Approach to the Patient with Gastrointestinal Disease

Background
- Main GI tract is mouth, pharynx, esophagus, stomach, small intestines, large intestines, anus
- Accessory organs included in GI system are the salivary glands, liver, gallbladder, and pancreas
- Common GI signs and symptoms (including alarm symptoms):
  - abdominal pain:
    - types:
      - visceral pain is poorly localized
      - somatic pain is initiated by pain receptors in the parietal peritoneum and is sharp, well-localized, and increased by changes in pressure or tension
      - referred pain is a visceral pain felt elsewhere because visceral and somatic afferents frequently converge on the same neurons in the spinal cord
    - investigation:
      - differential: acute pancreatitis, acute cholecystitis, acute appendicitis (begins with periumbilical pain that settles in the RLQ), diverticulitis, intestinal ischemia (great pain after eating), peptic ulcer disease, bowel obstruction, infectious diarrhea, incarcerated hernia
      - must differentiate acute vs. chronic pain
  - altered bowel habits: includes diarrhea, constipation
  - nausea and vomiting
  - bleeding: hematemesis, melena (old blood in stool = maroon or tarry), or hematochezia (BRBPR), coffee ground emesis (old blood from the stomach)
  - pyrosis: heartburn; exposure of the esophageal epithelium to gastric acid
  - dysphagia: an ALARM symptom
  - odynophagia
  - early satiety: an ALARM symptom for pancreatic and colorectal malignancies
  - jaundice
  - anorectal symptoms
  - anemia
  - weight loss > 10% TBW
  - history of PUD
  - FH of gastric malignancy
  - abdominal mass
- Investigation:
  - GI history: be sure to ask about bowel habits, travel, extra-intestinal manifestations, meds, diet
  - PE: does disease encourage or resist movement by the patient, look for signs of telangiectases or other hallmarks of liver disease, rectal exam if needed
  - diagnosis of GI disease is complex are symptoms can be localized or diffuse
  - many diagnoses must be done by exclusion
  - many disorders are “functional” = lacking laboratory or radiographic evidence of disease
    - causes can be altered gut motility, exaggerated visceral responses to noxious stimuli, altered processing of visceral stimuli
    - ex. atypical chest pain, IBS, dyspepsia, functional bloating, functional constipation or diarrhea

Causes of Chronic Abdominal Pain
A.) GERD
B.) Non-ulcer dyspepsia: chronic or recurrent pain in the upper abdomen
  - different from GERD in that pain is the primary feature
  - investigation:
patients > 55 or with alarm symptoms → prompt endoscopy
patients < 55 with no alarm symptoms → test and treat for H. pylori + PPI (or PPI trial only)
treatment only needed if patients have chronic symptoms

C.) IBS
D.) IBD
E.) Chronic pancreatitis
F.) Infectious diarrhea

Diagnostic Methods

☐ Common GI Labs
1.) 24-hour urine 5-hydroxyindolacetic acid (HIAA): a breakdown product of serotonin that is associated with carcinoid syndrome when excreted in large amounts
   -patient prep: must avoid serotonin-rich foods like bananas, pineapple, avocado, mushrooms, walnuts
2.) Pancreatic labs
   a.) amylase: made by pancreas and salivary glands to break down starch
      -can be obtained from serum, urine, pleural fluid, peritoneal fluid
      -pronounced elevation in acute pancreatitis, pancreatic pseudocyst
      -mod elevation in pancreatic cancer, mumps, salivary gland inflammation, perforated peptic ulcer
   b.) lipase: made mostly by the pancreas to break down TG
      -serum
      -released into the bloodstream with disease or injury to pancreas
      -elevation is highly specific for pancreatic disease
      -pronounced in acute pancreatitis, pancreatic pseudocyst
      -mod in pancreatic cancer
3.) Liver labs:
   a.) total bilirubin: increased production from heme + defective removal
      -bilirubin is a product of RBC breakdown
      -normally the heme → unconjugated bilirubin by the spleen
      -then the bilirubin is further processed by the liver → conjugated bilirubin
      -enters the bile
      -most is excreted in feces
      -smaller amount excreted in urine
      -blockage of bile duct → enters the blood instead
      -insoluble bilirubin = unconjugated = indirect
      -kidneys won’t filter this!
      -soluble bilirubin = conjugated = direct
      -kidneys will filter this, so if urine is dark this is why
      -total and direct bilirubin is what is measured from the blood, and indirect bilirubin is calculated from this number
      -unconj bili elevated from increased heme (hemolysis), hepatitis, drugs
      -conj bili elevated from biliary cirrhosis, drugs, hepatocyte damage, bile duct obstruction
      -elevated from liver cause: impaired uptake, defective bili metabolism, hepatocyte damage, obstruction
   b.) alanine aminotransferase (ALT) and aspartate aminotransferase (AST): enzymes normally within the hepatocytes that are released when they are damaged
      -chronic hepatitis = elevation to the 100s
      -acute hepatitis = elevation > 1000
      -ALT:
      -high content in liver but also in kidney, heart, skeletal muscle
      -low content in pancreas, spleen, lung, RBCs
      -more specific for liver injury than either AST or ALP
      -more elevated injury than obstruction or cirrhosis
      -AST:
      -high content in liver, heart, brain, and skeletal muscle
-mod content in RBCs
- can be increased following MI, PE, skeletal muscle trauma, alcoholic cirrhosis, viral
  or drug-induced hepatitis
- can be altered by drugs and patient conditions like hemolysis

→ interpreting and ALT/AST elevation:
- how high are they?
  - if only mildly elevated:
    - repeat labs (half will be normal)
    - review history and consider causes of hepatitis
    - d/c drugs and alcohol and recheck labs
    - consider testing for hepatitis, hereditary diseases
  - if mod-high:
    - think hepatitis, drug injury, toxin injury, muscle injury
    - uncommon: viruses, extrahepatic biliary obstruction
  - if ALP is elevated out of proportion to ALT/AST, evaluate for cholestasis

  c.) alkaline phosphatase (ALP): isoenzymes present rapidly dividing or metabolically active cells in the
     liver, bone, intestine, and placenta
    - elevated in biliary obstruction, pregnancy, active bone formation
    - if elevated, consider following up with 5' nucleotidase: more specific to the liver than ALP
    - associated with cholestasis, liver mets
    - not as subject to elevation from drugs
    - if this comes back normal, the source is outside the liver!

d.) \(\gamma\)-glutamyl transpeptidase (GGT): present in liver and biliary tract, and in low amounts in the kidney,
    spleen, heart, intestine, brain, and prostate
    - useful in assessing cholestasis and biliary obstruction
    - confirms liver etiology when ALP is elevated
    - elevated in alcohol-induced hepatic changes, and in most liver and hepatobiliary diseases

e.) serum albumin: the portion of total serum protein formed WITHIN the liver
    - has a half-life of 14-20 days = lags behind disease
    - serum prealbumin has a half-life of 2 days so it is more sensitive to assess acute liver
      damage

f.) INR and PT: pertain to liver because clotting factors are synthesized there
    - prothrombin time will not be prolonged until one of the associated clotting factors decreases to <
      30-40% of normal

g.) \(\alpha\)-fetoprotein (AFP): elevated with inflammation or hepatocellular carcinoma

h.) total protein: includes prealbumin, albumin, globulins
    - increased in dehydration, globulinopathies
    - decreased in pregnancy, excess IVF, cirrhosis, other liver disease, chronic alcoholism, CHF,
      nephrotic syndrome, burns

i.) “hepatic function panel!”: typically includes Na, K, Cl, CO2, glucose, urea, creatinine, Ca, albumin, P

4.) Biliary labs: ALP, GGT, bili

- Paracentesis
  - Normally peritoneal fluid is ~ 50 mL, clear, and straw-colored
  - Paracentesis fluid is evaluated for cells, Gram stain, glucose, amylase, NH3, ALP
    - ↑ WBCs and neutrophils indicate bacterial peritonitis
    - ↑ amylase indicates pancreatic ascites
    - bloody fluid without traumatic tap indicates malignant peritonitis
  - Serum albumin: ascites albumin gradient/ratio:
    - high in cirrhosis, CHF, alcoholic hepatitis, myxedema, portal vein thrombosis
    - low in bacterial peritonitis, malignancy, nephrotic syndrome, pancreatitis, TB, peritonitis

- Peritoneal Lavage: instillation and aspiration of sterile saline into the abdominal cavity
  - Indicated for eval of abdominal trauma, intraperitoneal hemorrhage, intestinal perf, organ perf
  - Evaluates cells and chemicals
Fecal Occult Blood Testing
1.) Plain old FOBT:
- qualitatively measures presence of blood by oxidation of guaiac (extract impregnated in the paper) to hydrogen peroxide when exposed to heme → blue color
- the “Sensa” brand has an enhancer that gives a more intense blue for greater sensitivity and ease of interpretation
  - requires 3 serial stools
  - can be used to detect bleeding associated with colorectal cancer
  - false + with red meats, NSAIDs, aspirin, excess alcohol, steroids, anticoagulants, chemotherapeutics, iodine preparations
    - must avoid red meats for 3 days
    - must avoid NSAIDs (including aspirin over 325 mg) for 7 days prior to collection and during collection
  - false neg with vit C supplements, excess natural vit C,
  - timeframe:
    - wait 3-5 minutes if immediate development of fresh sample is needed
    - specimens should be tested within 14 days of first stool collection
  - green results may be due to bile in specimen
2.) Immunochemical FOBT:
- specific for human globin = fewer false + from red meat, drugs, etc.
- nice because there is no patient prep needed and fewer specimens are needed

Fecal Leukocyte Testing
- Methylene blue stain detects leukocytes (mostly neutrophils)
- neutrophils are indicative of inflammation
  - presence varies by etiology
    - present with Shigella, Campylobacter, EIEC, UC, Crohn’s, radiation colitis, ischemic colitis
    - variably present with Salmonella, Yersinia, Vibrio, C. diff, Aeromonas
    - ABSENT in norovirus, rotavirus, CMV, ETEC, EHEC, Giardia, Entamoeba histolytica, Crypto, Staph aureus, Bacillus cereus, Clostridium perfringens
- Don’t get in patients hospitalized > 3 days, because they would have manifested symptoms of inflammatory diarrhea by then (unless they got it while in the hospital)

C. diff Testing
- suspect in patients passing 5+ liquid stools per 24 hours
1.) Toxin test
  - predominant enterotoxin is toxin A, toxin B is less common
  - an ELISA test
  - false neg is possible, reduce this risk by testing serial stools: 3 specimens on 3 different days
2.) Tissue culture
  - the gold standard but is rarely performed
  - requires anaerobic culture of biopsy

Bacterial Stool Cultures
- Covers Salmonella, Shigella, and Campylobacter
  - need to specially request media for Vibrio, Aeromonas, Yersinia
  - EHEC is a stool toxin test, so don’t ask for a culture for it!
- When to order?
  - severe or persistent illness
  - again, don’t get in patients hospitalized > 3 days, because they would have manifested symptoms of infectious diarrhea by then (unless they got it while in the hospital)
- Takes 3 days for a final negative result

Ova, Cysts, and Parasites
1.) Fecal acid fast stain for Cryptosporidium parvum and Cyclospora cayetanensis
-Crypto is a veterinary pathogen seen in immunocompromised patients and kids in daycare
-Cyclospora stains as “ghost cells”

2.) Giardia lamblia immunofluorescence assay, need UV microscope to do
3.) Cryptosporidium parvum immunofluorescence assay

> Testing caveats:
- only allowed per hospitalization
- not indicated in immunocompetent patients over age 6 that have been hospitalized for > 3 days

☐ Summary: Tests to Order in Acute Diarrhea
- Fecal leukocytes, routine stool culture
  - order with acute diarrhea < 7 days + severe illness:
    - temp > 38.5 C (101.3 F)
    - bloody diarrhea
  - greater than 6 stools a day, dehydration, abdominal pain
- order with persistent illness for 7-10 days or worsening of symptoms
- Add C. diff toxin if recent hospitalization or antibiotic use
- Add ova and parasite testing if diarrhea is > 10 days, travel to endemic area, community water outbreak, HIV infection, homosexual male

☐ Helicobacter pylori Testing

 *** concurrent use of a PPI, antibiotics, or bismuth can cause false neg in these tests! ***
1.) Serologic ELISA test that detects IgG or IgA
- non-invasive test of choice for diagnosing H. pylori in an untreated patient
- positive in 50% of adults over age 60
- antibodies persist for years after treatment = can’t discern active vs past infection
2.) Gastric biopsy urease test
- best invasive test
3.) Urea breath test: patient ingests radioactive carbon-13 urea, labeled CO2 is exhaled and detected
- best non-invasive test for documenting successful treatment of H. pylori
4.) Stool antigen

☐ Fecal Viral Studies
1.) Rotavirus ELISA
2.) Norovirus PCR: only performed for epidemiology!

