Demystifying Pancreatitis

Bonnie Slayter RN,BS
Staff Nurse, MGH Endoscopy Unit
Boston, MA
Bonnie Slayter BS, RN

MGH Staff RN 13 years

Endoscopy Unit 8 years

ERCP team member 3 years

Deep sedation RN for EUS and ERCP procedures 4 years
(Department of Anesthesia now provides sedation for advanced endoscopy procedures)
MGH Endoscopy unit performs approximately 30,000 procedures/year

- 2,000 advanced endoscopic procedures/year
- Average 80 cases/day – main campus/ Blake 4
  – Average 40 cases/day Charles River Plaza 9
- 2 Fluoroscopy equipped procedure rooms
  – ERCPs, fluoroscopy guided esophageal and colonic stents
- 3 EUS procedure rooms – cancer staging, FNAs, pancreatic evaluation
OBJECTIVES for Demystifying Pancreatitis

• Epidemiology

• Etiology

• Pathophysiology

• Symptoms and signs

• Diagnostic tests and labs

• Treatment plans for mild and acute pancreatitis

• Alternative/Complementary medicine treatment

• Health promotion
Epidemiology of Pancreatitis
• 210,000 people admitted annually with pancreatitis/ US

• Mortality rate for acute pancreatitis 10-15%; Patients with severe disease, organ failure, mortality rate approximately 30%

• Acute pancreatitis - males > females - cause in males often r/t EtOH, average age 39

• Pancreatitis in females frequently biliary tract disease/gallstones, average age 69
Etiology of Pancreatitis
Etiology of Pancreatitis

- EtOH – 35% acute pancreatitis cases, 60% chronic pancreatitis cases

5-8 alcoholic drinks/day significantly ↑ risk for pancreatitis

- ? EtOH → overstimulation of pancreas, activation of digestive enzymes before excreted out of pancreas

- EtOH → spasm of sphincter of Oddi, → reflux of duodenal contents into pancreatic duct, activating digestive enzymes within pancreas

- Chronic pancreatitis - repeated bouts of pancreatitis, ongoing exocrine + endocrine dysfunction
• Biliary tract disease - 40% of acute pancreatitis cases

• Gallstones obstructing bile duct - most common cause of acute pancreatitis

• Gallstones flowing down bile duct get lodged at ampulla of Vater, obstruction → bile backing up into pancreas → activation of digestive enzymes → autodigestion

• Gallstones also block pancreatic secretions from emptying into duodenum, leads to enzyme activation within pancreas
• Pancreatitis of unknown origin 10-30% of cases
• Up to 70% of cases of idiopathic pancreatitis - biliary microlithiasis
• Post-ERCP pancreatitis - 4% of cases
• Trauma - 1.5% of acute pancreatitis cases
  Abdominal trauma - stab and bullet wounds; blunt injury - steering wheels, horseback riding, bicycle injuries;
• Medications - 2% of acute pancreatitis cases - azathioprine, sulfonamides, tetracycline, valproic acid, estrogens, corticosteroids, thiazide diuretics, methyldopa
• Infection < 1% of acute pancreatitis cases
• AIDS - opportunistic infections or drug therapies
• Hereditary pancreatitis < 1% of reported cases
• Hypercalcemia < 1% of cases
• Developmental abnormalities of pancreas < 1% of cases
• Hypertriglyceridemia < 1% of cases
• Tumors obstructing pancreatic ductal system <1% of cases
• Toxic exposure to organophosphate insecticides <1% of cases
Several experimental studies have shown that smoking induces pathological and functional changes in the exocrine pancreas (mfg/secretion of digestive enzymes).

Nicotine induces damage through signal pathways in pancreatic acinar cells, leading to increased levels of intracellular calcium release and/or impaired pancreatic blood flow.

Nicotine also alters gene expression in the exocrine pancreas, which affects the ratio of trypsinogen to its endogenous inhibitor leading to autodigestion.
• Postoperative pancreatitis - < 1% of surgical procedures

• Autoimmune pancreatitis → acute pancreatitis < 1%, usually age <40, inflammatory bowel disease is comorbidity

• Vascular abnormalities < 1% acute pancreatitis cases - can cause pancreatic ischemia; Systemic lupus erythematosis associated with this type of pancreatitis
Pathophysiology of Pancreatitis
• Endocrine pancreas - insulin and glucagon production

• Exocrine pancreas - manufacturing, secreting digestive enzymes

• 80% exocrine function (metabolizing carbohydrates, fats and proteins)

• 15 different enzymes produced in pancreatic acinar cells.

