Gastrointestinal and hepatobiliary system pathology

Gastrointestinal system

Structure and function [Fig. 10-1]

- **Function**
  - absorption of nutrients, excretion of waste
- **Structure**
  - 4 layered tube
    - mucosa [epithelium, lamina propria, muscularis mucosae]
    - submucosa
    - muscularis propria
    - serosa [peritoneum]
  - blood vessels, lymphatics, nerves (ANS)
  - MALT

Oral cavity pathology

- **Cleft lip and palate**
  - congenital anomalies of the lips and palate due to failure of fusion of facial processes
  - multifactorial disorders, varying severities
- **Dental caries (cavities)** [Fig. 10-2]
  - disease of teeth due to bacterial erosion of tooth structure
  - *Streptococcus mutans* thrives in saliva with sugar
  - plaque promotes attachment of bacteria
  - **Complications**
    - pulpitis
    - apical abscess
    - periapical granuloma
    - radicular cyst
- **Periodontitis**
  - inflammation of periodontal recesses (gingiva, periodontal membrane, alveolar bone)
  - most common cause of tooth loss
- **Stomatitis**
  - inflammation of the mouth (oral mucosa)
  - infectious causes
    - viruses [herpes], bacteria, fungi [candida]
  - non infectious causes
    - aphthous ulcers
    - immunologic

Oral cavity neoplasms

- Leukoplakia is clinical term for a persistent white lesion
- Erythroplakia is clinical term for a persistent red lesion
- Malignant oral neoplasms
  - arise from epithelium in the oral cavity
  - usually squamous cell carcinomas (>95%)
  - risk factors include tobacco, alcohol
  - may present as leukoplakia
  - most common locations are anterior 2/3 of tongue, lower lip
  - metastasize to regional lymph nodes
  - treatment with surgery and radiation (5 yr survival = 45%)
Gastrointestinal system pathology
Salivary gland pathology

• Sialadenitis
  – inflammation of a salivary gland, usually the parotid gland
  – infectious causes
    • viral [mumps]; bacterial [Staphylococcus aureus]
  – autoimmune causes
    • Sjogren’s syndrome is immune mediated inflammation of salivary + lacrimal glands

• Neoplasms
  – Pleomorphic adenoma
    • benign salivary neoplasm of both epithelial and stromal elements
    • most common salivary gland tumor
    • needs proper excision, may recur locally

Esophageal pathology [Fig. 10-4]

• Esophagitis
  – inflammation of the epithelial lining of the esophagus
  – infectious causes [viral (Herpes), fungal (Candida)]
  – chemical causes [GERD]

• Gastroesophageal disease [GERD]
  – reflux of gastric contents into esophagus resulting in inflammation
  – relaxed tone of lower esophageal sphincter allows reflux of acid
  – Barrett’s esophagus
    • presence of metaplastic intestinal type epithelium in lower esophagus
    • increased risk of developing adenocarcinoma of the esophagus
    • requires regular evaluations

• Hiatus hernia
  – displacement of portion of the stomach above the diaphragm
    • sliding hernia (90%) refers to “sliding” of stomach upwards
    • paraesophageal hernia (10%) refers to portion of stomach protruding upward beside esophagus

• Achalasia
  – disorder of esophagus resulting in increased resting tone of LES
  – food is unable to enter stomach due to increased tone of LES

• Esophageal varices
  – dilation of submucosal veins of the distal esophagus
  – often due to portal hypertension secondary to hepatic cirrhosis
  – significant morbidity and mortality associated with rupture

• Malignant esophageal neoplasms
  – usually carcinomas
    • either squamous cell carcinoma or adenocarcinoma
  – risk factors for squamous carcinoma include tobacco, alcohol
  – risk factors for adenocarcinoma include Barrett’s esophagus
  – typically occur in lower portion of esophagus
  – presents as ulceration or a mass
  – lymphatic invasion
Gastrointestinal system pathology

Stomach pathology

• Gastritis
  – inflammation of the mucosal lining of the stomach
  – Acute gastritis
    • acute erosive inflammation of the mucosal lining of the stomach
      – stress, drugs (aspirin), alcohol
  – Chronic gastritis
    • chronic inflammation of the mucosa with acute exacerbations
    • Helicobacter pylori infection
      – H. pylori is a bacteria that survives in the acidic gastric environment
      – associated with one type of chronic gastritis
      – chronic H. Pylori infection associated with increased incidence of gastric adenocarcinomas and lymphomas