☐ Fecal Fat Studies: a screening tool for detection of malabsorption disorders resulting in steatorrhea
1.) Quantitative stool fat test: pt is on a high-fat diet for 2 days before and during collection
- gold standard
2.) Qualitative stool fat test: pt is put on a high fat diet and stool is examined using Sudan stain to look for fat droplets

☐ Common GI Imaging and Procedures
1.) X-ray:
   a.) plain films
   - abdominal flat and upright
   - ileus: multiple loops of dilated large and small bowel without a transition point
   - SBO: abnormal air-fluid levels with paucity of distal colonic gas
   - CXR: calcifications, foreign bodies, free air, obstruction
   - free air best visualized in LLD or upright
   → not helpful for evaluation of reflux or colorectal screening
   b.) + barium = fluoroscopy (aka barium swallow, barium esophagram)
   - evaluate transit times, mucosal abnormalities
2.) CT:
   - indicated for trauma, unexplained pain, infectious or inflammatory lesions, pancreatitis, obstruction
   - indicated for primary malignancies of the liver and pancreas
3.) MR:
- superior soft tissue resolution
- good for liver lesions
- not typically used in acute setting because it takes too long, with the exception of pregnancy
  - magnetic resonance cholangiopancreatogram (MRCP): evaluates biliary tree and pancreatic duct
    - noninvasive and no radiation

4.) Transabdominal US
- usually test of choice for liver and biliary disease
- test of choice in pediatric appendicitis and intussusception
- commonly indicated for cholecystitis, cirrhosis

5.) Endoscopies
   a.) esophagogastroduodenoscopy (EGD): goes from mouth up through the duodenum
   b.) colonoscopy: goes from anus to terminal ileum, allows for visualization of entire colon
      - study of choice for colorectal screening
      - also indicated for eval of anemia, bleeding, assessment of IBD
      - extensive patient bowel prep and liquid diet for 24 hours prior to procedure
      - requires sedation
   c.) sigmoidoscopy: examines descending colon, sigmoid colon, and rectum
      - useful for patients with inflammatory diarrhea who only need a view of the distal colon
      - more effective than fecal occult for colorectal cancer screening, but less effective than colonoscopy
      - less patient prep than colonoscopy
   d.) endoscopic US: allows for transluminal imaging
      - study of choice for staging of rectal, esophageal, and gastric tumors
      - study of choice for identifying pancreatic tumors
      - can also be used to do aspiration biopsies through endoscope
   e.) endoscopic retrograde cholangiopancreatogram (ERCP): endoscope is inserted from the mouth to the duodenum, and contrast is shot through it while x-rays are taken
      - evaluates the biliary tree and pancreatic duct endoscopically, can also intervene with stents, ductal dilation, or brushings
      - diagnostic uses: choledocholithiasis, biliary strictures, sphincter of Oddi dysfunction, recurrent acute or chronic pancreatitis, pancreatic cancer, pancreatic ampullary adenomas
      - therapeutic uses: removal of gallstones, sphincterectomy, stent placement, stricture dilation, fluid drainage, biopsy
   f.) enteroscopy: small bowel endoscopy
   g.) video capsule endoscopy: pill-sized camera for imaging small bowel
      - small bowel indications: tumors, obscure bleeding, polyposis syndromes, refractory malabsorption syndromes
      - esophageal indications: screening for varices, screening for GERD complications, esophagitis
      - avoid in patients with GI distress, fistulas, pregnancy, or swallowing disorders

6.) Nuclear medicine
   a.) hepatobiliary scintigraphy (aka HIDA scan): injection of radioactive tracer into vein → removal by liver → tracer enters bile
      - gallbladder not visualized with cystic duct obstruction or inflammation
      - delayed gallbladder emptying with biliary dyskinesia
   b.) tagged RBCs: uses technitinum-99 to detect obscure bleeding

 Liver Biopsy
- Indicated for evaluation of abnormal LFTs, suspected neoplasm, confirmation of diagnosis (hepatitis C, primary biliary cirrhosis, alcoholic cirrhosis, NAFLD), evaluation of granulomatous disease, unexplained jaundice or suspected drug reaction, management of post-transplant care
- Percutaneous, laparoscopic, or transjugular
- Gold standard for evaluation of liver inflammation or fibrosis
- Outpatient
- Complications rare but serious
- Contraindications: increased PT, thrombocytopenia, ascites, difficult body habitus, suspected hemangioma
Miscellaneous GI Complaints and Anorectal Disorders

Diverticular Disease
- A 20th century disease associated with the Western lifestyle of low fiber, red meat, obesity, and increasing age
- Includes diverticulosis (presence of small outpouchings of the mucosa and submucosa through the muscular layer of the colonic wall; of unknown pathophysiology) and diverticulitis (inflammation of the diverticula)
- Occurs in areas of weakness where the intramural vasa recta penetrate the submucosa
- Presentation of diverticulitis:
  - Pain that is LLQ and suprapubic +/- palpable mass = looks like a left-sided appendicitis
  - Can be mild to severe
  - Fever, diarrhea, nausea, vomiting, dysuria, urinary frequency
- Investigation of diverticulitis:
  - Leukocytosis with left shift
  - CT is imaging of choice to assess severity
  - Plain films for free air, ileus, or obstruction
- Treatment of diverticulitis:
  - 7-10 day course of antibiotics that must cover aerobes and anaerobes: cipro + metronidazole
  - Clear liquids diet
  - Surgical consult if no improvement in 72 hours
- Complications of diverticulitis:
  - Lower GI bleed
  - Intra-abdominal abscess or peritonitis secondary to diverticula perforation
  - Fistulas into the bladder, ureter, vagina, or abdominal wall
  - Obstruction

Diarrhea
- Causes: disordered intestinal motility, malabsorption
  - Malabsorption presents as diarrhea with nutrient deficiencies
    - Fat malabsorption → bulky, frothy, oily stools
    - CHO malabsorption → bloating, soft diarrhea
    - Protein malabsorption → edema, muscle wasting
- Diarrhea may be osmotic, secretory, or inflammatory and weight loss
  - Infectious diarrhea is secretory or inflammatory
- Acute if < 6 weeks
  - 80% of cases are infectious: mostly viral, but occasionally bacterial or parasitic
    - Diarrhea NOT improving within 3 days of onset is less likely to be viral
    - Risk factors: travel, antibiotic use, day care, hospitalization, long-term care facility, immunosuppression therapy, MSM, vigorous/strenuous exercise
  - 20% of cases are medication-induced or due to poorly absorbed sugars
- Chronic if > 6 weeks
  - Pathogens associated with persistent infection: E. coli, Aeromonas, Yersinia, Giardia, Entamoeba, Cryptosporidium

Constipation
- May refer to infrequent stools (< 3 per week), difficult-to-pass/splashing stools, sense of incomplete evacuation, abdominal distension, bloating, or pain
- Rome criteria: for at least 12 weeks in the past year there is < 3 BMs per week as well as straining, hard stools, sense of incomplete evacuation, sense of anorectal obstruction, or need to use manual maneuvers to facilitate evacuation with more than 25% of BMs
  - Loose stools are not present and there are insufficient criteria for IBS
- Generally considered to be a functional disorder with 3 subtypes:
  - Slowed transit through colon
  - Obstructive defecation
  - Constipation-predominant IBS
- Causes:
-functional: low fiber, sedentary activities, slow transit time
  -consider if there is a long PMH of constipation
-d rugs: Ca channel blockers, diuretics, anticholinergics
-endocrine/metabolic disorders: diabetes, renal failure, hypercalcemia, hypothyroidism, hypokalemia
-neuro disorders: MS, Parkinson’s, spinal cord disorders, Hirschsprung’s disease, psychosis
-structural lesions: anorectal lesions, colonic strictures or lesions
-recent onset → organic cause: malignancy, meds

-Investigation:
  -PE: rectal and abdominal exam
  -labs: CBC, TSH, metabolic panel
  -procedures rarely needed

-Treatment (after ruling out causes such as drugs or lesions):
  -no data: increase fiber and water intake, regular exercise
  -bowel training
  -increase number of daily meals
  -laxatives
  -severe cases:
    -digital disimpaction
    -meds: lubiprostone, prokinetic agents such as erythromycin

- Nausea and Vomiting
-Acute: appendicitis, cholecystitis pancreatitis, peritonitis, small or large bowel obstruction
-Chronic: esophageal disorders, PUD, gastric malignancy

- Anorectal Anatomy
  -Sensory fibers end at the dentate line

- Common Anorectal Symptoms
A.) Hemorrhoids: occur when increased venous pressure (from straining, prolonged sitting or standing, pregnancy) causes prolapse of the subepithelial pillows of smooth muscle → pain, bleeding, discharge
  -internal hemorrhoids: painless bleeding after defecation
    -visible with anoscopy
    -treatment: 1% hydrocortisone, rubber band ligation if prolapsed, infrared coagulation for severe cases
  -external hemorrhoids: rare bleeding but extremely painful, especially if thrombosed
    -visible externally on perianal exam
    -treatment: sitz bath, 1% hydrocortisone, stool softeners
    -may need to remove thrombosed clot
    -prolonged recovery

B.) Anal itching: can lead to lichenification, fissures, and infection
  -causes: diabetes, malignancies, thyroid disease, or triggers such as diarrhea or constipation, anorectal lesions, wipes, tight-fitting clothes, over-cleansing, ingested irritants (tomatoes, citrus foods, caffeinated drinks), atopic dermatitis, lichen planus, psoriasis, infections (intertrigo, HPV, HSV, scabies, pinworms), meds (colchicine)
  -treatment: good hygiene, removal of offending agents, 1% hydrocortisone, antihistamine, antipruritic

C.) Rectal pain
  -causes:
    -fissure: clue is severe pain with or immediately after a bowel movement
    -inflamed internal hemorrhoids: clue is dull, aching pain after a bowel movement
      • proctalgia fugax: spasmatic anal pain unrelated to BMs, may only occur a few times a year

D.) Lump or mass
  -causes: external hemorrhoids (painful), skin tags (usually painless), polyps, genital warts, molluscum contagium