• Digestive enzymes - packaged into storage vesicles (zymogens)

• Pro-enzymes - inactive enzymes with acidic pH, low calcium concentration, guards against premature activation

• Post-prandial enzymatic cascade stimulated, pro-enzymes released into pancreatic duct via ductal cells, then secreted into small intestine to begin metabolism
• Trypsin – an enzyme(catalyst) - facilitates activation of other pro-enzymes, normally helps break down proteins in food to aid digestion, inactive within pancreas

• Feedback mechanism limits pancreatic enzyme activation after appropriate metabolism occurs

• EtOH can lead to elevated levels trypsin, → premature activation within the pancreas, increases risk of acute pancreatitis significantly

• Disruption of protective mechanisms of pro-enzymes → intracellular activation, pancreatic auto-digestion → PANCREATITIS.
PANCREATITIS:

• Injury to acinar cells or protective constitution of pro-enzymes

• Cellular injury → disruption in cellular membrane trafficking

• Pro-enzymes converted in pancreas to active enzymes by trypsin

• Cascade of inflammatory mediators (neutrophils, proteolytic enzymes and macrophages) → increased pancreatic vascular permeability → edema, hemorrhage and potentially, pancreatic necrosis
• Absence of a well-developed pancreatic capsule allows inflammatory process to spread

• Undeterred inflammatory cascade → bacteremia, ARDS, pleural effusions, gastrointestinal hemorrhage, renal failure, SIRS, shock and possibly, death
Pathogenesis of Acute Pancreatitis

PRECIPITATING FACTORS

- Alcohol Abuse
- Infections
- Trauma
- Biliary disease
- Drugs
- Surgery
- Hyperlipidemia
- Hypercalcemia
- Hereditary pancreatitis

↓

MECHANISMS FOR ACTIVATING PANCREATIC ENZYMES

- Injury to acinar cell
- Duct obstruction
- Activation of pro-enzymes

↓

ACTIVATION OF PROTEOLYTIC ENZYMES

- Trypsin, Elastase, Lipases

↓

Inflammation
- Edema
- Hemorrhage
- Necrosis
- Vascular Damage

↓

AUTODIGESTION

↓

ACUTE PANCREATITIS
Symptoms of Pancreatitis
• Upper abdominal pain, severe enough for ER visit

• Gaseous abdominal fullness, swollen abdomen

• Pain r/t EtOH pancreatitis 1-3 days after binge drinking/cessation

• Biliary colic r/to gallstone pancreatitis - post-prandially, foods with high fat content

• ½ of patients describe band-like radiation to back

• Severe pancreatitis - Cullen’s sign – blue discoloration around umbilicus (hemoperitoneum); Turner’s sign – blue-red-purple or green-brown discoloration at flanks (tissue catabolism of hemoglobin)
• Abdominal pain, nausea + vomiting, 90% of patients

• Diarrhea

• Restlessness and agitation

• Chronic pancreatitis - chronic weight loss, diarrhea, nausea + vomiting, fatty, oily or pale, clay colored stools
Signs of Pancreatitis
• Fever, tachycardia, ↑ serum amylase and lipase (3X > ref range)

• ↑ LFTs such (alk phos, Tbili, AST, ALT)? gallstone pancreatitis and biliary duct system injury

• Hypercalcemia and hyperlipidemia can cause pancreatitis
• Lytes, BUN/Cre, glucose - electrolyte imbalances, renal insufficiency, damage to pancreas impairs insulin production

• CBC - hemoconcentration (HCT > 47%) - severe pancreatic disease

• C-reactive protein - acute-phase reactant, inflammation; double digit values (>10mg/dL) = severe pancreatitis; often correlates with organ failure

• IgG4 levels - evaluate for autoimmune pancreatitis
Diagnostic Tests

Visualization of inflammation within pancreas confirms diagnosis, answers specific clinical questions
• Abdominal ultrasound – sound waves bounce off organs. Echoes make electrical impulses that create a picture.
  - Hyperechoic (more echogenic/brighter than normal)
  - Hypoechoic (less echogenic/darker than normal)
  - Isoechoic (the same echogenicity as another tissue)

• Diffusely enlarged, hypoechoic pancreas = acute pancreatitis

• Sound also bounces off gallstones showing their location

• Ultrasounds do not measure severity of pancreatitis - bowel gas can obscure pancreas

