

Acute and Chronic Pancreatitis

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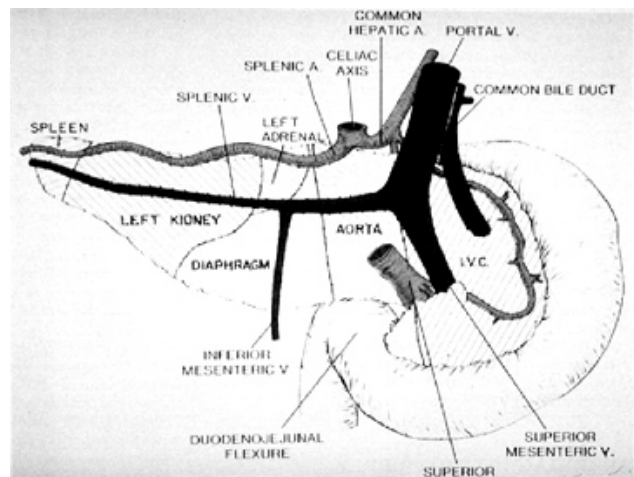
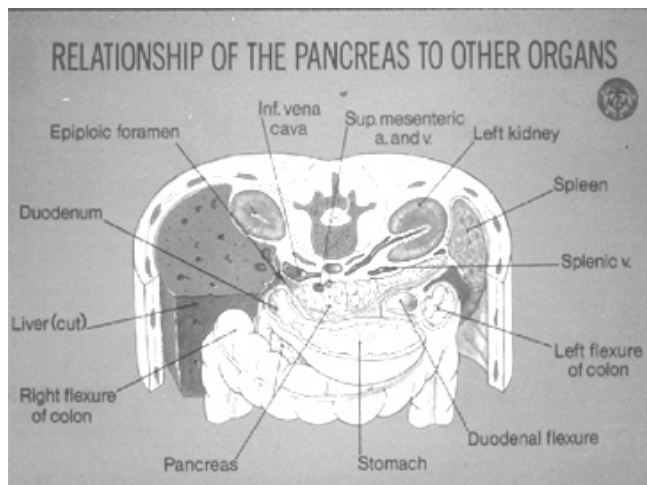
Objectives

1. Appreciate the spectrum of inflammatory diseases of the pancreas
2. Understand aspects of pancreatic anatomy, histology, and function that relate to acute and chronic pancreatitis
3. Know the distinction between acute and chronic pancreatitis
4. Learn important clinical features of acute pancreatitis and chronic pancreatitis including: etiology, clinical pathophysiology, diagnosis, and complications. Clinical management/therapy will be addressed only briefly.

I. Brief Review

Anatomy

- A. The pancreas is a deep centrally located retroperitoneal organ extending from the "C" loop of the duodenum to the splenic hilum with the mid-body of the pancreas lying just anterior to the 1st and 2nd lumbar vertebrae. In this location the pancreas receives a rich blood supply from the celiac axis and superior mesenteric artery and is juxtaposed to many important structures.
- B. Review the diagrams below to understand the relationship of the pancreas to surrounding structures including:
 1. Stomach, duodenum, proximal small bowel loops, colon
 2. Spleen, left kidney, left adrenal, diaphragm, common bile duct
 3. Aorta, inferior vena cava, portal vein, superior mesenteric vein and artery, splenic vein and artery, right and left renal vein



- C. The anatomic location of the pancreas makes this organ less accessible to exam, diagnostic studies, and surgical intervention. Its central location and involvement of adjacent structures often influence the signs, symptoms, and outcome of pancreatic disorders.

Histology

- A. The pancreas consists primarily of exocrine glands (80%) with the remaining pancreas divided into endocrine tissue (2%), and support (18%) tissues
 1. Exocrine acinar cells manufacture and secrete numerous digestive enzymes including proteases, lipases, and nucleases
 2. Endocrine cells secrete insulin, glucagon, somatostatin, pancreatic peptide, and vasoactive intestinal peptide
 3. Support tissues include duct cells, nerves, blood vessels, lymphatics, and connective tissue
- B. Anatomy of the exocrine pancreas