E.) Rectal bleeding
  -common causes:
    -younger patients: internal hemorrhoids, fissures, polyps (rare)
-older patients: must also consider malignancy
-causes of BRBPR: hemorrhoids, diverticuli, UC, infectious diarrhea, AVMs, fissures, fistulas, polyps
-fissures are caused by tears or erosion in the epithelium of the anal canal
-usually caused by large or hard-to-pass stool, rarely due to trauma
-very tender and bleed easily
-most commonly posterior
-if lateral, think chronic fissuring, TB, syphilis, occult abscesses, or carcinoma
-diagnosed by appearance
-treatment: stool softeners, protective ointments, sitz baths, 1% hydrocortisone, 2% NG, Botox
-if no healing after 6 weeks, need surgical consult
-fistulas may be caused by cryptoglandular infection, obstetrical injury, TB, Crohn’s, cancer, radiation therapy
-treatment is antibiotics and surgical referral
-abscesses are a medical emergency! can become septic quickly
-begin as an infection of the anal glands
-pathogens: E. coli, Proteus vulgaris, Bacteroides, Staph, Strep
-causes of occult blood: gastritis, gastric ulcers, gastric and esophageal malignancies, esophageal varices, diverticuli, polyps, colorectal carcinomas

Colon Cancer

-95% of primary colon cancers are adenocarcinomas
-Polyps:
-some polyps are adenomatous (malignant potential) while some are hyperplastic (not pre-malignant)
-transformation from adenomatous polyps to colon cancer occurs over many years
-patients with hyperplastic polyps do not need frequent screening
-Tumors occur in the inner mucosa, muscularis mucosa, and possibly the submucosa
-Incidence decreasing since mid-1980s
-Risk increases with age, FH, DM2, metabolic syndrome, ethnicity, IBD, high red meat/processed meat consumption, inactivity, obesity, smoking, heavy alcohol use
-Genetic risks: up to 30% of colorectal cancers have some familial component
-FAP: also incurs increased risk of thyroid, pancreas, duodenal, gastric cancers
-HNPCC: also associated with endometrial, ovarian, gastric, urinary tract, renal cell, biliary, and gallbladder cancers
-Most occur after age 50
-Slightly more common in men
-Prevention:
-diet with plant foods
-healthy BMI
-limit red meats
-physical activity
-vit D/Ca?
-screens
-stool tests: occult blood, stool DNA
-these generally only detect cancer
-guaiac-based fecal occult blood test has the best mortality benefit data
-should be done annually
-can’t be used with a digital rectal exam sample when used for screening
-if positive, should always be followed by colonoscopy
-structural exams: colonoscopy, CT colonography, flexible sigmoidoscopy, double-contrast barium enema
-these detect polyps as well as cancer
-colonoscopy: direct inspection of entire colon with conscious sedation
extensive and thorough bowel prep needed
-can miss large adenomas and some cancers
-but overall much more likely to detect any neoplasia than by fecal immunochemical testing alone
-complications: bleeding post-polypectomy, perforation
-should be done every 10 years, or every 3-5 years with detected cancer or polyps, or every 5 years with FH, or yearly once IBD is present for 15+ years
-flex sig: examines left colon
-some bowel prep is needed
-adenomas found will need a colonoscopy follow-up
-needs to be done every 5 years
-CT colonography: no sedation
-requires some bowel prep
-reimbursement varies
-positive results require f/u colonoscopy
-needs to be done every 5 years
-an emerging technology with lower specificity and sensitivity
-MR colonography: unable to detect lesions < 5 mm
-non-invasive tests are an option but they are less likely to prevent cancer and a colonoscopy must be done if they come back abnormal
-ACS guidelines:
-avg patient → begin at 50
-FH in 1st degree relative or many 2nd degree relatives → begin screening 10 years younger than youngest affected family member
-screening interval determined based on test results and presence of risk factors
-USPSTF guidelines:
-use fecal occult blood, sigmoidoscopy, or colonoscopy beginning at age 50 and continuing through age 75

Presentation: few symptoms!
-rectal bleeding
-iron deficiency anemia
-fatigue and weight loss
-obstruction
-change in stool quality or caliber
-abdominal mass or pain
-weakness
-weight loss
-unusual presentations than can happen:
-invasion of adjacent organs or formation of malignant fistula
-fever of unknown origin or intra-abdominal or retroperitoneal abscesses
-Strep bovis or Clostridium septicum sepsis can be due to underlying colon cancers
-20% of cases will have metastatic disease, most commonly to the liver and lung

Investigation:
-evaluation of metastatic disease:
-colonoscopy is the gold standard for visualization and biopsy of the tumor
-abd/pelvis CT to help with staging
-see classic “apple core” lesions
-CXR
-labs: CBC, CMP, baseline CEA for follow-up
-PET

Treatment
-surgery
-very early stage tumors may be removed endoscopically
-polypectomy decreases colon cancer death rate by 53%
-hemicolectomy (usually ¼ of the colon) with lymph node dissection
-may need colostomy
isolated mets to other organs may be removed
-local treatment of mets
- radiofrequency ablation
- ethanol ablation
- cryosurgery
- hepatic artery embolization for liver mets to make them necrose
- chemo to eradicate micromets
- begin considering at stage II
- standard of care for stage III, metastatic disease, or unresectable tumors
- radiation is not typically used for colon cancer due to high toxicity in the gut, but may be used for rectal cancer

GI Bleed

Background
- Defined as an intraluminal blood loss anywhere from the oropharynx to the anus
- An “obscure” bleed is one whose source is not identified after upper and lower endoscopies
- An “occult” bleed is detected in an asymptomatic patient
- Occurs more commonly in men
- Acute or chronic, upper or lower (separated by ligament of Treitz)
- Chronic may present as hemoccult + stool, Fe deficiency anemia, or both
- Assessing the GIB patient:
  - how sick are they?
    - vitals
      - resting tachycardia with 10% of intravascular vol lost
      - orthostasis with 10-20% intravascular vol lost
      - shock with 20-40% of intravascular vol lost
    - HPI:
      - frequency, amount of stool
        - blood is cathartic = will accelerate defecation
        - melenic stool means it has been in the GI tract for at least 12-14 hours
      - other symptoms
      - meds associated with GIB: NSAIDS (even baby aspirin), Goody or BC powders, steroids in setting of NSAIDs, warfarin, heparin, enoxaparin, clopidogrel
- PMH: prior bleeding episode, underlying disease (liver), history of radiation to the pelvis, results of previous endoscopies/colonoscopies, prior surgical history
- PE: blood in nose or throat, abdominal exam, signs of liver disease (jaundice, ascites, spider angiomas, caput medusiae, palmar erythema), rectal exam
- Investigation:
  - in a known GIB patient, stool guaiac has no utility because it doesn’t tell you where the bleed is coming from
  - labs:
    - H/H: remember that during a GIB the pt is bleeding whole blood, so the hematocrit won’t change until you start adding fluids and compare
      - can also take up to 2 hours for hct to reflect the extent of bleeding
    - MCV should be normal in acute blood loss
    - BUN rises as blood is broken down to urea with digestion
      - differentiate from a kidney cause by a rise without a proportional rise in creatinine
    - INR
    - platelets
  - rectal exam
- determine source of bleeding and stop active bleeding: EGD, colonoscopy, others
  - NG lavage: dropping an NG tube in to aspirate fluid to look for blood
    - helps delineate upper from lower source
- problem: false negative in ¼ of upper GIBs, does not give information about etiology
- endoscopy: EGD, enteroscopy, and/or colonoscopy
  - both diagnostic and therapeutic potential
  - tagged RBC scan; can pick up a slower GIB (0.1 mL/min) in a safe and non-invasive way but can’t intervene with
  - pre-test for angiography
- angiography: can pick up a bleed of 0.5 mL/min or greater
  - usually only done with positive tagged RBC scan
  - can use to perform coil microembolization of a bleeding vessel

-Treatment:
  - stabilize patient
  - resuscitate with IVF to gain normal BP
  - blood products for hypotensive or tachycardic pts, active bleeding, or those with low hemoglobin
  - d/c anticoagulants and antiplatelets
  - give PPI if suspecting upper GIB
  - if bleeds are variceal → octreotide drip, antibiotics
  - give platelets in renal patients and clopidogrel users, even if #'s are good their platelets don’t work so well
  - treat underlying source of bleeding
  - prevent re-bleeding

☐ Upper GIB
- Causes:
  - common:
    - ulcers: esophageal, gastric, duodenal
      - bleeding occurs from erosion into a vessel
    - risk factors: NSAIDs, H. pylori, acid, steroids with NSAIDs, anticoagulation, alcohol
    - esophageal varices
    - less common causes: malignancy, vascular abnormalities, Mallory-Weiss tear (laceration in the mucosa usually from throwing up a lot, usually near the GE junction), tumors, erosions, Dieulafoy’s lesion (dilated submucosal artery erodes into the mucosa with subsequent rupture of the artery), esophagitis, aorto-enteric fistula
- Presentation:
  - usually acute
  - most commonly hematemesis, but can also have melena or hematochezia depending on speed of bleed
- Investigation:
  - endoscopy to assess risk of re-bleed
- Treatment: most are self-limiting and only require supportive care but requires close follow-up
  - if ulcers are present → PPI, H. pylori eradication if needed, endoscopic therapy (clips, banding, etc)
  - second-line: angiogram, other surgery
  - if bleed is from varices, this can be massive!
    - airway management
    - octreotide, antibiotics if cirrhosis is present
    - EGD with banding
    - compression with Minnesota tube
    - if EGD fails, treat portal HTN causing the bleed → transjugular intrahepatic portosystemic shunt, establishes communication between the inflow portal vein and the outflow hepatic vein
    - if bleed is from vascular lesions:
      - Mallory-Weiss tears are usually self-limiting
- Prognosis:
  - mortality is 8-10%, especially in the elderly

☐ Lower GIB
- Causes:
  - common: diverticular disease, neoplasms, colitis (infectious, ischemic, radiation, IBD)
  - less common: angiodysplasia, hemorrhoids, fissures

- Upper GIB
- Causes:
  - common:
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☐ Lower GIB
- Causes:
  - common: diverticular disease, neoplasms, colitis (infectious, ischemic, radiation, IBD)
  - less common: angiodysplasia, hemorrhoids, fissures
-Increased incidence with age
-Many cases are underreported as most people do not seek medical care
-Presentation is usually hematochezia
  -if diverticular cause ➔ acute and painless hematochezia
-Investigation:
  -procedures:
    -anoscopy
    -flexible sigmoidoscopy
    -colonoscopy: role is not well established for acute lower GIB
      -may have poor visibility and may cause bowel purge during active bleeding
    -tagged RBC scan: can help localize the bleeding
    -angiography
-Treatment:
  -diverticular bleeds usually stop spontaneously but can recur, especially with increasing age
  -fix during scope or angiography
  -further surgical resection: colectomy, hemorrhoidectomy

Iron Deficiency Anemia
-Can result from blood loss, decreased intestinal absorption of iron, or increased red cell destruction
-Check labs
-When unexplained, upper/lower GIB evaluation needs to be conducted

Liver Disease

Background
-History for liver patient:
  -meds: include herbals
  -FH of hemochromatosis, Wilson’s disease, α-1 antitrypsin deficiency
  -alcohol, drugs
  -HIV status
  -exposures: hepatitis, blood products, sex, IVDU or intranasal, travel
-PE:
  -HEENT: icteric sclera, Kayser-Fleischner rings
  -chest: gynecomastia from overproduction of estrogen in cirrhosis
  -abdomen: ascites, small liver, splenomegaly, caput medusae
  -GU: testicular atrophy
  -extremities: edema, palmar erythema, spider angiomata from elevated estrogens
  -neuro: asterixis, coma, encephalopathy
-Liver diseases:
  • hepatitis: inflammation of the hepatocytes
    -can be viral (most commonly), alcohol-related, metabolic, toxin, or medication-related
    -can be acute or chronic
  • fulminant liver failure: a progression to liver failure in < 14 days in a patient without previous liver disease
    -can be viral, autoimmune, ischemic, toxin-related
  • cirrhosis: fibrotic bands and nodules as a result of long-standing liver damage
-Common liver disease presentations:
  • jaundice: yellowing of the skin, conjunctiva, and mucous membranes due to increased bilirubin
    -clinically apparent when bilirubin > 2.5 mg/dL
    -first appears in the eyes and oral mucosa
    -may also have dark urine and light stool
  -malaise/fatigue
  -light stools, dark urine
  -pruritus
  -GIB
-confusion
-edema
-weight loss or loss of appetite
-nause & vomiting
-fever