• Chronic gastritis
  – Autoimmune gastritis
    • autoimmune destruction of parietal cells in the stomach
    • associated with increased risk of gastric adenocarcinoma

• Peptic ulcer disease [Fig. 10-6]
  – localized chronic ulceration of gastric or duodenal mucosa
  – due to action of acid on weakened gastric or duodenal mucosa
  – factors include H. pylori, stress, hormones
  – complications
    • hemorrhage [melena, iron deficiency anemia, hematemesis]
    • perforation [peritonitis]
    • scarring [stenosis, obstruction]

Stomach neoplasms

• Malignant gastric neoplasms
  – Gastric carcinoma [Fig. 10-7]
    • incidence is decreasing in North America
    • risk factors include nitrosamines, Japanese, H. pylori,
    • adenocarcinomas
    • classification
      – on basis of gross appearance (polypoid, fungating, ulcerating, diffuse)
      – on basis of histological appearance (intestinal type, signet cell)
    • poor prognosis [5 year survival 20%]
    • lymphatic spread [Virchow node]
  – Lymphoma
    • stomach is common site for extra-nodal malignant lymphoma
    • MALToma is a low grade lymphoma arising in chronic H. pylori

Small bowel pathology

• Meckel’s diverticulum
  – developmental disorder of small bowel due to persistence of the omphalomesenteric (vitelline) duct
  – 2 % of population, 2 ft. from ileocecal valve, 2% ectopic gastric mucosa, 2 % develop symptoms

• Malabsorption
  – inability of body to absorb nutrients
    • maldigestion, decreased absorption, impaired transport
  – Celiac disease
    • damage to small bowel mucosa due to hypersensitivity reaction to gluten, a protein present in wheat
    • malabsorption results from the damage to the small bowel mucosa
    • treatment is a gluten free diet
Gastrointestinal system pathology

Small bowel pathology

- Infections of the small bowel
  - Girardia
    - Parasite
    - beaver fever

- Neoplasms
  - neoplasms of small bowel are rare
  - Malignant neoplasms
    - carcinoids
      - low grade malignant neoplasm of neuroendocrine cells
      - may produce carcinoid syndrome (diarrhea, flushing, bronchospasm)
      - locally invasive
    - lymphomas

Inflammatory bowel disease

- Two diseases of unknown etiology where inflammation plays key role

- Crohn’s disease
  - skip lesions, transmural inflammation, granulomas
  - may affect any part of the gastrointestinal tract (mouth to anus)
  - complications
    - fissures, strictures, fistulas, adhesions
    - dysplasia less common than ulcerative carcinoma
    - extra-colonic manifestations
      - arthritis, eye involvement, primary sclerosing cholangitis, skin lesions

- Ulcerative colitis
  - confluent involvement from rectum proximal to cecum
  - small bowel is not involved
  - inflammation is confined to mucosa
  - complications
    - toxic megacolon
    - dysplasia
    - extra-colonic manifestations
      - arthritis, eye involvement, primary sclerosing cholangitis, skin lesions

Large bowel pathology

- Hirschprung’s disease
  - congenital absence of colonic nerve ganglia resulting in portion of colon with no peristalsis
  - dilation of colon proximal to aganglionic segment

- Diverticular disease [Fig. 10-8]
  - disease, generally of the elderly, characterized by outpouchings of colonic mucosa (pseudodiverticulum)
  - diverticulosis is term for presence of diverticula
  - diverticulitis is term for inflammation of a diverticulum
  - complications
    - pericolonic abscess
    - peritonitis
    - colonic stenosis
Gastrointestinal system pathology

Large bowel pathology

• Inflammation
  – infectious
    • pseudomembranous colitis
      – acute colitis characterized by formation of a pseudomembrane
      – due to toxin produced by bacterium *Clostridium difficile*
      – due to broad spectrum antibiotic use
  – inflammatory bowel disease
  – ischemic bowel disease
    • certain parts of bowel susceptible to ischemia (watershed areas)
    • ischemia may result from atherosclerosis

• Hemorrhoids
  – variceal dilation of veins in the submucosa of the anorectal area