• Ultrasounds cannot detect necrosis
• Abdominal radiography – X-RAYS detect free air in abdomen (perforated viscus) and calcifications in pancreas (chronic pancreatitis)

• Generalized ileus and ascites present with severe disease

• Abdominal CT scan – non-invasive image of choice for assessing complications of pancreatitis

• Prognostic information is gained

• Pancreatic enlargement, inflammation, and fluid collections are visualized
Normal Anatomy by CT

- Pancreas arcing anteriorly over spine
- Head adjacent to duodenum
- Tail extending toward spleen
- Splenic vein posterior to body and tail
- Portal vein confluence immediately posterior & left of pancreatic neck
50 year-old woman

CT scans of normal kidneys and pancreas
Chronic Pancreatitis

Calcifications
Recommendations for Contrast-Enhanced CT

Clinical diagnosis in doubt

Severe clinical pancreatitis

Ranson score > 3

APACHE score > 8

Failure to rapidly improve within 72 hours of conservative medical therapy, initial improvement with later deterioration
Ranson Criteria

Used for more than 30 years – reliable predictor of severity of pancreatitis, organ failure and mortality. One point given for each applicable category. A score > 3 is considered to be severe pancreatitis and a score > 5 increases risk of mortality to > 50%

**At admission**
- Age > 55
- WBC > 16,000
- Blood glucose > 200
- Serum AST > 250
- Serum LDH > 350

**After 48 hours**
- Hematocrit ↓ > 10%
- ↑ BUN ≥ 1.8 after rehydration
- Serum calcium < 8.0
- PO2 < 60
- Base deficit > 4
- Estimated fluid sequestration > 6L
Clinical Scoring system: BISAP (2008)

- **BUN** > 25 mg/dL
- **Impaired mental status** (GCS < 15)
- **SIRS**
  1. Temperature < 36°C or > 38°C
  2. Respirations > 20/min or PaCO2 < 32 mmHg
  3. Heart rate > 90/min
  4. WBC < 4,000/mm³ or WBC > 12,000/mm³ or more than 10% bands found on blood smear.
- **Age** > 60
- **Pleural effusion**

BISAP Validation Cohort 2004-2005 (N=18,256)

![BISAP Score](image.png)
Gallstone-induced pancreatitis in 27 year-old woman

Transverse CT scan obtained with intravenous and oral contrast material reveals a large, edematous, homogeneously attenuating (73-HU) pancreas (1) and peripancreatic inflammatory changes (white arrows). Although the attenuation values are low, there is no pancreatic necrosis. Calcified gallstones are seen in gallbladder (black arrow). 2 = liver (140 HU).
47-year-old man with severe pancreatitis

Fluid collection replacing pancreatic body and tail
• MRCP (magnetic resonance cholangiopancreatography)

• MRCPs - images categorize fluid collections, differentiate between abscesses, hemorrhages, pseudocysts, necrosis

• MRCPs - more sensitive than CTs in detecting mild acute pancreatitis; visualize pancreatic and bile ducts better than CT scans.
• Procedures for Diagnosing and Treating Pancreatitis

• Endoscopic Ultrasound – Endoscope with ultrasound balloon attached to the end of scope passed into small intestine - visualizes pancreas and bile ducts

• High frequency transducer introduced adjacent to pancreas, provides an excellent view

• Fine needle aspirations performed through endoscope – needle passes trans-gastric/duodenal - differentiates between infected and sterile necrosis or pseudocysts
EUS image/pancreatitis

Pancreas is diffusely enlarged, image is hypoechoic (less echogenic, darker image than normal pancreas)
Endoscopic Retrograde Cholangiopancreatography

- Side-viewing endoscope used in conjunction with XRAY evaluates biliary and pancreatic ductal system.
- ERCP used in pancreatitis cases secondary to choledocholithiasis
- Sphincterotomy and stone extraction may cure pancreatitis
- ERCP itself poses the risk of pancreatitis
ERCP Image/ CBD Stones

CBD Stone Extraction
ERCP/ CBD Stone
ERCP/ CBD
Stone
ERCP/ Stone/
Basket Extraction
ERCP/ XRAY of Stone Extraction
PANCREATIC CYSTS/PSEUDOCYSTS
Pancreatic cysts are both a risk factor for pancreatitis and are often caused by pancreatitis.