-Liver labs: AST/ALT, ALP, bili

-Liver transplant
- indicated for hep C, alcoholic cirrhosis (if abstinent at least 6 months), cryptogenic cirrhosis, NASH, PBC, PSC, autoimmune hepatitis, hep B

-assessments:
- **Child-Pugh score**: takes into account ascites, bili, albumin, INR/PT, encephalopathy
- estimates one and two-year survival rates
- **MELD score**: takes into account bili, INR, creatinine
- used to rank liver transplant candidates and assess surgical risk
- scores of 12-15 have a better survival living with the disease than getting a transplant but can be put on the list at this time
- scores of 22+ are ready for transplant
- one year survival is 85%, 3 year 70%

### Viral Hepatitis

<table>
<thead>
<tr>
<th>Source</th>
<th>A</th>
<th>B</th>
<th>C</th>
<th>D</th>
<th>E</th>
</tr>
</thead>
<tbody>
<tr>
<td>Incubation</td>
<td>15-30 days</td>
<td>45-180 days</td>
<td>2-26 weeks</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Transmission</td>
<td>Fecal-oral</td>
<td>Percutaneous/mucosal Transplacental</td>
<td>Percutaneous/mucosal</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Prevention</td>
<td>Immunization, esp for travelers, MSM, drug users, chronic liver disease</td>
<td>Immunization of all adolescents and adults in high risk groups, perinatal prevention</td>
<td>Blood donor screening, don’t share needles, barrier protection during sex</td>
<td>Immunization for HBV</td>
<td>Safe drinking water</td>
</tr>
<tr>
<td>Presentation</td>
<td>ACUTE RUQ pain, n/v</td>
<td>CHRONIC in 5% unless you clear it</td>
<td>Usually no acute flare, just becomes chronic Silently progressive</td>
<td>CHRONIC</td>
<td>ACUTE</td>
</tr>
<tr>
<td>Investigation</td>
<td>† ALT/AST + IgM if acute + IgG if prior/vacc</td>
<td>+ surface Ag with active infection + surface AB with previous infect/vacc + core AB with active or prior infect (NOT vac) + E Ag with active viral replication + E AB in chronic infect w/o replication, + blood DNA in infection</td>
<td>+ AB in present or previous infection + RNA in active infection</td>
<td>+ AB in present or previous infection + RNA in active infection</td>
<td></td>
</tr>
<tr>
<td>Treatment</td>
<td>IFN, antivirals Usually clears spontaneously</td>
<td>Type 1 ➔ direct antivirals, pegylated IFN, ribavirin Type 2 or 3 ➔ pegylated IFN, ribavirin</td>
<td></td>
<td></td>
<td>Benign and self-limiting</td>
</tr>
<tr>
<td>Chronic infection?</td>
<td>No</td>
<td>Yes, especially in kids under 5</td>
<td>Yes in 70%</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Special notes</td>
<td>“Infectious hepatitis” Complications of fulminant hepatitis, cholestatic hepatitis Prevalent in Alaska natives, American Indians</td>
<td>“Serum hepatitis” Chronic increases risk for cirrhosis and HCC #1 cause for liver transplant 6 genotypes, with 1 most common and hardest to treat Liver biopsy useful for staging chronic Requires coinfection with hep B</td>
<td></td>
<td></td>
<td>Increased severity in pregnant women Rare in US Endemic in India, Mexico, Iraq, North Africa, etc.</td>
</tr>
</tbody>
</table>
Viral hepatitis labs:
- WBCs normal to low
- super high AST/ALT
  - followed by ↑ total bili
  - followed by ↑ ALP
- pathogen-specific antigens and antibodies
- proteinuria

Other Causes of Chronic Hepatitis
A.) Hemochromatosis from iron overload
   - labs: high ferritin, Fe saturation, HFE gene testing
B.) Autoimmune hepatitis
   - labs: ANA, anti-smooth muscle, IgG levels
   - treat with prednisone and azathioprine
C.) Wilson’s disease → copper overload
   - labs: low ceruloplasmin
D.) α-1 antitrypsin deficiency
   - lung and liver manifestations
E.) Medication side effects

Alcoholic Liver Disease
A.) Acute alcoholic hepatitis
   - presentation: RUQ pain, n/v, jaundice
   - investigation:
     - labs:
       - AST 2x higher than ALT, but not as high as other etiologies of hepatitis
       - elevated bili
       - elevated INR
   - treatment:
     - prednisone +/- pentoxifylline if discriminant function is calculated to be > 32
B.) Alcoholic cirrhosis
   - average consumption of 8 12 oz beers, 1L wine, or ½ pint of spirits per day for 20 years

Nonalcoholic Fatty Liver Disease: a spectrum of diseases ranging from asymptomatic fat in the liver to NASH to cirrhosis
A.) Non-alcoholic steatohepatitis (NASH): resembles alcoholic liver disease but patients have no history of significant alcohol consumption
   - usually seen in patients with metabolic syndrome
   - presentation:
     - mostly asymptomatic, found incidentally in labs or after development of cirrhosis
     - treatment: weight loss, exercise, tight glucose control, HTN treatment, hyperlipidemia treatment (can use statins in this case!)
     - current research on use of glitazones, vit E
B.) Non-alcoholic cirrhosis: end result of chronic inflammation from a variety of etiologies = alcoholic cirrhosis will also manifest in same way
   - presentation:
     - portal HTN
     - ascites: + fluid wave and shifting dullness
       - can have bacterial infection on top of ascites → abdominal pain, fever, renal insufficiency
     - gastro-esophageal varices
     - splenomegaly → thrombocytopenia
     - encephalopathy from lack of toxin clearance → euphoria, confusion, asterixis, coma
       - can be precipitated by infection, bleeding, hyponatremia, hypokalemia, sedatives, azotemia, blood transfusion, TIPS (shunts blood away from the liver, leading to ineffective clearing of toxins)
-investigation:
  -labs:
    - high INR and low albumin from decreased ability to make proteins
      = low total protein
    - elevated conjugated bili followed by elevated unconjugated bili due to inability of liver to process bilirubin
      - initially problems getting the conjugated bili into bile, then problems conjugating at all?
    - US to check for ascites, portal vein thrombosis (cause of acute ascites)
  - diagnostic paracentesis:
    - truly ascites from portal HTN if difference between serum albumin and peritoneal fluid albumin is > 1.1
    - bacterial peritonitis if > 250 neutrophils
  - histology: fibrosis, regenerated nodules, vascular distortion

-treatment:
  - screen for varices with EGD
    - if present, start on β-blocker to reduce portal pressures
  - ascites:
    - salt restriction, but no fluid restriction
    - diuretics
    - therapeutic paracentesis
    - TIPS procedure if refractory
    - if bacterial infection → 3rd gen cephalosporin, hold diuretics
  - encephalopathy:
    - rule out infection
    - correct electrolytes
    - lactulose: decreases pH to favor NH4+ formation with removal by the gut
    - rifaxamin to kill GI tract bacteria and keep NH4+ levels low
  - transplant

- Predominantly Biliary Liver Disease
  A.) Primary sclerosing cholangitis: inflammation of larger bile ducts leads to scarring and obstruction
  B.) Primary biliary cirrhosis: inflammation of the small bile ducts
    - labs: + anti-mitochondrial AB

- Liver Masses
  A.) Benign
    - solid: in most cases, if patient is otherwise healthy, manage expectantly, but if patient has malignancy elsewhere consider a needle biopsy
      i.) hemangioma: most common benign liver tumor
        - small, asymptomatic, incidental finding
      ii.) hepatic adenoma: associated with long-term estrogen use
        - can rupture and bleed = should be resected
      iii.) focal nodular hyperplasia: may be a response to a congenital vascular malformation
        - resect
      iv.) hamartoma:
        - cystic:
          i.) simple cyst:
          ii.) infectious cyst:
          iii.) polycystic liver:
          iv.) biliary cystadenoma:
          v.) Von Meyenburg complex:
  B.) Malignant
    i.) mets:
    ii.) hepatocellular carcinoma: usually occurs with chronic liver disease or cirrhosis
-diagnostic imaging shows multiphasic tumor (arterial phase hypervascularity with delayed phase washout)
-treat by resection, embolization (temporary measure), radiofrequency ablation, or transplantation

iii.) cholangiocarcinoma:
iv.) rare tumors:
  • hemangioendothelioma:
  • soft tissue sarcoma:
  • primary hepatic lymphoma:
  • non-Hodgkin lymphoma:

Consideration of liver masses
-think about underlying liver disease or primary malignancies present
-symptomatic patient vs incidental finding
-risk factors: age, gender, travel, exposures, medications
-imaging is key

Esophageal Disease

Background
- Anatomy of the esophagus
  -spans from about C6 to T11
  -cricopharyngeus muscle is closed except during swallowing and emesis
  -descends between the trachea and the vertebral column
  -lumen is collapsed at rest and distends with food bolus
  -innervated by the recurrent laryngeal nerve and sympathetic trunks
  -blood supply from aortic branches
- Common esophageal symptoms:
  • pyrosis: heartburn, with pain being substernal, can radiate to the neck
  • dysphagia: difficulty in swallowing liquids and or solids
  -etiology can be oropharyngeal or esophageal, or lie outside of the GI tract
  -esophageal: motility disorder (difficulty swallowing liquids and solids) or mechanical obstruction (difficulty swallowing solids)
  -oropharyngeal: difficult in transferring food bolus to back of mouth
  -may be a neurologic dysfunction (CVA, ALS)
  -can also be caused by Zenker’s diverticulum
  • odynophagia: painful swallowing from inflammation of esophageal mucosa
  -a sign of infectious esophagitis
  -other causes:
    -pill-induced esophagitis
    -meds: doxycycline, tetracycline
    -ingestion of caustic substances
  -chest pain: could be GERD, diffuse esophageal spasm, nutcracker esophagus, achalasia

Esophageal Diagnostic Studies
1.) Barium esophagram: patient swallows barium sulfate to get a better sense of the anatomy of the esophagus and stomach
2.) EGD
3.) Esophageal manometry: catheter with multiple pressure-sensing regions is introduced via the nose or mouth into the esophagus to measure swallowing and peristalsis pressures
  -senses pressures in the pharynx, upper esophageal sphincter, esophageal body (3 areas), and the lower esophageal sphincter
  -assesses function of peristalsis and sphincters prior to any surgical or endoscopic correction for reflux
4.) Ambulatory esophageal pH monitoring: standard procedure for detecting pathologic acid reflux into the esophagus
  -measures frequency of acid contact and duration to correlate to symptoms
-indicated for refractory GERD with normal EGD, atypical symptoms, failure to respond to pharmacologic therapy, and patients being considered for antireflux surgery

**GERD and Complications**

- Involves dysfunction of sphincters and reflux of caustic materials (acid, pepsin, bile, pancreatic enzymes)
- Specific causes: incompetent lower esophageal sphincter, transient lower esophageal sphincter relaxation, refluxate, delayed gastric emptying, impaired swallowing, impaired peristalsis (Raynaud’s, scleroderma), impaired salivary secretion (Sjogren’s), hiatal hernia