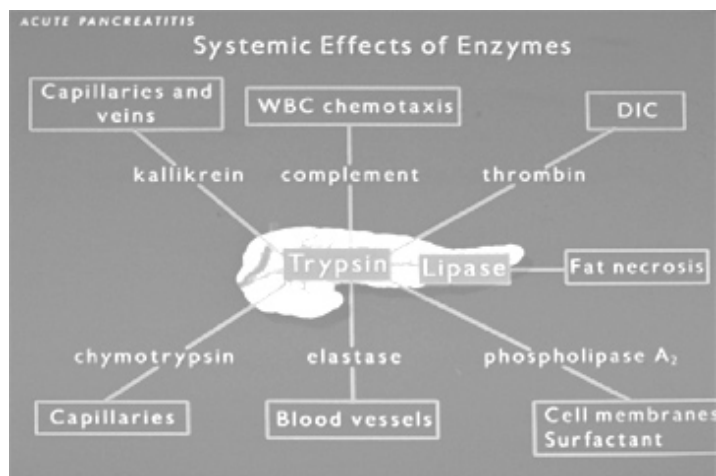
1. The basic unit of the exocrine pancreas is the acinus
 - a. The acinus is a glandular collection of acinar cells
 2. Multiple acini are arranged into lobules
 3. Ductules from acini merge into intralobular ducts then into interlobular ducts that coalesce into branches of the main pancreatic duct
 4. Throughout the course of the pancreatic duct, duct cells secrete bicarbonate rich fluid
 - a. The secreted volume is approximately 2.5 liters per day
- C. Because the enzymes produced and secreted by the acini have the ability to digest the pancreas and all surrounding tissues, the pancreas and acinar cell has elaborate protective mechanisms to deter the intracellular and intraglandular activation of digestive enzymes.
1. Enzymes are synthesized in an inactive zymogen form
 2. Enzymes are segregated into membrane bound compartments
 3. The acinar cell contains enzyme inhibitors
 4. Activating enzyme kept geographically separate from pancreatic parenchyma

II. Acute pancreatitis

Pathophysiology

Acute pancreatitis is a vicious cycle of inappropriate activation of pancreatic enzymes and cellular/glandular destruction

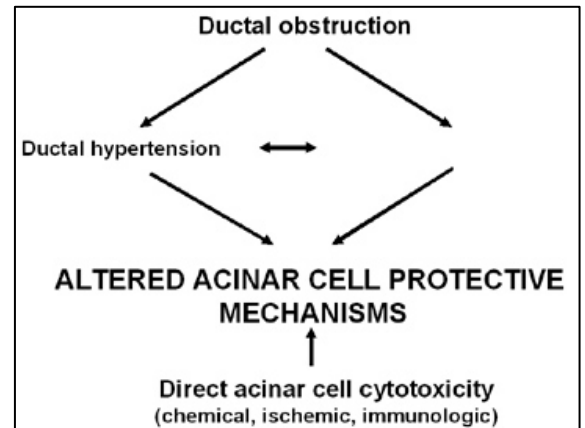
- A. Cellular
 1. The primary event in acute pancreatitis is altered acinar cell protective mechanisms that lead to intracellular activation of digestive enzymes
 2. The intracellular activation of digestive enzymes initiates a self perpetuating cascade of cellular and glandular inflammation and injury including
 - a. Dissolution of organelles and cell membranes
 - b. Release of cellular components (phospholipase, lysolecithin, elastase)
 - c. Release of soluble mediators (cytokines): PAF, TNF α , IL-1b, IL-2R, IL-6, IL-8, iNOS, MIF, Sub P, ICAM-1
- B. Glandular (including local extension of inflammatory process)
 1. Increased vascular permeability
 2. Granulocyte and macrophage influx and activation
 3. Formation of reactive metabolites
 4. Dissolution of blood vessels and extracellular matrix
 5. Massive fluid loss into abdominal cavity
 6. Hemorrhage, thrombosis
 7. Tissue necrosis
- C. Systemic
 1. Systemic effect of released cellular components and cytokines
 2. Respiratory failure
 - a. Phospholipase A₂ degrades surfactant and alveolar membranes
 - b. Subdiaphragmatic inflammation prevents adequate diaphragmatic excursion
 - c. Shallow respirations with decreased tidal volume secondary to pain with inspiration
 - d. Hemorrhage reduces oxygen carrying capacity
 3. Renal failure
 - a. Hypovolemia



- i. Lack of adequate oral fluid intake
 - ii. Capillary leak with massive intrabdominal fluid loss
 - iii. Hemorrhage
 - iv. Kallikrein mediated peripheral vasodilation
- 4. Disseminated intravascular coagulation (DIC)
 - a. Systemic effect of released cellular mediators leading to diffuse activation of fibrinolytic and coagulation pathways.
- 5. Shock
 - a. Activation of kallikrein and bradykinin
 - b. Hypovolemia, hemorrhage
 - c. SIRS

