</td>
<td>yes</td>
</tr>
<tr>
<td>Slaff (1984)</td>
<td>uncoated</td>
<td>yes</td>
</tr>
<tr>
<td>Halgreen (1986)</td>
<td>coated</td>
<td>no</td>
</tr>
<tr>
<td>Mossner (1992)</td>
<td>coated</td>
<td>no</td>
</tr>
<tr>
<td>Malesci (1995)</td>
<td>coated</td>
<td>no</td>
</tr>
</tbody>
</table>
Chronic Pancreatitis

Splenic Vein Thrombosis

- Associated with chronic disease
- Splenomegaly
- Large gastric varices without esophageal varices
- Splenectomy for bleeding
Diabetes

- Loss of insulin and glucagon
- Only in severe disease
- Brittle
- Insulin requirement low
- Ketoacidosis rare
CHRONIC PANCREATITIS
CHRONIC PANCREATITIS

Treatment of Steatorrhea

- Ingest potent enzymes
- Protect enzymes, reduce H⁺ (H-2 blocker) or ingest enteric-coated
- Decrease dietary fat
Autoimmune Pancreatitis

Presentation

Symptoms

- Asymptomatic or mild pain
- Acute pancreatitis, rare
- Obstructive jaundice

Imaging

- Incidental pancreatic mass
Autoimmune Pancreatitis

Patient Characteristics

Gender
- Male > female

Age
- Wide range (20-80 years), most > 50 years

Comorbidity
- Autoimmune diseases
Autoimmune Pancreatitis

**Diagnostic Criteria: I**

**Imaging**
- Diffuse pancreatic duct narrowing
- Diffuse pancreatic enlargement

**Immunity**
- Autoantibodies
- Elevated gammaglobulins or IgG4

**Histology**
- Periductular lymphoblastic infiltrate
- Phlebitis
- Fibrosis
Autoimmune Pancreatitis

Diagnostic Criteria: II

Other organ involvement
- Biliary
- Liver
- Kidney
- Lung

Response to steroids
Modified Biliary Classification

A = Elevated liver tests on 1 or more occasions

B = Dilated Common Bile Duct

Biliary Type I – A+B

Biliary Type II – A or B

Biliary Type III – Pain only
<table>
<thead>
<tr>
<th>Type</th>
<th>Features</th>
<th>Cancer risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pseudocyst</td>
<td>Macrocystic</td>
<td>None</td>
</tr>
<tr>
<td></td>
<td>Thick wall</td>
<td></td>
</tr>
<tr>
<td>Serous cystadenoma</td>
<td>Micro- or macrocystic</td>
<td>Low</td>
</tr>
<tr>
<td>Mucinous cystadenoma</td>
<td>Macrocystic</td>
<td>High</td>
</tr>
<tr>
<td>Mucinous cystadenocarcinoma</td>
<td>Macrocystic</td>
<td>Cancer present</td>
</tr>
<tr>
<td></td>
<td>Thick wall</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Intracystic mass</td>
<td></td>
</tr>
</tbody>
</table>
Cystic Neoplasm

Clinical clues
- No prior pancreatitis
- Unexplained pancreatitis
- Cyst present on 1st CT

Diagnosis
- Fluid analysis
- EUS, ERCP
- Resection