- Presentation:
  - Heartburn 30-60 minutes after a meal
  - Sour brash
  - Dysphagia
  - Relief with antacids
  - Esophagitis: does not correlate with severity of heartburn complaint
  - Extra-esophageal manifestations: exacerbation of asthma, cough, non-cardiac chest pain, laryngitis, hoarseness, loss of dental enamel

- Investigation:
  - Diagnosis is usually clinical
  - Procedures:
    - EGD: documents type and extent of tissue damage from GERD, including strictures and Barrett’s
      - Will be normal in up to half of patients with reflux symptoms and won’t detect mild disease
    - Barium studies: limited role in reflux, but will detect strictures, ulceration, and abnormal folds
    - Reveals abnormal motility or esophageal clearance
    - Esophageal manometry
    - 24 hour esophageal probes

- Treatment/management:
  - Uncomplicated ➔ PPI empirically
    - No need for further workup unless there is treatment failure, > 10 year duration of symptoms, warning/atypical symptoms (dysphagia, weight loss, hematemesis, melena, anemia unresponsive to medications)
    - BUT symptom onset after age 50 warrants further invest
  - Lifestyle modifications: elevate HOB, lose weight, stop tobacco, no late night eating, limit alcohol/fatty foods/caffeine/chocolate
  - Acid suppression: decreases acid but NOT reflux!
  - Motility agents
  - Surgical procedures:
    - Nissen fundoplication: tightens area around sphincter in an attempt to make it close more tightly
    - Must screen for Barrett’s with EGD in those with symptoms > 10 years, those over 50, white males

- Complications of GERD:
  - Esophageal/peptic stricture: narrowing or tightening of the esophageal lumen that causes dysphagia
    - May need to be dilated with a balloon to relieve symptoms
  - Increased risk for adenocarcinoma
    - Even symptoms > once per week increases risk by 8x
    - Frequent symptoms increase risk by 44x
  - Barrett’s esophagus: change from squamous to columnar epithelium in esophagus, puts patient at 30-60x risk for adenocarcinoma of the esophagus
    - Chronic reflux ➔ esophagitis ➔ squamous epithelial injury ➔ metaplasia
    - Risk related to extent of Barrett’s
    - On EGD looks like salmon-colored patches with irregular borders, erythema
    - Treat with acid suppression therapy, anti-reflux surgery, endoscopic ablation therapy, esophagectomy

**Infectious Esophagitis**
- Pathogens: CMV, herpes, Candida
- Think AIDS or other immunosuppressive disease with idiopathic ulceration
- Presentation: odynophagia, dysphagia, chest pain, +/- fever
- Investigation: EGD with biopsy, especially if fever

**Structural Disorders**

A.) Esophageal stenosis/strictures
- causes:
  - rings and webs: vaguely describes lesions that can be found anywhere in the esophagus
    - Plummer Vinson syndrome: symptomatic proximally located webs found in middle-aged women with evidence of Fe deficiency anemia
    - Schatzki ring: web occurring in the distal esophagus
  - reflux esophagitis
  - tumors
  - caustic ingestions
  - infections
  - iatrogenic: pills, radiation, sclerotherapy, NG tubes
- treatment: widen stenotic area with balloon
  - can’t be done with active inflammation or ulceration due to risk of perforation

B.) Zenker’s diverticulum: herniation of posterior pharyngeal wall
- most common cause of transfer dysphagia
- usually occurs in men over 60
- presentation: regurgitation, dysphagia, halitosis

C.) Eosinophilic esophagitis: allergic or idiopathic infiltration
- associated with asthma, allergic rhinitis, urticaria, hay fever, atopic dermatitis, food or medication allergy
- presentation: dysphagia, food impaction, reflux
- investigation:
  - EGD or imaging shows strictures, mucosal rings, linear furrowing, “feline” esophagus, eosinophilic abscesses, esophageal polyps
- treatment:
  - initially try PPI as symptoms can be related to GERD
  - allergy testing and elimination diet
  - topical corticosteroids (swallowed fluticasone) or systemic corticosteroids
- complications: perforation

**Motility Disorders**

A.) Achalasia: absence of normal esophageal peristalsis with increased tone of the lower esophageal sphincter (won’t relax)
- causes: Chagas disease, others?
- develops in patients ages 25 to 60
- presentation: months to years of symptoms
  - gradual, progressive dysphagia of both solids and liquids
  - regurgitation of undigested foods, sometimes nocturnally
  - substernal discomfort or fullness after eating
  - poor esophageal emptying
- investigation:
  - manometry is the gold standard
    - shows complete absence of peristalsis, incomplete or absent relaxation of LES
- CXR showing air-fluid level in an enlarged, fluid-filled esophagus
- barium swallow: shows “bird’s beak” from acute tapering of LES at gastro-esophageal junction, esophageal dilation, loss of peristalsis
- EGD to look for cause: stricture, cancer, ring, obstruction
- treatment:
  - meds: smooth muscle relaxers like Ca channel blockers, nitrates
  - balloon dilation of LES: highest perf rate of any esophageal procedure!
  - surgical myotomy
-Botox injection to relax LES

B.) **Diffuse esophageal spasm:** simultaneous, nonperistaltic contractions of the esophagus

- uncommon
  - presentation:
    - intermittent dysphagia
    - anterior chest pain unrelated to exertion or eating
    - provoked by stress, large food boluses, hot or cold liquids
  - investigation:
    - barium swallow shows corkscrew contractions or “rosary bead appearance”
    - manometry shows intermittent, simultaneous contractions of high amplitude not related to swallowing along with periods of normal peristalsis

-treatment: disease is usually self-limiting

C.) **Nutcracker esophagus:** abnormally high pressures during peristalsis

- presentation: chest pain
- investigation:
  - manometry

D.) **Scleroderma esophagus:** atrophy and fibrosis of esophageal smooth muscle ➔ loss of LES competency, decreased peristalsis, delayed gastric emptying

- can also occur in progressive systemic sclerosis, Raynaud’s, or CREST
- presentation: severe acid reflux, strictures, erosions, heartburn, dysphagia

- investigation:
  - manometry: diminished peristalsis with low pressures, hyper-relaxed LES
  - barium swallow: very dilated, flaccid esophagus

- **Esophageal Cancer**

- Recent trend towards adenocarcinoma vs squamous cell carcinoma

- squamous cell carcinoma:
  - risks: alcohol, tobacco, achalasia, caustic-induced esophageal injury, head and neck cancers, Plummer-Vinson syndrome, black ethnicity, male
  - occurs in proximal 2/3 of the esophagus

- adenocarcinoma:
  - risks: Barrett’s esophagus, white ethnicity, males
  - occurs in lower 1/3 of the esophagus

- Usually occurs in ages 50-70
- Presentation: progressive solid food dysphagia, weight loss

- usually is late stage by the time patient is symptomatic

- Investigation:
  - CXR showing mediastinal widening, lung or bony mets
  - barium swallow showing many infiltrative or ulcerative lesions, strictures
  - chest CT
  - endoscopic US for staging

- Complications:
  - tumor fistula into the tracheo-bronchial tree
  - chest or back pain
  - laryngeal nerve impingement
  - pneumonia
  - malnutrition

- Treatment:
  - surgical resection with gastric pull-up or colonic interposition (5-year survival of 20-50%)
  - palliative radiation (5-year survival of 21%)
  - chemo
  - palliative stenting or photodynamic therapy via endoscopy

- Prognosis: overall 5-year survival is 17%
Pancreatic Disease

Background

- Anatomy
  - retroperitoneal, lies behind the stomach against the spine
- Functions
  - exocrine: acinar cells make pancreatic enzymes and zymogens, duct cells make HCO3
  - endocrine: alpha cells make glucagon, beta cells make insulin

Acute Pancreatitis: a syndrome defined by inappropriate activation of trypsin within the pancreas → enzymatic damage to the pancreas → discrete episodes of abdominal pain as well as release of systemic pro-inflammatory mediators

- Numerous causes
  - gallstones are most common
  - alcohol use, although temporal relationship is uncertain
  - obstructions: gallstones, pancreatic or ampullary tumors, sphincter of Oddi dysfunction, pancreatic divisum (malformation of pancreatic duct)
  - medications: diuretics, azathioprine, 6-mercaptopurine, sulfa drugs, ACE inhibitors, HIV meds
  - infections: mumps, rubella, Coxsackie virus, echovirus, EBV, HIV
  - metabolic: ↑ TG, hypercalcemia
  - toxins: ethanol, methanol, scorpion sting in Trinidad
  - vascular: vasculitis, ischemia
  - abdominal trauma: pancreatic contusion, pancreatic duct damage
  - post-ERCP
  - inherited causes: hereditary pancreatitis, cystic fibrosis
  - idiopathic: microlithiasis?

- Presentation: range of severity from mild illness to multiorgan failure
  - constant, epigastric pain radiating to the back
  - nausea and vomiting
  - tachycardia secondary to hypovolemia from leaky blood vessels and third-spacing
  - fever within 1-3 days of onset from retroperitoneal irritation or inflammation
  - sepsis
  - icterus or jaundice with biliary obstruction
  - decreased breath sounds with pleural effusion
  - abdominal tenderness with guarding and rebound tenderness
  - acute interstitial pancreatitis: mild, with pancreatic edema
  - acute necrotizing pancreatitis: severe, with necrosis of parenchyma and blood vessels
    - Gray-Turner’s sign: flank ecchymosis from retroperitoneal hemorrhage
    - Cullen’s sign: periumbilical ecchymosis

- Diagnosis:
  - labs:
    - elevated amylase:
      - problem: not specific, can be elevated in other conditions such as appendicitis, cholecystitis, perforation, ectopic pregnancy, renal failure
      - decreases after the first 24 hours of pancreatitis
    - elevated lipase:
      - more specific for pancreas, but can be elevated in renal failure and other problems
      - elevated for 3 days
      → elevated amylase or lipase alone without clinical signs are NOT pancreatitis!
    - bilirubin will be elevated if there is an obstruction blocking it from leaving the liver
    - elevated BUN if there is volume depletion
    - increased hematocrit if there is volume depletion
  - US showing enlarged, hypoechoic pancreas
  - also look for gallstones, biliary duct dilation
  - CT scan showing pancreatic enlargement, peripancreatic edema
imaging of choice for pancreatic parenchyma: can assess necrosis, extrapancreatic fluid, assess complications
-can be normal in some patients with mild disease
-MRCP
-ERCP

-Treatment:
-NPO? uncertain, feeding the stomach may have an anti-inflammatory effect
-lots of IVF to recover vol from 3rd spacing
-pain meds
-if severe, may need antibiotics (carbapenems) to prevent necrosis, and early jejunal feeds to decrease mortality

Complications:
-pro-inflammatory cascade may cause ARDS, sepsis, renal failure
-fluid collections → no treatment
-pancreatic necrosis → antibiotics
-if infected tissue, also surgical debridement
-pancreatic abscess → antibiotics and CT-guided drainage
-pancreatic pseudocyst (collection of pancreatic juice encased in granulation tissue) → drain after 4-6 weeks to allow rind formation