Etiology

- A. Postulated events triggering acute pancreatitis
 - 1. Ductal obstruction
 - 2. Ductal hypertension damages the apical surface of acinar and duct cells
 - 3. Altered acinar cell or duct cell permeability
 - 4. Direct cytotoxic effect on the acinar cell or duct cell
- B. Principal clinical etiologies of acute pancreatitis fall into four categories
 - 1. Common duct stones (50%)
 - 2. Alcohol (30%)
 - 3. Idiopathic (7%)
 - 4. Other (13%)
 - a. Partial duct obstruction
 - i. Tumors of pancreas, ampulla, duodenum
 - ii. Sphincter of Oddi dysfunction or stenosis
 - iii. Pancreatic cyst, stone, stricture
 - iv. Helminthic infection
 - v. Pancreas divisum, annular pancreas
 - vi. Choledochoceles
 - b. Medications
 - c. Metabolic
 - i. Hypertriglyceridemia
 - ii. Hypercalcemia
 - d. Iatrogenic
 - i. ERCP
 - ii. Surgery (abdominal, cardiac bypass, transplant)
 - e. Toxins
 - f. Trauma
 - g. Vascular
 - i. Hypoperfusion
 - ii. Vasculitis
 - h. Autoimmune
 - i. Infectious
 - i. Mumps, coxsackie, parasites (HIV: CMV, MAI, cryptosporidium)
 - j. Genetic
 - i. Trypsinogen (PRSS1), SPINK1, CFTR



Clinical Presentation

- A. Symptoms
 - 1. Abdominal pain, nausea, vomiting, low-grade fever, dehydration

- B. Physical exam
1. Tenderness, mild distension, decreased or absent bowel sounds

Diagnosis

A. Clinician's base the diagnosis of acute pancreatitis on history, physical exam, elevated pancreatic enzymes, and imaging.

B. Laboratory

1. Amylase (sensitivity 80-90%, specificity 70%)
2. Lipase (sensitivity 90%, specificity 90%)
3. Because amylase may arise from many different organs an isolated elevated amylase should lead to consideration of diseases involving
 - i. Ovaries, fallopian tubes, salivary glands, lungs
 - ii. Renal insufficiency
4. Simultaneous elevations in amylase and lipase greatly increases specificity for a pancreatic etiology
 - a. The small intestine however may contain can be the source of systemic absorption of both amylase and lipase. Acute injury of the small bowel can therefore present with elevated amylase and lipase as well as symptoms that mimic acute pancreatitis
 - i. SBO, perforation, infarction
5. Amylase rises over 2-12 hours, declines over 3-5 days. Lipase persists for 7 days.
6. Magnitude of amylase and lipase elevations are of **no** prognostic significance

| | Amylase | Lipase |
|--|---------|--------|
| Paroditis | yes | no |
| Tumors | yes | no |
| Biliary disease | yes | slight |
| Pancreatitis | yes | yes |
| Renal failure | yes | slight |
| Intestinal obstruction, ulceration, ischemia | yes | yes |
| Ectopic pregnancy | yes | no |
| Macroamylasemia | yes | no |
| Perforated viscus | yes | yes |

C. Radiology

1. Plain film - used to rule out other causes of abdominal pain
2. Ultrasound - poor study to evaluate pancreas due to surrounding bowel gas
3. Computed tomography
 - a. Method of choice
 - b. 92% sensitivity, 90% specific
 - c. Can determine severity: presence and extent of necrosis (requires contrast)
 - d. Detects complications
4. MRI not generally used in the setting of acute pancreatitis
 - a. Currently only advantageous in pregnant patients and those with contrast allergies.