Heavy alcohol use and gallstones are risk factors for pancreatitis, and pancreatitis is a risk factor for pseudocysts — the most common type of pancreatic cyst.

Pseudocysts are often watched via CT scan OR

Drained via EUS

In extreme circumstances, when the pseudocyst is infectious Naso-cystic drainage and irrigation may help
Dr. Forcione’s nasal-cystic irrigation protocol

Irrigation options:
• Boluses, to be pushed via endoscope or Nasal-Cystic Tube: hydrogen peroxide 3%, diluted 20 ml hydrogen peroxide to 40 ml normal saline or sterile water.

• Via NCT for continuous irrigation: hydrogen peroxide 3%, diluted 10:1 with normal saline or sterile water, infused by pump at 50mm/hr. Inject 100 ml into a 1L bag of IV fluid.
Nasal cystic irrigation set
Case Study
Case Study

JB is a 61 year old female complaining of nausea, vomiting and mid-epigastric pain X 3 days

JB decides to visit her PCP’s office for an assessment. NP assessment yields the following information:

HR: 103 (baseline for JB is 68); BP 102/58 (baseline 128/70);
T: 100.0 F;

Physical exam: Abdomen is swollen and tender. JB is tolerating sips of gingerale, but reports vomiting X 3 days with solids.
JB’s NP orders labs:

- CBC - JB’s HCT is WNL
- Lytes, glucose, BUN/Creatinine - JB is WNL
- Calcium, magnesium, cholesterol, triglycerides - JB is WNL
- Liver function tests (LFT’s), amylase/lipase - JB’s amylase is elevated
- Serum alanine aminotransferase (ALT) - useful parameter in predicting gallstone etiology
  
  • Serum ALT concentrations 150 IU/L (3X normal value) positive predictive value 95% - JB’s ALT is significantly elevated
NP suspects pancreatitis - probable cause gallstones

JB - admitted to MGH for IV fluids, abdominal U/S, pain management

JB c/o 5/10 abd pain, (her husband assures is 8/10, since JB never complains)

JB notes pain is slightly relieved when she leans forward - it’s hard to find a comfortable resting position

Leaning forward, or assuming fetal position decreases stretching the pancreas, which alleviates pain
In house, medical team writes the following orders:

• Morphine Sulfate 2mg IV q4° PRN for pain
• Omeprazole 40mg IV BID
• NPO except sips of clear liquids as tolerated
• Compazine 10mg IV q6° PRN for nausea
• Zofran 4mg IV q4° PRN for nausea
• D51/2NS@100cc/hr continuous/ or per Dr. Forcione, LR
• CBC, Electrolytes, Glucose, BUN/Cre, Amylase/Lipase, Calcium, Magnesium, Phosphorous QD X 3D
• Diagnostic test: Abdominal ultrasound shows choledocholithiasis

• Treatment: ERCP for gallstones – sphincterotomy and balloon sweep of the bile duct.

• D/C to home following ability to tolerate clear liquids. Advance diet to low-fat, full liqs for 1 day then advance diet as tolerated.
Gallstone Pancreatitis

- Gallstones
- Fluid
- Pancreas
Stone Types

Pure cholesterol

Black pigment

Brown pigment

Mixed
Four common stone types

• Pure cholesterol stones - most common, originate in the gallbladder

• Black pigment stones consist of bilirubin metabolites - seen in chronic hemolytic conditions and cirrhosis

• Mixed stones and brown pigment stones - usually seen in the setting of cholestasis and cholangitis
Treatment Plan/Mild Pancreatitis
• Pancreatic rest → reduce pancreatic enzyme synthesis + secretion, prevent infectious complications

• Hospitalization - alert watch for local complications and progression of severity

• Patient NPO until pain and anorexia resolve

• N/V treated with PPIs and anti-emetics - NG used to empty and decompress stomach

• ADAT – initiate feeding with clear liqs → full liquid, low-fat → low-fat, low protein solids → resume usual diet

• IVF (often D51/2 NS) - fluid resuscitation critical to offset third spacing and decrease hypovolemia-related complications. Dr. Forcione prefers LR, and often orders 2L post ERCP.

• Indomethacin 100mg PR (post ERCP pancreatitis prophylaxis)
Indomethacin:

Bioavailability 80-90% rectal

Non-steroidal anti-inflammatory drug, not particularly an analgesic

Works by inhibiting the production of prostaglandins

Allergy to NSAIDS is a contraindication

Severe pre-existing renal and liver damage is a contraindication

Let patients know post procedure if they’ve received indocin…

They may have a feeling they have to move their bowels
Does fluid type matter?

