Pancreatitis

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What is Pancreatitis?
Pancreatitits
The Burden of Pancreatitis

- Incidence: 80/100,000/year
- 250,000 admissions per year for acute pancreatitis
- 1.7 billion for hospital facility costs
- 250 million/year in loss productivity due to patient hospitalization
- Mortality in severe disease (SAP) has remained high for over 30 years.
Classification of Pancreatitis

Acute
- Acute inflammation
- Acute abdominal pain
- Elevated serum pancreatic enzymes
- Self-limiting

Chronic
- Chronic inflammation
- Chronic abdominal pain
- Progressive loss of pancreatic endocrine and exocrine function
Definition and Pathogenesis

AP may be defined as an acute inflammatory process of the pancreas with associated serologic and clinical criteria.

Exact mechanism is unknown.

Early events:
- Inability to secrete pancreatic zymogens
- Early activation of pancreatic enzymes
Mechanisms of Acute Pancreatitis

- **Reflux theory**: Bile reflux up the pancreatic duct activates trypsinogen. Postulate interstitial (as opposed to intracellular) trypsin leads to pancreatitis.

- **Co-localization theory**: Missorting of digestive enzymes and lysosomal enzymes within the acinar cell. Lysosomal enzymes, e.g. cathepsin B, prematurely activates trypsinogen to trypsin thus activating the cascade.
Pathogenesis of Acute Pancreatitis

Cellular Destruction

Fusion of lysosomes and zymogens

Early Release of PSTI

Zymogen granules

PSTI

α1 – antitrypsin

β2-microglobulin

Early release of trypsin

Enterokinase or trypsin

Trypsin

α1 – antitrypsin
β2-microglobulin

Cellular Blockade of secretion

Premature activation

Fusion of lysosomes and zymogens

Cathepsin B

Golgi Complex

RER

Nucleus

Lumen

 Protein plug

Gallstone sludge

Trypsin

Early release
Etiology

- Alcohol
- Gallstones
- ERCP induced
- Ideopathic

- Hereditary Pancreatitis
- Hyperlipidemia
- Pancreas Divisum
- Medications (Thiazides, Valproic Acid, Azothiaprine)
- HIV
- Mass effect (tumor, diverticula)
- Hypercalcemia
A 60 year old 275 pound man presents to the emergency room with abdominal pain. While entertaining friends the night before, he developed a sharp, stabbing epigastric pain acutely an hour after eating BBQ pork. Eventually the pain radiated to the back and did not subside, prompting a visit to the ER early in the AM where he developed nausea, vomiting and generalized malaise. He has not defecated since but had voided a scant amount of tea-colored urine. He has not had any fever or chills. He does note that he has had upper abdominal pain in the past, just not to the extent that he sought medical advice.
What Now?

What is the differential?

What is the etiology?

How do you prove your diagnosis?

How do you treat this man?
Manifestations of Acute Pancreatitis

- Pain is always present.
- Peritoneal signs are absent - retroperitoneal organ.
- Ileus may arise secondary to extension into small intestinal and colonic mesentary.
- Nausea/Vomiting.
- Fever to 101°F.
- Hypocalcemia - rarely see tetany.
- CBD compression, gastritis, duodenitis, pulmonary manifestations.
### Clinical Features

<table>
<thead>
<tr>
<th>Signs and Symptoms</th>
<th>Labs</th>
<th>Differential Diagnosis</th>
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</thead>
<tbody>
<tr>
<td>Abdominal pain</td>
<td>Leukocytosis</td>
<td>Choledocholithiasis</td>
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<tr>
<td>Abdominal tenderness</td>
<td>Hyperamylasemia</td>
<td>Perforated ulcer</td>
</tr>
<tr>
<td>Fever</td>
<td>Hyperlipasemia</td>
<td>Mesenteric ischemia</td>
</tr>
<tr>
<td>Tachycardia</td>
<td></td>
<td>Intestinal obstruction</td>
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<td></td>
<td></td>
<td>Salpingitis/ectopic pregnancy</td>
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</tbody>
</table>
Ranson’s Criteria