• Polyps (generic term for protruberant mass)
  – hyperplastic polyp
    • most common colonic polyp, no malignant potential
  – hamartomatous polyp
    • occur in children
    • Peutz-Jeghers syndrome
      – autosomal dominant, characterized by multiple hamartomatous polyps and pigmented lesions on lips, peri-oral skin
      – increased risk of malignancies
  – adenomatous polyps
    • benign neoplasms (tubular, villous, tubulovillous)
    • increased risk of carcinoma if villous or high grade dysplasia
    • familial adenomatous polyposis is autosomal dominant hereditary tumor syndrome

• Colonic carcinoma [Fig. 10-16]
  – 3rd most common malignant tumor in North America
  – 3rd most common cause of cancer-related death in North America
  – peak incidence in 60 - 80 years age group
  – rare before age 40 unless predisposing condition
  – risk factors include FAP, IBD
  – histologically adenocarcinomas
  – metastasize via lymphatics or blood stream
  – staging takes into account depth of penetration, nodes, mets
  – majority occur in distal colon
  – digital rectal exam as part of routine physical exam

Appendiceal pathology

• Appendicitis
  – acute bacterial infection of appendix secondary to luminal obstruction (fecolith, lymphoid hyperplasia, pinworms)
  – abdominal pain (McBurney’s point, rebound tenderness), systemic features, leukocytosis
  – rupture leads to peritonitis

• Neoplasms
  – carcinoid is most common neoplasm of appendix
  – adenocarcinomas also occur
Hepatobiliary system

Structure and function [Figs. 11.1 & 11.2]

- **Function**
  - detoxify metabolic waste products
  - remove old red blood cells (with spleen)
  - produce bile
  - synthesize plasma proteins
  - synthesize plasma lipoproteins
  - detoxify drugs

- **Structure**
  - hepatocytes are arranged in lobules
    - portal triad
    - central vein

- **Blood flow**
  - portal vein, hepatic artery supply the sinusoids
  - blood drains through sinusoids in lobule into central vein
  - blood exits via hepatic vein into IVC

- **Bile**
  - function is to solubilize fat
  - made in liver
  - stored in gall bladder

- **Bilirubin**
  - breakdown product of hemoglobin
  - conjugated (solubilized) in liver
  - excreted into bile
  - bile excreted into bowel
  - altered by bacteria present in bowel
    - urobilinogen
      - reabsorbed (yellow urine)
    - stercobilinogen
      - not reabsorbed (stool brown)

Hepatobiliary pathology

Cirrhosis [Figs. 11-7, 11-12]

- End stage liver disease characterized by fibrosis and regenerative nodules

- **Causes**
  - alcohol
  - viral hepatitis (HBV&HCV)
  - metabolic and hereditary (hemachromatosis, Wilson’s disease)
  - drugs
  - biliary cirrhosis

- **Complications**
  - Portal hypertension [Fig. 11-3]
    - varices, ascites, splenomegaly
Hepatobiliary pathology

Hepatitis

- Inflammation of the liver parenchyma
- Non-infectious causes: metabolic disorders
  - hemochromatosis
    - autosomal recessive disorder of iron metabolism resulting in increased deposition of iron in various organs including liver, heart, pancreas
  - Wilson’s disease
    - autosomal recessive disorder of copper metabolism resulting in increased deposition of copper in various organs including liver, brain, and eye
  - Alpha 1 antitrypsin deficiency
    - autosomal recessive disorder resulting in decreased alpha 1 antitrypsin, may cause emphysema, cirrhosis
- Non-infectious causes: drug/toxin induced
  - acetaminophen
    - dose related necrosis of liver cells
  - alcohol
    - three pathologic changes linked to alcohol use
      - fatty liver (steatosis)
        - all alcoholics show steatosis [fatty yellow liver]
    - alcoholic hepatitis
      - acute inflammation with fibrosis
    - cirrhosis
- Viral hepatitis (usually due to hepatotropic viruses [Hepatitis virus A,B, C, D, E, G])
  - hepatitis A
    - fecal oral transmission
    - no chronic state
    - rarely lethal
    - vaccine available
  - hepatitis B
    - parenteral, perinatal, sexual transmission
    - 5-10% progress to chronic hepatitis
    - massive hepatic necrosis and death are uncommon
    - increased incidence of hepatocellular carcinoma
    - vaccine available
  - hepatitis C
    - parenteral, sexual transmission
    - 50-70% progress to chronic hepatitis
    - increased incidence of hepatocellular carcinoma
    - no vaccine
  - hepatitis D
    - parenteral, possibly sexual transmission
    - requires coinfection with hepatitis B
  - hepatitis E
    - fecal oral transmission