Chronic Pancreatitis:
-chronic inflammation leads to irreversible fibrosis of the pancreas
-Causes: chronic alcohol use, chronic pancreatic duct obstruction (strictures, tumor, papillary stenosis), tropical chronic pancreatitis (due to malnutrition), autoimmune pancreatitis, hereditary pancreatitis, idiopathic
-Presentation:
-persistent or recurrent episodes of epigastric and LUQ pain
-steatorrhea due to fat malabsorption
-fat soluble vitamin deficiency
-diabetes
-Investigation:
-labs:
-no blood tests to diagnose chronic pancreatitis
-amylose and lipase won’t be elevated because the pancreas is burned out by now
-fecal fat
-fecal elastase will be low because it comes from the pancreas
-secretin stimulation test: give secretin and see if pancreas responds with bicarb secretion
-imaging:
-abdominal x-ray showing pancreatic calcifications (classic)
-CT showing pancreatic calcifications, atrophied pancreas
-MRCP/ERCP showing “chain of lakes” or areas of dilation and stenosis along the pancreatic duct
-endoscopic US

-Treatment:
-abstain from alcohol
-pancreatic enzyme replacement + PPI + low fat diet
-narcs for pain
-insulin
-surgical options:
-ERCP with sphincterectomy or stent placement to open up pancreatic duct
- Puestow procedure: filleting the pancreas, then hotdogging the jejunum in between and connecting it to the pancreatic duct for ease of pancreatic juice flow into the jejunum
-subtotal pancreatectomy of the tail or head
-total pancreatectomy +/- autologous islet cell transplantation into the liver

Pancreatic Adenocarcinoma
-Typically occurs in 70s-80s
-Slightly more common in males
- Most common location is the head of the pancreas
- Risk factors: tobacco use, chronic pancreatitis, exposure to chemicals in dye manufacturing, DM2 in nonobese person arising after age 50, history of partial gastrectomy or cholecystectomy, genetic factors including BRCA 2
- Presentation: jaundice, weight loss
  - cancer in pancreatic head → painless jaundice as it compresses the common bile duct
  - can cause Courvoisier’s sign: palpable gallbladder due to compression of bile duct
  - cancer in pancreatic tail → abdominal pain due to retroperitoneal invasion into the celiac plexus
  - Troisseau’s sign: hypercoagulable state created by the malignancy causes a migratory thrombophlebitis = clots forming, resolving and then appearing again elsewhere in the body
- Investigation:
  - labs: ALP, bili, CA 19-9
  - imaging:
    - CT for “double duct sign” = dilation of common bile and main pancreatic ducts
    - MRI
    - endoscopic US if negative CT/MRI but high clinical suspicion
    - tissue diagnosis: not always needed if imaging is convincing
    - ERCP with brushings and intraductal biopsy
    - CT-guided biopsy: incurs risk of seeding
    - best option is endoscopic US with FNA
- Treatment:
  - surgical resection + radiation if there is no vascular invasion, lymphatic involvement, or mets
  - cancer of pancreatic head → resection of head, common bile duct, gallbladder, gastric antrum, duodenum, proximal jejunum (Whipple procedure)
  - cancer of pancreatic tail → distal pancreatectomy and splenectomy
  - locally advanced disease: radiation only
  - metastatic disease: chemo, pain control, palliative stents
- Prognosis:
  - resectable disease survival is less than 1.5 years
  - locally advanced disease survival is 6-10 months
  - metastatic disease is 3-6 months
  - half of pancreatic cancers are metastatic by time of diagnosis

### Biliary Diseases

#### Background
- Liver makes bile, the gallbladder stores it
  - bile is mostly water, bile salts, pigments, a little bilirubin
  - functions as fat emulsifier, bactericidal properties, neutralizes stomach acid
- Each time bile is released, 95% of it is recycled at the terminal ileum back into the liver → multiplied by 5-15x per day = 20-30% of bile excreted in feces each day
- Risk factors for developing disease: obesity, bariatric surgery or rapid weight loss, multiparity, female sex, FH, certain drugs including TPN, Native American or Scandinavian, ileal disease, increasing age
  - the “5 F’s” are Fat, Female, Forty, and Fertile, and FH
  - the “2 C’s” are Crohn’s, cirrhosis
  - the “2 D’s” are diabetes, drugs

#### Labs in Biliary Disease
- Hepatocellular disease:
  - causes very high AST, ALT
  - mildly high or normal ALP
  - increased unconjugated bilirubin
- Biliary disease:
  - high AST, ALT
  - very high ALP
-increased conjugated bilirubin

**Imaging in Biliary Disease**

- Gallbladder US: good for detecting gallstones and evaluating dilated bile ducts
  - less sensitivity with obesity
  - hard to assess liver or pancreas
- CT or MRI
  - MRI better than CT for detecting gallstones in the bile duct
- ERCP: used before an MRCP for diagnosis
  - very sensitive and can use to perform therapy
  - requires sedation or anesthesia
  - risks of bleeding, infection, pancreatitis, and perforation
- MRCP: the most sensitive non-invasive test for detection of gallstones
  - costly = used for diagnosis only if there is uncertainty
- Percutaneous transhepatic cholangiogram (PCT): needle inserted externally into right hepatic duct, contrast injected, x-rays taken
  - can do therapy like ERCP but much more uncomfortable = used when ERCP is not feasible
- Endoscopic US
- HIDA scan

**Gallbladder Disease**

-Diseases are on a spectrum:
  a.) asymptomatic cholelithiasis
  b.) biliary colic (symptomatic cholelithiasis): gallbladder is contracting against an obstruction in the gallbladder or cystic duct
    - types of stones:
      - cholesterol: located within the gallbladder, think five F’s
      - black pigment stones: located within the gallbladder, made of calcium bilirubinate, think cirrhosis or chronic hemolysis (sickle cell)
      - brown pigment stones: form in bile ducts, made of unconjugated bilirubin, think bile duct infection
        - most common kind of stone
    - presentation: RUQ or epigastric pain for 30 min to several hours (until gallbladder manages to squeeze stone out of the way), nausea or vomiting
      - triggered by fatty foods
    - labs are normal
    - imaging: no dilated ducts seen with this
      - US to look for hyperechoic mobile stones, acoustic shadow from obstruction of flow
      - test of choice!
    - can also do CT
    - treatment: elective cholecystectomy if complications or symptoms are severe enough
      - bile duct is not removed, so patients can still form bile duct stones (choledocholithiasis)
  c.) acute cholecystitis: when stone impacts in cystic duct or gallbladder neck → gallbladder distension, inflammation, and edema → secondary bacterial infection → necrosis
    - presentation: fever, nausea, vomiting, RUQ and epigastric pain/riidity/guarding > 6 hours
      - Murphy’s sign: inspiratory arrest with palpation of RUQ
      - referred pain to shoulder not frequently seen
    - labs: ↑WBCs with left shift, mild AST/ALT, bili, ALP, ↑ amylase, ↑ lipase
    - imaging: no dilated ducts
      - US: detects gallbladder wall thickening, pericholecystic fluid, impacted stone
      - can do US Murphy’s sign
      - first-line test
      - HIDA scan if US is negative but high clinical suspicion
    - treatment: IV antibiotics, IV fluids, analgesia, cholecystectomy in 2-3 days
  d.) choledocholithiasis: when gallstone travels to the common bile duct → decreased bile flow
-presentation similar to symptomatic cholelithiasis

-investigation:
  -labs: mild bili, mod ↑ ALP (distinguish from other causes via elevated ALP), transient ↑ALT/AST
  -imaging: dilated ducts

-treatment: ERCP with stone extraction followed by cholecystectomy

-complications: cholangitis, pancreatitis

e.) ascending cholangitis: when choledocholith creates a blockage → bacterial infection

-presentation:
  -Charcot’s triad: RUQ pain, jaundice from no bile to excrete bilirubin, fever
  -Reynold’s pentad: Charcot’s + hypotension and mental status changes, suggests sepsis

-investigation:
  -labs: ↑WBCs, ↑ AST/ALT, ↑direct bilirubin and ALP
  -may have + blood cultures
  -imaging: dilated ducts

-treatment: IV antibiotics, IVF followed by urgent biliary decompression via ERCP, followed by cholecystectomy if etiology was stones

e.) gallstone pancreatitis: when stone blocks pancreatic duct

-Other diseases:
  a.) acalculous cholecystitis: occurs in the absence of gallstones in critically ill patients, progresses to gangrene and perforation if untreated
    -can also present as emphysematous cholecystitis: infection of gallbladder with gas-forming organism
    -US will show bubbles in gallbladder wall
    -in this case emergency surgery is required
    -ALP is often elevated unlike typical cholecystitis
    -treatment: IV antibiotics, cholecystectomy or percutaneous cholecystostomy tube if too ill
  
b.) malignant biliary obstruction: insidious onset of painless jaundice due to malignancy causing obstruction of the bile duct
    -presentation:
      -overall the presence of Courvoisier’s sign is rare
    -investigation:
      -labs: ↑ ALP, ↑ direct bili
      -imaging for dilated duct proximal to obstruction, mass lesions, double duct sign with pancreatic cancer
      -tissue diagnosis via ERCP with brushing, endoscopic US with FNA, guided biopsy for liver mets
    -prognosis: generally poor for cancers that cause this symptom

Infectious Diarrhea

-What is diarrhea?
  -greater than 3 BMs per day (or > 200 g/day) that are loose or liquid
  -“acute” diarrhea is present for < 14 days and is infectious
  -“persistent” diarrhea lasts 14-30 days
  -“chronic” diarrhea has been going on for > 1 month
  -think malabsorption, motility disorders, inflammation

-Kinds of diarrhea:
  • osmotic diarrhea: acts in lumen to suck water into the gut
    -diarrhea should stop with removal of offending agent
    -ex. lactose malabsorption
  • secretory diarrhea: a result of enhanced anion secretion from gut enterocytes
    -can be massive
    -doesn’t stop with fasting
-ex. enterotoxin-induced diarrhea

-Clinical evaluation of diarrhea:
  -most are self-limiting and last < 1 day
  -assess severity of disease:
    -volume status: general appearance, vitals, mucous membranes, skin turgor, cap refill
    -duration of symptoms: concerning if > 2 weeks
    -inflammatory components: fever, bloody stools, tenesmus
    -alarm symptoms: severe abdominal pain, hospitalized patient, recent antibiotic use, elderly,
      immunocompromised, systemic signs (especially if pregnant)
  -investigation:
    -want to determine viral, bacterial, or parasitic
      -travel, day care, hobbies, antibiotics, sick contacts, recent dietary habits
    -stool studies: only send if diarrhea is persistent or recurring, h/o fever or tenesmus, other warning
      signs!
      -cultures: costly and diagnostic yield is very low
      -fecal leukocytes can be helpful in determining inflammatory diarrhea
  -initial treatment:
    -rehydration: oral solutions
    -BRAT diet
    -avoid lactose

-**Infectious Diarrhea**
-**The 3 most common causes are Shigella, Salmonella, and Campylobacter**
-**Bloody? MESSY CACA!**
  -M = medical disease
  -E. coli:
    -0157:H7
      -associated with warm weather
      -transmission: undercooked beef, unpasteurized juice, spinach
      -incubation period depends on whether it produces toxin or not
      -presentation: mild or severe symptoms
        -fever
        -toxin \( \rightarrow \) hemorrhagic colitis: severe abdominal pain, bloody diarrhea
      -treatment: don’t give antibiotics because it can cause/worsen HUS
      -complications: HUS, ARF, thrombocytopenia, microangiopathic hemolytic anemia
        -usually in kids < 10
      -traveler’s diarrhea = usually ETEC
        -occurs in less developed areas
        -treatment: antibiotics (cipro or rifaximin) may decrease duration of illness
  -Shigella:
    -features a Shigatoxin that confers high virulence
    -associated with day care, nurseries, long-term care
    -more common in peds
    -transmission is fecal-oral
    -incubation of 1-3 days
      -low inoculum needed
    -presentation: lower abdominal cramps, diarrhea, fever, bloody and purulent stool, tenesmus
    -treatment: should be self-limiting in less than 7 days, but antibiotics are recommended (cipro or
      Septra)
      -antibiotics decrease duration by 2.4 days, decrease fever, decrease tenesmus, reduce
      excretion of organism
      -complications: Shigatoxin may cause HUS
  -Salmonella:
    -food poisoning salmonellosis (many species)
      -increased incidence in kids < 5 and adults > 60
-transmission: animals, ingestion of contaminated foods (poultry, eggs, dairy), or fecal-oral
-high inoculum needed
-incubation of 6 hours to 3 days
-presentation: fevers, myalgia, abdominal cramping, headache
-worse illness in the very old, young, or immunosuppressed
-complications: septicemia or bacteremia, osteomyelitis (esp sickle cell), endocarditis, arthritis

