Harvard-MIT Division of Health Sciences and Technology
HST.121: Gastroenterology, Fall 2005
Instructors: Dr. Jonathan Glickman

Anatomy of the biliary tract

Figure removed due to copyright reasons.

- **Biliary secretions contribute up to 40% of bile volume**
- **Regulated by secretin**

Exocrine Pancreas- Anatomy

- **Acini**
  - **secretion of zymogens**
  - **regulated by CCK**

Figure removed due to copyright reasons.

- **Ductal system**
  - **secretion of HCO_3 rich fluid**
  - **regulated by secretin**

Pathology of the exocrine pancreas

- Cystic fibrosis
- Acute pancreatitis
- Cysts and pseudocysts
- Neoplasms
  - Exocrine
  - Endocrine

Acute pancreatitis

- Severe condition characterized by acute necrosis of pancreatic parenchyma
- Adults, M>F
- Etiology
  - alcohol
  - gallstones
  - trauma
  - ischemic damage
- Pathogenesis: autodigestion; ?mechanisms of activation

Acute pancreatitis- pathogenesis

Figure removed due to copyright reasons.

Acute pancreatitis- pathology

- **Early**
  - Congestion, edema
  - Vascular thrombi, parenchymal necrosis
  - Acute inflammation, fat necrosis
- **Late:** Scarring, chronic pancreatitis
- **Complications**
  - peritonitis
  - hypocalcemia
  - disseminated fat necrosis

Acute pancreatitis

Figure removed due to copyright reasons.

Chronic pancreatitis

- Secondary to recurrent pancreatitis
- Pathogenesis
  - recurring acute pancreatitis (alcoholism, biliary tract disease, cystic fibrosis)
  - familial
  - autoimmune
- Complications
  - exocrine pancreatic insufficiency
  - diabetes mellitus

Chronic pancreatitis- pathology

- Pancreatic parenchymal atrophy, fibrosis
- Focal acute pancreatitis, fat necrosis
- Duct ectasia
- Calcifications
- Pseudocysts

Cystic fibrosis

- CF: 1/3000 live births, Caucasians
- Gene defect: CFTR transmembrane cAMP-activated Cl^- channel; common mutations results in impaired trafficking of protein and loss of surface expression
- Expressed in many epithelia (airway, pancreas, sweat glands)
- Results in inability to reabsorb Cl, and increase in viscosity of secretions

Cystic fibrosis- pancreatic and GI pathology

- Dilated ducts filled with inspissated secretions
- Exocrine pancreatic atrophy with fibrosis (i.e chronic pancreatitis)
- Exocrine pancreatic insufficiency
- Diabetes relatively late
- GI tract: meconium ileus in infants

Pancreatic cysts and pseudocysts

- Most cystic lesions are pseudocysts associated with acute or chronic pancreatitis
- Congenital (associated with polycystic kidney disease, von Hippel Lindau sydrome)
- Neoplastic
  - cysts lined by serous (pancreatic duct-like) or mucinous epithelium
  - benign or malignant

Pancreatic pseudocyst

Images removed due to copyright reasons.

Pancreatic neoplasms

- Vast majority are epithelial in origin
- Exocrine
  - ductal-type adenocarcinoma
  - acinar cell carcinoma (unusual)
  - Serous cystic tumors
  - mucinous neoplasms (unusual)
- Endocrine
  - functional
  - non-functional

Pancreatic carcinoma

- Majority arise from ductal epithelium
- Peak age >50 years, slight M>F
- Symptoms: weight loss, painless jaundice; may be asymptomatic until relatively advanced
- Pathology: tubular adenocarcinoma showing a range of differentiation
- Aggressive neoplasm with poor prognosis

Pancreatic endocrine tumors

- Arise from islet cells
- May be functional or non-functional
- Gastrinomas (from delta cells) associated with Zollinger-Ellison syndrome
- Insulinomas: associated with hypoglycemia
- Pathology similar to GI carcinoids
- Liver metastasis common

Gallbladder

- **Anatomy**
  - **Mucosa**
  - **Submucosa**
  - **Muscularis**
  - **Serosa**
- **Functions**
  - **Storage and concentration of bile**
  - **Regulated by CCK, secretin**

Gallstones

- Extremely common in U.S.
- Risk factors: female gender, obesity, parity
- Etiology likely multifactorial
- Classification
  - Cholesterol
  - Bilirubinate
  - Mixed
- Effects: 80% asymptomatic; acute cholecystitis, gallstone ileus, ?gallbladder CA

Acute Cholecystitis

- **Clinical: 90% a/w gallstones**
  - **acalculous**
  - **HIV-associated**
- **Gross: distended, hemorrhagic, exudate**
- **Microscopic: AI, necrosis**
- **Variants:**
  - **vasculitis**
  - **emphysematous**
  - **gangrenous**

Chronic cholecystitis

- Usually due to repetitive acute cholecystitis
- Most associated with gallstones, may also be associated with bacterial infection in biliary tract
- Gross appearance: Fibrotic gallbladder with wall thickening contraction
- Microscopic: Fibrosis, chronic inflammation, mucosal hyperplasia with Rokitansky-Aschoff sinuses

Gallbladder carcinoma

Clinical

- Most common GB malignancy, incidence 1/100K
- F:M 2:1, peak in 8th decade
- Risk factors: ethnicity, gallstones, abnormal CDP junction, UC, porcelain GB, chemicals
- Symptoms: pain, jaundice, weight loss

Gross

- Mostly fundus; nodular, polypoid or infiltrative

Gallblader carcinoma- pathology

- 75-90% adenocarcinoma NOS
  - Well differentiated (50%) >95% glands
  - Moderately differentiated glands 50-94%
  - Poorly differentiated 5-49% glands
  - Undifferentiated <5% glands
- Adenocarcinoma variants- papillary, mucinous, adenosquamous, signet ring cell
- Other: pleomorphic/giant cell, small cell, squamous cell
- Special studies: mucin+;CK7+CK20+/-; CEA+
  - 30-40% focally positive for NE markers

Cholangitis

- Primary sclerosing cholangitis
- Secondary cholangitis (more common)
  - choledocholithiasis
  - prior procedure, surgery
  - infection
  - pancreatitis
  - toxic injury
- Two types usually difficult to distinguish histologically

Primary Sclerosing Cholangitis

- Clinical: middle aged adults, M>F
  - 70-90% of pts have IBD (usually UC)
  - other associated conditions
- Radiology: Stricture ("beading") of BDs
- Indications for biopsy:
  - BD biopsy: exclude malignancy
  - liver biopsy: confirm diagnosis or r/o others; evaluate progression of liver disease

Primary Sclerosing Cholangitis- Pathology

- Periductal and periglandular lymphocytic inflammation
- Mild ductular distortion, concentric fibrosis
- Progression: obliteration of lumen
- Ddx:
  - invasive carcinoma
  - secondary cholangitis