Prognosis

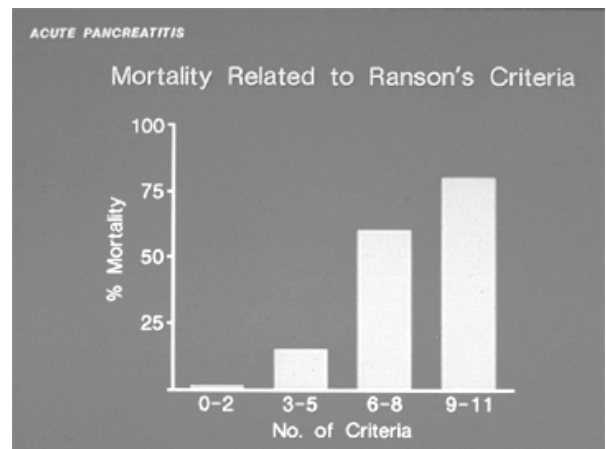
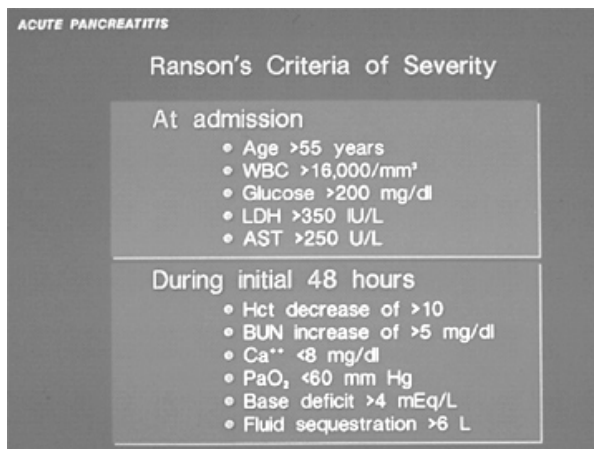
A. General

1. Eighty percent of patients have mild-moderate pancreatitis
 - a. Not associated with organ dysfunction or complications.
 - b. Recovery is uneventful
 - c. Disease related mortality is low
2. Twenty percent of patients have severe pancreatitis
 - a. Associated with impaired pancreatic function and local and systemic complications
 - b. Complicated recovery common
 - c. High mortality.
3. Overall mortality is 9%

B. Important to clinically distinguish patients with mild to moderate disease from those with severe disease

1. Level of monitoring and treatment strategies change with disease severity.
 - a. Patients with severe disease are more likely to develop respiratory failure, renal

- failure, and pancreatic infections
- b. Early institution of intensive care monitoring and antibiotics in this group of patients may decrease mortality.
- C. Clinical assessment - the methods of evaluating the severity of acute pancreatitis early in the course of the disease include bedside assessment, clinical scoring systems, CT criteria, and serum markers.
 1. Bedside assessment
 - a. Underestimates disease severity
 - i. When a patient appears acutely ill, the patient usually has severe disease and requires intensive care monitoring.
 - Assessment modalities other than CT scan usually do not add significant information.
 - b. Bedside assessment most often fails in the young patient or in a patient with good functional reserve.
 - i. In these situations, methods other than bedside assessment must be used to provide an accurate estimate of severity and prognosis.
 - c. The following bedside parameters should precipitate a guarded prognosis and intensive monitoring plan.
 - i. Tachycardia (Heart rate > 120/min)
 - ii. Hypotension (Systolic blood pressure < 90 mmHg)
 - iii. Hemoconcentration (Hematocrit > 50%)
 - iv. Oliguria (UO < 400 cc/24 hours)
 - v. Tachypnea (Respiratory rate > 30/min)
 - vi. Hypoxemia (O₂ saturation < 90%)
 - vii. Encephalopathy
 2. Scoring systems
 - a. Ranson criteria



- b. Glasgow scale
- c. Apache score
- 3. Findings on CT scan
 - a. Degree of inflammatory changes, presence of complications, and extent of pancreatic necrosis.
 - b. A scoring system has been devised to translate these features into prognosis

Treatment

- A. There are no specific treatments that can attenuate the pathophysiologic inflammatory cascade of acute pancreatitis.
- B. Assessment of severity and appropriate triage
- C. Supportive care
- D. Prevention and treatment of complications

E. Seek etiology

Supportive care

1. Aggressive hydration and electrolyte replacement
2. NPO
3. Monitoring
 - a. Physical exam, vital signs, urine output, O₂ saturation
 - b. Intravascular volumes (swan-ganz catheter)
 - c. Anticipate complications
 - i. Hypovolemia
 - ii. Acute renal failure
 - iii. Acute respiratory distress syndrome (ARDS)
 - iv. Hemorrhage
 - v. Sepsis
 - vi. Disseminated intravascular coagulation
 - vii. Infected necrosis
4. Pain control, anti-emetics
5. Antibiotics
 - a. Recent data suggests that antibiotics should not be used prophylactically but only if infection is suspected
6. Nutritional support
 - a. Start early in severe disease as severe disease is associated with prolonged course
 - i. Nasojejunal tube is preferred modality to deliver nutrition
 - ii. TPN appropriate but less desirable
7. Organ failure support
 - a. Mechanical ventilation, dialysis, pressors