- **Lactated Ringers vs NS**
  - LR associated with lower CRP levels
  - LR associated with less SIRS
  - WHY??
    - Better electrolyte balance
    - More pH balanced

NS -> Non gap met acidosis -> trypsinogen activation
Analgesics for pain relief:

PO medications (for mild pancreatitis):
Tylenol, Darvocet, Ultram (as PO intake is tolerated)

IV Demerol, Dilaudid, Morphine, Fentanyl
Treatment Plan/Moderate → Severe Pancreatitis
Moderate to Severe Pancreatitis:

- Patient is NPO - NJ feedings initiated when oral feeding not tolerated within 7 days (ACG)

- TPN - patients who cannot maintain caloric needs with enteral nutrition, or if NJ access cannot be maintained

- Role of nutritional support - reduce burden of pancreatitis on the body

- Severe acute pancreatitis - negative nitrogen balance associated with poor clinical outcomes

- ↑ catabolic nitrogen loss, ↑ mortality

- Successful nutritional support maintains positive nitrogen balance without over-stimulating pancreatic fluid secretion

- Enteral nutrition (EN) preferred - fewer complications than parenteral nutrition, more cost effective
• NJ feeding - nutrients bypass stomach and duodenum (↓ pancreatic stimulation)

• EN aids immune function, preserves lean muscle mass, ↓ risk for metabolic complications

• EN transitions better back to oral feeding

• EN maintains baseline gut permeability, ↓ transfer of gut bacteria to surrounding organs

• EN less expensive than TPN

• ACG guidelines advise EN as the initial route of nutritional support

• TPN causes hyperglycemia, necessitates the use of insulin more frequently than EN
Complementary/Alternative Medicine
• Antioxidant Diet Therapy

• Oxidative stress - production of free radicals

• Free radicals - by-products of metabolism, harmful to cells

• Antioxidant deficiency may exacerbate chronic pancreatitis

• EtOH induced pancreatitis linked with low levels of antioxidants

• Antioxidant rich foods: blueberries, cherries, tomatoes, green vegetables, squash, peppers.

• Antioxidant rich herbs: green tea, holy basil, rhodiola, cat’s claw, reishi mushroom, indian gooseberry, grapeseed extract, licorice root, ginger root, Asian ginseng, peony root, cinnamon Chinese bark.
Lower sepsis rates for patients given enteral nutrition (via NJ tube) enriched with omega-3 fatty acids, probiotics (lactobacillus plantarum) arginine, nucleotides and glutamine

Inflammation and bacterial invasion complicate pancreatitis, vitamins and probiotics help suppress pathogenic bacterial overgrowth and inflammation

Treatments shown to decrease the chance of septic complications and reduce length of hospitalization.
Acupuncture

- Blockage of normal energy movement (qi) restored by inserting sterile needles into points of the body
- Used for several thousand years in China
- Needle placement releases endorphins, stimulates inhibitory descending pathways in the brain and activates opioid receptors on the spinal level
- Reduces opioid requirements, contributes to overall wellbeing
- Well-tolerated, few adverse effects
- Promising outcomes demonstrated in research studies
Health Promotion

• Gallstone pancreatitis or idiopathic recurrent pancreatitis - cholecystectomy

• EtOH abuse - Alcoholics Anonymous

• Smoking cessation - risk factor for both chronic and acute pancreatitis

• Hypertriglyceridemia - risk factor for pancreatitis; low-fat diet + exercise

• Type II diabetic patients 18 - 45 (5X more likely to develop pancreatitis than patients > 45);

• Glycemic control important
Thank you!!!
Reference Sources

UpToDate.com

DAVEPROJECT.org

National Institute of Diabetes and Digestive and Kidney Diseases: digestive.niddk.nih.gov

University of Maryland Medical Center: umm.edu/cgi-bin

Medline Plus: nlm.nih.gov/medlineplus

eMedicine Clinical Knowledge Base, Institutional Edition: imedicine.com


Brugge WR, MGH Endoscopy Unit, EUS slides and video.


Forcione D, MGH Endoscopy Unit, ERCP video and images


Pillay Y. Probiotics in severe acute pancreatitis. The Lancet 2008; 371: 634-635

Schapiro RH, MGH Endoscopy Unit, Pancreatitis images