-Salmonella enterica serovar Typhi
-bacteria pass through intestinal epithelia to enter the liver, spleen, and bone marrow
-prevention: vaccine for travelers
-presentation:
-typhoid fever = fever with bradycardia
-10-14 days after ingestion → fever, headaches, myalgia, malaise, anorexia, followed by GI symptoms from colonization of the gallbladder and reinfection of the intestines
-can become a chronic carrier due to gallbladder colonization

-Yersinia enterocolitica:
-affects the terminal ileum
-transmission by ingestion of contaminated food or water
-presentation: diarrhea, fever, abdominal pain for 1-2 weeks, enlarged lymph nodes
-may mimic appendicitis
-can be chronic for months
-prognosis: high mortality with systemic disease

-Campylobacter jejuni:
-most produce a toxin that prevents infected cells from dividing and alerting an immune response
-transmission by animals (esp chickens), contaminated food, milk, or water
-incubation of 1 weeks
-presentation: dysentery, bacteremia
-treatment: illness is usually self-limiting but can last a week or longer
-consider antibiotics (azithromycin) in AIDS or immunocompromised
-must be started within 4 hours of onset
-complications: Guillain-Barre syndrome, reactive arthritis

-Amoeba → Entamoeba histolytica
-C. difficile:
-most common cause of nosocomial diarrhea
-considered to be an antibiotic-induced diarrhea
-transmission by spores
-diagnose with toxin test
-treatment: Flagyl or oral vancomycin

-Aeromonas:
-Water?
-viruses: rotavirus, norovirus, adenovirus
-most common is norovirus
-usually occurs in winter, except for adenovirus which is year-round
-fecal-oral, person-to-person, or contaminated foods
-usually self-limiting
-bacteria: Staph aureus, Bacillus cereus, Vibrio

-Staph aureus, Bacillus cereus, Clostridium perfringens → illness caused by ingestion of pre-formed toxin = fast onset
-Staph aureus:
-transmission by ingestion of contaminated food (from carrier’s skin or nose)
-likes potato salad, meats, custard-filled pastries, ice cream
-presentation: symptoms within 4 hours that are short-lived
-Bacillus cereus:
-prevention: refrigeration
transmission by ingestion of contaminated fried rice, meats, sauces
-presentation: emesis within 1-6 hours of ingestion, longer for diarrheal illness

-Clostridium perfringens:
-prevention: heating to destroy toxins
-transmission by ingestion of contaminated meats and poultry
-incubation of 8-24 hours
-presentation: abdominal cramps, watery diarrhea, nausea, vomiting, NO fever
-lasts less than 24 hours

-Vibrio:
-activates intestinal adenylate cyclase → blocks Na and Cl absorption and promotes Cl excretion → severe profuse diarrhea
-transmitted in contaminated seafood or contaminated water (developing countries)
-incubation of 12-24 hours
-at risk: patients with liver disease and iron overload
-presentation: watery “rice-water” diarrhea, abdominal cramping, hypotension
-can also infect wounds
-treatment: oral rehydration, single dose fluoroquinolone
-prognosis: mortality is 50% if untreated!

-parasites: Giardia, Crypto, Entamoeba histolytica
-diarrhea lasts longer than 7 days

-Giardia:
-associated with contaminated streams, day care centers, and well water
-presentation: diarrhea is foul and watery, also have cramps and farts
-infection can become chronic in those with hypogammaglobulinemia, IgA deficiency, and even in the immunocompetent
-diagnose with antigen stool testing

-Entamoeba histolytica:
-causes necrosis of the large intestine
-more common in tropical areas
-at risk: travelers, MSM
-presentation: abdominal pain, cramping, colitis, diarrhea (can be bloody), fevers
-immunocompromised → think Cyclospora, Isospora, Cryptosporidium, Microsporidia
-present in environment and water supply

-Don’t use anti-motility agents in inflammatory diarrheas like Shigella, C. diff, E. coli 0157
-Loperamide: an opiate without systemic effects that inhibits peristalsis
-helpful to use in conjunction with antibiotics for traveler’s diarrhea
-Bismuth subsalicylate
-good in kids and traveler’s diarrhea, slightly helpful in norovirus

-Antibiotics
-may be used in Shigella, traveler’s diarrhea, C. diff, Campylobacter
-need to weigh risks and benefits
-may prolong shedding of Salmonella or C. diff and can worsen Shigatoxin of EHEC
-make sure there are no risk factors for EHEC before giving (visible blood without fever, June-September presentation, ground beef, petting zoos, etc)
-best if started early
-bottom line: if concerned for severe infectious diarrhea, first choice is cipro or other FQ, second choice is Septra, if Campylobacter use azithromycin
-otherwise, just treat supportively!

Inflammatory Bowel Disease

-IBD = Crohn’s disease or ulcerative colitis
-Pathophysiology: exact etiology unknown
  -both are autoimmune, chronic inflammatory disorders of the GI tract
  -tends to run in families
  -may be response to environmental triggers (infection, drugs, other agents) interacting with a genetically susceptible individual

-Epidemiology:
  -incidence is highest in Westernized countries, with a bimodal distribution in 15-40 year-olds and > 60 year-olds
  -Crohn’s more common in Caucasians, with higher risk in Ashkenazi Jews, and lower incidence in Latinos and Asians
  -UC: Ashkenazi Jews and Caucasians have higher incidence rates than other ethnic groups

-Presentation:
  -diarrhea (often bloody), fatigue (may be anemia), weight loss, fever, anorexia, n/v, crampy abdominal pain
  -tend to have a relapsing & remitting course
  -extraintestinal manifestations: generally limited to the eye, skin, liver, and joints
    a.) primary sclerosing cholangitis: a chronic liver disease caused by progressive inflammation and scarring of the bile ducts of the liver → stricturing
      -usually symptomatic, may have puritus
      -usually initially detected as an ↑ ALP
      -confers high risk for colon cancer! get a colonoscopy ASAP and screen annually
    b.) arthritis: spondylitis & sacroiliitis
      -usually asymptomatic, or pain/stiffness in back and buttocks
    c.) skin manifestations
      -erythema nodosum: raised, tender, red-purplish nodules
        -most commonly on the extensor surfaces of the extremities
        -may parallel IBD therapy
        -may need to treat with steroids
      -pyoderma gangrenosum: necrotic inflammation, from papules to widespread necrosis
        -parallels IBD activity half the time
        -don’t biopsy!
        -may require topical therapy
        -colectomy may be needed
    d.) eye manifestations
      -uveitis: inflammation of the middle layer of the eye
        -eye pain, blurred vision, photophobia, headaches
        -requires prompt diagnosis and treatment to prevent complications
        -topical and systemic steroids
      -episcleritis: superficial inflammation of the sclera
        -treat with topical therapy or IBD-directed therapy
e.) aphthous ulcers

-Investigation:
  -differential: infectious diarrhea (always think of this if symptoms are less than 2-3 weeks), ischemia (elderly, PVD, thrombosis), meds (NSAIDs, penicillins, mycophenolate), diverticulosis
  -no gold standard for diagnosis!
  -relies on a combination of endoscopy, histology, radiography, labs, and clinical data
  -possible studies:
    -colonoscopy with ileal intubation and biopsy
    -small bowel follow-through
    -enteroclysis +/- CT
    -MR enterography
    -capsule endoscopy?

-General principles of IBD management:
  -not everyone needs continued treatment or any treatment at all
  -mild disease may be better than taking daily pills
  -infrequent disease may respond to short steroid treatment
  -treat the affected area: proctitis, ileal disease, etc.
-not everyone responds to the same treatment
-response to any given therapy is 30-70%
-high placebo effect
-lots of trial and error
-drugs:
-use as little steroids as possible, and try to get on another therapy as quickly as possible
-use sparingly to induce remission
-modest doses are all that is needed
-patients can become steroid-dependent
-side effects of steroids: cataracts, hyperglycemia, weight gain, loss of bone density, easy bruising, striae, moon-facies, acne
-assess risk for osteoporosis using questionnaire
-may need PCP prophylaxis
-yearly eye exams
-bone density monitoring
-vit D/Ca supplementation
-blood glucose monitoring
-6-mercaptopurine ↔ azathioprine: impair T cell function
-takes 2-4 months to work, so begin with steroids and wean them off
-TNF antibodies: inhibit TNF
-high risk for TB reactivation
-must adhere to treatment to prevent side effects
-malignancy risk

-remember that live vaccines are contraindicated for patients on immunosuppressive therapy such as high-dose steroids, anti-TNF agents
-screening for colon cancer:
-begin 8 years after onset of symptoms
-colonoscopies every 1-2 years
-or every year if there is concomitant primary sclerosing cholangitis
-risk increases with time and degree of inflammation

-surgical procedures:
-colectomy may be needed for dysplasia, cancer, toxic colitis
-watch for complications!
-extra-ocular manifestations
-frequent UTIs/pneumaturia → fistula to bladder
-high fever or abdominal mass → abdominal or liver abscess
-severe abdominal pain → perf
-nausea and vomiting → obstruction
-severe rectal pain → perirectal abscess
-drug side effects

-Management of an acute flare:
-compare to previous flares to look for worrisome features
-rule out infection, obstruction
-check WBCs, H/H
-consider if it is a medication side effect
-short course of steroids
-follow-up
-endoscopy if not improving

☐ Crohn’s Disease
-Can affect any portion of the GI tract from lips to the anus and can involve entire thickness of bowel wall (transmural)
-Disease tends to skip areas → skip lesions
-Presentation:
-aggravated by smoking
-Complications:
- Fistulas around the anus and internally → abscesses
- Must be surgically repaired
- Abdominal strictures → obstruction

-Treatment:
- Drugs:
  - Corticosteroids
    - Budesonide is directed at the terminal ileum = fewer side effects
  - 6-mercaptopurine/azathioprine
  - Methotrexate
  - Infliximab, adalimumab, certolizumab, natalizumab (risk of JC virus)
- Surgery: General principle is to try to avoid surgery unless absolutely necessary!
  - May need segmental resection for fibrotic structures, obstructions, fistulas

Ulcerative Colitis
- Disease begins in the rectum and is limited to the colon, and has only superficial penetration of the mucosal wall
- Disease is usually continuous
- Characterization:
  - “Mild” if ≤ 4 BMs per day, no signs of systemic disease (fever, tachycardia, anemia), normal ESR
  - “Severe” if > 6 BMs per day and evidence of systemic disease
- Presentation:
  - Proctitis → tenesmus, lower abdominal or pelvic cramping
  - Bloody diarrhea
- Investigation:
  - H/H showing anemia
  - Low serum albumin
  - Elevated ESR
  - Negative stool cultures
  - Sigmoidoscopy
- Treatment:
  - DOC are 5-ASAs (sulfasalazine, mesalamine, etc)
    - Formulated for delivery to a specific area: colon, small intestine, etc.
    - Highly effective in mild-mod disease or for maintenance after induction of remission
  - Corticosteroids
  - 6-mercaptopurine/azathioprine
  - Infliximab
- Complications:
  - High risk for colon cancer

Irritable Bowel Syndrome

IBS
- Defined as chronic abdominal pain and altered bowel habits in the absence of any organic cause
  = A function disorder
  = A diagnosis of exclusion, need to rule out IBD, infections, cancer
- Subtypes:
  - Constipation-predominant = IBS-C
  - Diarrhea-predominant = IBS-D
  - Mixed = IBS-M
- Pathophysiology:
  - Altered bowel motility: Motor abnormalities may be detected in IBS such as increased frequency and irregularity of luminal contractions, prolonged transit time, exaggerated motor response after eating (or after being given CCK)
  - Visceral hypersensitivity: IBS patients may experience pain and bloating at lower thresholds than controls
    - There is also increased cerebral cortex activity during this time
• Intestinal inflammation: there is an increased number of lymphocytes in the colon and small intestine of patients with IBS.
  - Causes release of mediators such as nitrous oxide, histamine → stimulation of enteric nervous system.
  - Increased mast cells.
  - Increased serine protease activity.