- On Admission
  - Age > 55
  - WBC > 16,000
  - Glucose > 200
  - LDH > 350
  - AST > 120

- During First 48 Hours
  - HCT Decrease > 10%
  - BUN Increase > 5
  - Calcium < 8
  - Arterial O2 < 60 mm Hg
  - Base Deficit > 4
  - Fluid Sequestration > 6L
Mortality and Ranson’s Criteria

Treatment of AP: Severity stratification

- Risk factors predictive of severe disease:
  - BMI > 30:
  - Hematocrit > 44 on presentation or non-decreasing after 24 hours hydration
  - Organ Failure: Atlanta Criteria
  - Apache II > 8
  - Radiographic Stratification
    - Balthazar CT Criteria
    - MRI
Change in Plans

8 hours later….

The patient is agitated, cotton-mouthed, short of breath, tachycardic and has made 40 ccs of urine since admission. His pain is getting worse.
How are you going to treat him?
Basic Tenents

- Fluids
- End organ support
- Nutrition
- Pain control
- Infectious control
HD Day 3

- WBC 20,000
- Bilirubin 3.8
- Alkaline Phosphatase 300
- Amylase 5200, Lipase 9800
- Temperature 103 degrees
- Requires vasopressor support
What’s the diagnosis?
Will ERCP help?
Indications for Biliary Sphincterotomy

- Severe pancreatitis – organ failure
- Ascending cholangitis
- Persistent biliary obstruction
- Poor candidate for cholecystectomy
- Post-cholecystectomy
HD #8

- ICU
- Intubated
- Febrile 102 degrees
- WBC 13,000
- Otherwise stable
Why is he still febrile?
HD # 15

- WBC 25,000 and rising
- Platelets 54,000
- Febrile 103 degrees
- Labile hemodynamics
A New Headache
Infection

- Pneumonia
- Line Sepsis
- Abscess
Pancreatic Infections

Only occurs in 5% of acute pancreatitis (80% Deaths)
Rare in interstitial (edematous) pancreatitis
Majority occur in setting of necrotizing variant

Types:
- Infected pseudocyst
- Pancreatic abscess
- Infected pancreatic necrosis
Pancreatic Necrosis

Diffuse or focal areas of non-viable pancreatic parenchyma, which is typically associated with peripancreatic fluid and inflammation.
Pancreatic Necrosis
Sterile Necrosis:
Operative Indications

- To perform a STAT autopsy!
- Demise is attributed to MSOF from the inception
- Allow for delineation of viable parenchyma over time
- Low mortality if avoided (< 2%)
- Ventillator/ICU dependant over one month
- Severe protracted pain, obstruction, or anorexia
Is this infected?
How do we know?
Clinical Signs of Infected Necrosis

- Fever past first week of onset of pancreatitis
- Increased leukocytosis
- Thrombocytopenia
- Metabolic acidosis
- Shock, capillary leak, tachycardia
- Deterioration of renal and pulmonary functions
- Persistent ileus
What about this?
How Do You Treat This?
Rational of Surgical Management

Remove vaso-active and toxic substances that account for multiorgan failure originating in devitalized pancreatic tissue and ascites

Prevent ultimate septic sequelae from infected necrotic tissue

Preserve viable pancreatic tissue as this has a major impact on long-term functional results
Indications for Surgery

- **Infected necrosis**: No role for medical management. Universally lethal

- **Non-surgical interventions**: More likely to resolve walled-off collections like infected pseudocysts or discrete pancreatic abscesses

- **Operative approaches**: Necessary due to particulate composition of necrotic collections

- **Sterile necrosis**: No benefit in survival or improvement of associated organ failure
HD # 25

Why is he still in the ICU?
Cytokines in Acute Pancreatitis

**Intracellular Events**
(Trypsin activation)

**Local Inflammation**
(IL-1, TNF, PAF produced in the pancreas. Tissue levels correlate with severity)

**Systemic Inflammation**
(Amplification of local effect)
Cytokines activated via liver kupfer cells and produced in affected organs such as lung

**Multiorgan failure**

**Death**
• Pulmonary
• Renal
• Cardiovascular
• GI
• Infection
• Rehabilitation
Pancreatic Pseudocyst
Pancreatic Pseudocyst
Three years later...