III. Chronic Pancreatitis

Definition

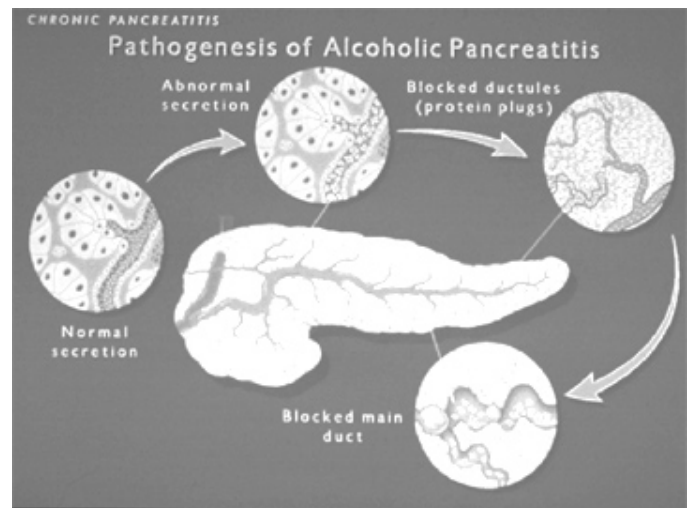
- A. Acute and chronic pancreatitis should be thought of as distinct clinical entities
 1. Acute pancreatitis is a defined event when a morphologically and functionally normal pancreas becomes acutely inflamed. Once the inflammation resolves the organ returns to normal
 2. Chronic pancreatitis is a persistent or progressive process. Changes in pancreatic structure and function usually precede symptoms and always persist even if the precipitating cause has been corrected.

Pathophysiology

- A. Acinar and duct cell damage results in increased membrane permeability
 1. Increased intraductal calcium and protein
 - a. Protein precipitates to form intraductal plugs
 - b. Calcium precipitates to form stones
 2. Patient develops partial duct obstruction
- B. Inflammation, fibrosis, atrophy, and disruption of ducts
- C. Inflammation, fibrosis, and destruction of exocrine and endocrine tissue
- D. Develop a hard fibrotic (cirrhotic-like) organ with reduction of number and size of acini and islets

Etiology

- A. Alcohol (95%)



1. Direct acinar cell toxicity
 - a. Alters membrane infrastructure (decreases GP2)
 - i. Increased membrane permeability (lysosome, zymogen, acinar cell membranes)
 - b. Increased basal protein secretion
 - c. Decreased trypsin inhibitor
 - d. Abnormal lithostatin
 - i. Precipitation of calcium
- B. Hereditary
 1. Mutation of the trypsinogen gene
 2. Mutation of the trypsin inhibitor gene
 3. Cystic fibrosis
 4. CFTR
- C. Chronic partial duct obstruction
 1. Partially reversible with relief of obstruction
- D. Autoimmune
- E. Idiopathic
- F. Tropical

Clinical Presentation

- A. Recurrent
 1. 50% recurrent acute attacks
- B. Insidious
 1. 35% insidious pain
 2. 15% insidious malabsorption, diabetes, jaundice
- C. Symptoms
 1. Pain
 - a. May be on the basis of ductal hypertension or neural inflammation
 - b. Constant, dull, radiates to back, worse with food
 - c. May maintain bent posture
 - d. May decrease with disease duration
 2. Nausea, vomiting
 3. Malabsorption
 - a. Diarrhea, steatorrhea
 - b. Late phase, requires 90% reduction of enzymes
 4. Diabetes
 - a. Late phase
 5. Weight loss
 - a. Fear of pain
 - b. Malabsorption
 - c. Diabetes
 - d. Continued EtOH abuse

Diagnosis

- A. History
 1. Recurrent episodes, chronic disease, EtOH
- B. Physical and laboratories may be suggestive but are not diagnostic
- C. Radiology
 1. Plain film – calcifications
 2. CT – calcifications, irregular glandular contour, dilated ducts, cystic lesions
 3. MRI with MRCP
 - a. Current gold standard
 - b. Ductal irregularity, dilated duct with strictures, cystic areas, calculi
 - c. Parenchymal fibrosis
- D. ERCP
 1. Reserved for therapeutic intervention

- E. EUS
 - 1. Increased echogenicity of parenchyma
- F. Secretin stimulation test

Complications

- A. Pain, malabsorption, weight loss, diabetes
- B. Narcotic addiction
- C. Pseudocyst formation
- D. Common bile duct obstruction, duodenal obstruction
- E. Splenic vein thrombosis

Treatment

- A. Alcohol abstinence
- B. Low fat diet
- C. Pancreatic enzymes +/- acid suppression
- D. Analgesics
- E. Insulin
- F. Surgical decompression
- G. Endoscopic decompression