Other infections

- Hepatic abscess
  - abscesses may form in liver parenchyma
  - maybe caused by bacteria or by ameba (a parasite)
- Hydatid disease
  - a disease of various organs cause by a parasite [echinococcus (cestode (tapeworm))] characterized by formation of cysts
- Schistosomiasis
  - liver disease results from schistosome (a parasite) depositing eggs in branches of portal vein
- Ascariasis
  - liver disease resulting from obstruction of bile ducts by the parasite
Hepatobiliary pathology

Immunologic disorders

• Primary sclerosing cholangitis
  – disease of unknown etiology characterized by destruction of intra-hepatic and extra-hepatic bile ducts by lymphocytes and macrophages
  – younger males
  – most also have inflammatory bowel disease (UC>CD)
  – increased incidence of cholangiocarcinoma

• Auto-immune hepatitis
  – chronic hepatitis in young females characterized by presence of autoantibodies to specific antigens
  – favorable response to steroids
  – associated with other autoimmune diseases

• Primary biliary cirrhosis
  – disease of unknown etiology characterized by destruction of small intra-hepatic bile ducts and eventual cirrhosis
  – possibly T-cell mediated
  – autoimmune disease affecting middle age females
  – antimitochondrial antibodies in 95%
  – cirrhosis develops over 10-15 yrs.
  – no cure

Neoplastic liver disease

• Benign neoplasms
  – cavernous hemangioma
    • benign neoplasm of endothelial (blood vessel) origin
    • most common benign neoplasm
  – hepatocellular adenoma
    • benign neoplasm of hepatocyte origin
    • young females on OCP

• Malignant neoplasms
  – hepatocellular carcinoma [HCC]
    • malignant neoplasm of hepatocytes
    • risk factors include cirrhosis, HBV, HCV, hemochromatosis, alpha 1 antitrypsin deficiency
    • tumors may be diffuse, solitary, or multiple nodules
    • AFP is a protein usually secreted by fetal hepatocytes
      – AFP levels are elevated in HCC and useful as tumor marker
  – metastatic carcinoma
    • most common malignancy of the liver
    • usual primary sites are GI tract, lung, breast
Hepatobiliary pathology

Gall bladder and biliary tract [Fig. 11-16]

• Bile is made in liver and stored in gall bladder
• Cystic duct (from gallbladder) empties into common hepatic duct forming common bile duct
• Bile duct travels through pancreas and empties into duodenum (ampulla of Vater)
• Pancreatic duct empties into bile duct
• Gallbladder stores bile

Biliary tract pathology

• Gallstones (cholelithiasis)
  – presence of stones in the gall bladder
  – types of stones
    • cholesterol stones (10%)
    • pigment stones (15%),
    • mixed stones (75%)
  – diagnose by ultra-sound
  – complications of cholelithiasis
    • cholecystitis
    • obstructive jaundice
    • ascending cholangitis
    • gallstone ileus

• Cholecystitis
  – inflammation of the gallbladder (acute vs. chronic)
  – usually due to gallstones
  – acalculous cholecystitis = no stone

• Choledocholithiasis
  – stone present in the common bile duct

• Primary sclerosing cholangitis (see above)

• Neoplasms
  – adenocarcinomas
  – cholangiocarcinoma
    • associated with PSC, clonorchiasis
Exocrine pancreas
Structure and function  [Fig. 12-1]

- Structure
  - exocrine glands consisting of epithelial cells arranged in lobules composed of acini
  - duct system emptying into common bile duct

- Function
  - secrete enzymes (lipase, amylase, peptidase) to aid in digestion of food

Pathology

- Pancreatitis
  - inflammation of the cells of the pancreas

- Acute Pancreatitis
  - acute inflammation with tissue necrosis due to release of pancreatic enzymes
  - alcohol and gallstones responsible for 80 % of cases
  - complications
    - abscess
    - pseudocyst
    - peritonitis
    - chronic pancreatitis
    - diabetes

- Chronic Pancreatitis
  - persistence of inflammation after original inciting agent removed
  - progressive fibrosis
  - alcohol important factor

- Pancreatic neoplasms
  - Malignant
    - pancreatic carcinoma
      - adenocarcinoma arising from duct epithelial cells
      - poor prognosis