The patient is unemployed and has taken to the bottle for the last few years.

He presents to the BIDMC ER with debilitating abdominal and back pain.

Labs are significant only for a bilirubin of 2.6. The amylase and lipase are normal. WBC: 11,000
Chronic Pancreatitis
Etiology of Chronic Pancreatitis

- Develops after attacks of relapsing acute pancreatitis
- Interstitial acinar and fatty tissue necrosis results in inducing peripancreatic fibrosis
- This causes stenosis and dilatation of the main and secondary pancreatic ducts
- Protein plaques form within interlobular ducts, causing periductal inflammation & fibrogenesis
Course of Chronic Pancreatitis

- Pain
- Calcification
- Malabsorption
- Diabetes

Tsiotos, 2002
Lankisch PG, Pancreatology 2001; 1:3
Mechanisms of pain

Ischemia

PD Obstruction with Increased PD pressure

Inflammation

Duodenal and common duct obstruction

Pseudocyst

Neural inflammation
Pathophysiology of Chronic Pancreatitis: Two discrete events lead to disease

DUCTAL OBSTRUCTION
Impaired HCO$_3$ secretion
1. Protein plugs
2. Strictures, tumors, SOD
3. Genetic factors
4. Pumps, channels

INTRAPARENCHYMAL ACTIVATION
of digestive enzymes within pancreatic gland
1. Obstruction
2. Membrane lipids
3. Free radicals
4. Hormones, messengers

Secondary involvement of Sphincter of Oddi or Ischemia may perpetuate disease
Chronic Pancreatitis
Non-operative Management

- Mandatory abstinence from alcohol
- Exogenous pancreatic enzyme supplements
- Insulin and diet modification
- Pain medications
- Endoscopic approaches
- Percutaneous nerve ablations
- Psychosocial rehabilitation

**DIAGNOSTIC WORKUP**
- Ultrasound
- CT Scan
- ERCP / MRCP
- Exocrine / Endocrine Function

Ultimately, 60-65% of Chronic Pancreatitis Patients will need Surgery
Indications for Surgical Treatment
Chronic Pancreatitis

- Medically intractable abdominal pain
- Local Anatomic complications
- Main Pancreatic duct Stenosis with dilatation in body and tail
- Suspected, but unproven, malignancy
Anatomic Classification of Chronic Pancreatitis

- Small Duct Disease
- Big Duct Disease
The “Pacemaker” of Chronic Pancreatitis

- Enlarged, Fibrotic and Inflammed Pancreatic Head
- PMN’s infiltrate perineural sheaths
- Local overexpression of pain transmitters
- Increased tissue and duct pressures
- 95% develop intractable pain
- Local Anatomic Complications
  - Common Bile Duct Stenosis – 60%
  - Duodenal Stenosis – 36%
  - Portal Vein Stenosis/Thrombosis – 17%
Chronic Pancreatitis
Surgical Management

• *Ductal Drainage Procedures:*
  – Seek to relieve ductal hypertension while preserving as much pancreatic parenchyma as possible
  – Usually 1st line procedures
Chronic Pancreatitis

Surgical Management

- **Ductal Drainage Procedures:**
  - Seek to relieve ductal hypertension while preserving as much pancreatic parenchyma as possible
  - Usually 1st line procedures

- **Pancreatic Resectional Procedures:**
  - Provide pain control by removing diseased pancreatic parenchyma
  - Consequently, endocrine & exocrine insufficiency will result
  - Usually, 2nd line procedures (with exceptions)
Chronic Pancreatitis

Ductal Drainage Procedures

- Longitudinal Pancreaticojejunostomy (Partington-Rochelle)
- Frey Procedure
- Caudal Pancreaticojejunostomy (Duval)
- Combined pancreatic, biliary and gastric bypass procedure (Warshaw)
- Transduodenal Sphincteroplasty
Aspiration of dilated duct

Dilated pancreatic duct
Puestow Procedure
### Long-Term Outcome after Duct Drainage

**5-year f/up of Pain Relief in Chronic Pancreatitis**

<table>
<thead>
<tr>
<th>Patients</th>
<th>Pain Relief</th>
<th>Pain, but Improved</th>
<th>Failure</th>
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<tbody>
<tr>
<td>205*</td>
<td>44%</td>
<td>31%</td>
<td>25%</td>
</tr>
<tr>
<td>85**</td>
<td>24%</td>
<td>31%</td>
<td>45%</td>
</tr>
</tbody>
</table>


**Adams, et.al. 1994.**
Chronic Pancreatitis

Resectional Procedures

- Duodenum-Preserving Pancreatic Head Resection
- Whipple Pancreaticoduodenectomy
- Limited Distal (Left-side) Pancreatectomy
- 95% Near-Total Pancreatectomy
- Total Pancreatectomy
  - Peterotopic pancreatic autotransplantation
  - Pancreatic islet transplantation
Traditional Pancreatic Head Resections

- Classic Whipple Pancreaticoduodenectomy
- Pylorus-Preserving Pancreaticoduodenectomy (PPPD)
- Higher M/M, Complications
- Overtreatment ??

Probably best for Suspected But Unproven Malignancy
The Whipple Procedure

- GI Disconnection
- Biliary Disconnection
- Pancreatic Disconnection
- Lymphadenectomy
- Fierce Vascular Disconnection
- Reconstruction
Afferent Limb Reconstruction

- Common Hepatic Duct
- Pancreatic Anastomosis
Duodenum-Preserving Pancreatic Head Resection (DPPHR)

• “Decompressive Resectional Procedure”
  ─ Transection of Pancreas at PV/SMV confluence
  ─ Subtotal Resection of Pancreatic Head (5-8mm shell remains at duodenum)
  ─ Roux-En-Y drainage of PD (2) and CBD (20%)

• Also Pseudocyst resections, long PD drainage

Best when large inflammatory mass
In Pancreatic Head is causing mechanical obstructions
Distal Pancreatectomy

Medial rotation of Pancreatic Tail & Body, together with Spleen off Retroperitoneum and Vessels
Distal Pancreatic Resections

NOT recommended for Diffuse Disease

BEST for Segmental, Localized Pancreatitis

Cystic Disease

Splenic Preservation
Chronic Pancreatitis

Summary

- Difficult disease
- Difficult patients
- Difficult operations

A careful multidisciplinary approach is always the key.
Pancreatitis

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Etiology of Acute Pancreatitis

- **Gallstones:** most common cause. 50-70 yrs of age. 1:2, male:female
- **Alcohol:** younger (30-35 yrs of age). 3:1, male:female
- **Drugs:** sulfonamides, furosemide, thiazides, valproic acid, estrogens with hyperlipidemia, azathioprim (6-MP), L-asparaginase, pentamidine, didanosine.
- **Trauma:** surgery, blunt trauma to the upper abdomen, ERCP, S.O. manometry.
- **Metabolic:** hypertriglyceridemia, ? hypercalcemia.
- **Obstruction:** gallstones, sludge/crystals, tumors, ascaris/clonorchis, choledochocele, annular pancreas, duodenal crohn’s, afferent loop obstruction, perhaps periampullary diverticula, pancreas divisum, ? S.O. spasm
Etiology of Acute Pancreatitis

- **Pregnancy:** Usually in 3rd trimester or postpartum. Coexisting cholelithiasis in 90%.
- **Infection:** Mumps, CMV, ?MAI and MTB, varicella, EBV.
- **ESRD:** High mortality. Incidence increases with yrs of HD.
- **Scorpions:** Excessive cholinergic stimulation. Seen mostly in the West Indies. Salivation, sweating, dyspnea, arrythmias.
- **Idiopathic:** 8-25% of cases. May be due to S.O. dyskinesia or microlithiasis.
- **Miscellaneous:** SLE, penetrating DU, CF.