• Post-infectious: there is a 6x greater risk of developing IBS after an episode of acute infectious gastroenteritis.
  - Risk factors: young age, prolonged fever, anxiety, depression.
  - May be due to development of bile acid malabsorption, increased T cells, or altered microflora.
  - Alteration in fecal microflora and bacterial overgrowth: abnormal breath tests with more hydrogen and methane in some but not all IBS pts.
  - Food sensitivity: IBS pts with elevated IgG may improve symptoms by eliminating certain food groups.
  - Potential overlap of IBS with lactose intolerance and celiac diseases.
  - Psychiatric: many IBS patients have psych comorbidities.
  - May be exacerbated by stress.

-Epidemiology:
  - Very common, in 10-15% of the population.
  - More common in females.
  - Most common in 20s-40s.
  - The #2 cause of work absenteeism.

-Triggers: infection, diet, lifestyle changes, psychological stress.

-Presentation and diagnostic criteria:
  - Manning criteria: pain relieved with defecation, more frequent stools at onset of pain, looser stools at the onset of pain, visible abdominal distension, passage of mucus, sensation of incomplete evacuation.
    - Highly specific but low sensitivity.
  - Rome criteria: for at least 3 days a month for at least 3 months (and at least 6 months prior to diagnosis), there is recurrent abdominal pain or discomfort plus ≥2 of the following:
    - Improvement with defecation.
    - Change in frequency of stool.
    - Change in form of stool.

-Other common symptoms supporting diagnosis: urgency, feeling of incomplete BM, bloating.

-Investigation:
  - Differential: diet cause, infection, inflammatory bowel, psychologic, malabsorption, tumors, endometriosis.
  - Fecal occult blood.
  - Labs:
    - All: CBC, CMP, ESR, serum albumin, consider TSH.
    - IBS-D: celiac panel +/- fecal fat, stool culture.
  - Imaging:
    - IBS-C: abdominal x-ray.
    - Consider flexible sigmoidoscopy if under 45 or colonoscopy if over 45.

*** Red flags for something that is NOT IBS: abnormal exam, fever, + fecal occult, weight loss, onset in older patient, nocturnal awakening, low hemoglobin, ↑ WBCs, ↑ ESR.
  - These patients definitely need a colonoscopy.

- Additional specialized studies: not routinely done in IBS patients.
  - IBS-C: colonic transit, anal manometry and balloon expulsion, rectal sensation and emptying, defecography.
  - IBS-D: stool osmolarity and electrolytes, laxative screen (if you suspect malingering), small bowel and colonic transit, rectal sensation, cholestyramine trial.
  - Symptoms of pain and bloating: small bowel series, antidepressant trial, CHO-H2 breath test, small bowel manometry.

- General principles for treatment:
  - Develop a therapeutic relationship.
  - No judgments.
  - Establish realistic expectations.
  - Involve patient in decision-making.
-patient education: no cure but no change in life expectancy
-dietary modification: 2 week trial of lactose avoidance, avoiding bloating foods, fiber trial
-psychosocial therapies: psychotherapy, biofeedback, hypnosis
-pharmacologic therapy is tailored to patient symptoms
  -not usually needed until IBS is moderate to severe
  -for abdominal pain:
    -antispasmodics: for PRN short-term relief
      -ex. dicyclomine, hyoscyamine, peppermint oil, pinaverium
    -antidepressants: reduce pain
      -ex. TCAs (most data), SSRI, SNRI
  -for diarrhea:
    -antidiarrheal: PRN, use cautiously if patient has mixed IBS
      -ex. loperamide
    -antibiotics? may improve global IBS symptoms
      -ex. rifaximin
  -for constipation:
    -1st line are bulking laxatives
      -ex. methylcellulose, psyllium
    -2nd line are stool softeners, osmotic laxatives, and simulant laxatives
      -ex. docusate, polyethylene glycol, lactulose, sorbitol, glycerol, mag cit, bisacodyl, Senna
  -for refractory cases → lubiprostone twice daily
-Prognosis: most remain symptomatic 5 years after diagnosis

**Peptic Ulcer Disease and Gastric Cancer**

**Background**
-PUD is defined as defects in the gastric mucosa that result from an imbalance between enzymatic activity and mucosal injury
-**Epidemiology:**
  -typically occurs between ages of 25-64
  -at risk: previous GI event, old age, use of anticoagulants, corticosteroids, NSAIDs, chronic diseases
-**Causes:** *H. pylori*, NSAIDs, excess acid
-**Prevention:** Cox-2 inhibitors vs NSAIDs, mucosal protection with 33isoprostol, PPIs, high-dose H2 blockers
-**Presentation:**
  -burning pain localized to the epigastrium that is non-radiating
  -gastric ulcers are worse after meals, duodenal ulcers are better after meals
  -pain that awakens patient from sleep between 2-3am
  -can also be asymptomatic
-**Investigation:**
  -upper GI series
  -EGD to characterize lesions and biopsy
  -**H. pylori** test
-**Treatment:**
  -meds:
  -surgery: rarely indicated
    -complete or partial gastrectomy
    -vagotomy
-**Complications:**
  -ulcer re-bleeding
    -higher for pigmented ulcers and adherent clots
  -hemorrhage
  -perforation of ulcer into adjacent peritoneum or organ
  -gastric outlet obstruction
PUD Caused by *H. pylori*

- Associated diseases
  - active chronic gastritis: can progress to atrophic gastritis
  - duodenal ulcers: 60-95% of patients with this have HP
  - gastric ulcers: > 80% of patients with this have HP
  - non-ulcer dyspepsia: 50% of patients with functional dyspepsia have HP
  - increased risk for gastric adenocarcinoma, MALT lymphoma

- Transmitted fecal-oral, with stomach being the only known reservoir
- Present in 40-50% of the general population
  - chance of getting gastritis from it increases with age
  - more common in blacks, Hispanics, lower SES, institutionalized individuals

- Treatment:
  - eradication of *H. pylori*
    - triple therapy:
      - confirmation of eradication by urease breath test or stool test
- Complications: up to 20% of cases may require retreatment
- Prognosis:
  - eradication reduces duodenal ulcer relapse to near zero, decreases rate of gastric ulcer relapse, and decreases risk of gastric cancer and MALT lymphoma

PUD Caused by NSAIDs

- Mechanism of injury:
  1. NSAIDs injure the gastric epithelium → interruption of mucosal barrier
     - occurs within one hour of ingestion
     - erosions develop with repeated doses in 24 hours
     - patients on chronic NSAIDs will have persistent findings of abnormal mucosa
     - degree of mucosal interruption is not predictive of ulcer development
  2. NSAIDs decrease prostaglandin synthesis → decreased mucin production, decreased mucosal blood flow, decreased bicarb production = loss of protective effects

PUD Caused by Excess Acid

- Parietal cells are stimulated to secrete HCl via histamine, Ach, and gastrin
- can act synergistically
- inhibited by somatostatin

- Causes:
  - Zollinger-Ellison syndrome: pancreatic gastrinoma → excess gastrin → excess HCl produced → peptic ulcers
    - causes can be sporadic or associated with MEN I syndrome
    - peptic ulcers will be in the duodenal bulb, distal duodenum, and jejunum
      = in the “gastrinoma triangle”
    - these ulcers will be resistant to treatment and will recur after gastric surgery
    - also associated with GERD, steatorrhea from large acid load (inactivates pancreatic enzymes)
    - investigation:
      - fasting gastrin or secretin test
        - secretin should have no effect on gastrin in normal patients but will ↑↑ gastrin in ZE
      - endoscopic US + somatostatin-R imaging
- Treatment:
  - high-dose PPI
  - surgical resection if no metastatic disease
  - metastatic disease → chemo, resection of liver mets, hepatic arterial embolization
- Prognosis: 15-year survival of 83% without mets
  - baseline fasting serum gastrin may have prognostic value
  - think of this in cases of multiple ulcers, refractory ulcers, or distal ulcers
Gastric Cancer
- High incidence in Korea, Japan, China
- More common in men and tobacco users
- Usually occurs after age 60
- Presentation:
  - early disease is asymptomatic
  - indigestion, nausea, early satiety, anorexia, weight loss
  - advanced: pleural effusions, GOO (?), gastroesophageal obstruction, SBO, bleeding
  - PE: palpable stomach, hepatomegaly, pallor, Virchow’s node and Sister Mary Joseph node
- Investigation:
  - EGD
  - endoscopic US
  - barium swallow
  - CT/MRI
- Treatment depends on stage
  - resection, chemo, radiation, adjuvants if needed
- Prognosis: difficult to cure, most die of recurrent disease even after resection
Gynecology Exam Notes

Gynecologic Anatomy

☑ Pelvic Anatomy
- Pelvic cavity bordered by the abdominal cavity and pelvic floor
  - Pelvimetry can be used to describe type of pelvis a woman has
    - but not correlated to outcome of childbirth
    - most common and “ideal” is gynecoid
  - Pelvic ligaments include the anterior & posterior sacroiliac ligaments, pubic symphysis, sacrotuberous ligament, sacrospinous ligament
    - loosen during pregnancy due to release of hormones
- Female erectile tissue: corpora cavernosa, bulbs of the vestibule, glans clitoris
- Glands:
  - Skene’s (paraurethral) are at 10 and 2 o’clock around the vestibule
  - Bartholin’s (greater vestibular) are at 4 and 8 o’clock around the vestibule
    - prone to abscess
  - Pelvic cavity muscles:
    - lateral wall: obturator internus, piriformis
    - floor: levator ani, coccygeus
    - weakness here can result in urinary or fecal incontinence
- Perineal body is located between the vagina and rectum
  - pelvic floor muscles and perineal membrane attaches here
  - where episiotomy is performed
  - “Uterine adnexa” = uterine tubes + ovaries
- Pelvic organs are draped in a fold of parietal peritoneum
- All lymphatic drainage in pelvic cavity (except for ovaries) goes from the external iliac nodes ➔ lateral aortic nodes
- Innervation via the sacral plexus (L4 to S4)
  - innervates pelvic floor and wall muscles
  - branches into the sciatic, gluteal, pudendal nerves
    - pudendal supplies the perineum
    - palpate ischial tuberosities to find right place for pudendal nerve block to perineum

☐ Development of Reproductive Organs
- Male ducts are Wolffian
  - testosterone causes regression of Mullerian ducts
- Female ducts are Mullerian
  - default sex
  - remnants of Wolffian ducts form Gartner’s duct (can form cysts)

☐ Vagina
- Recto-uterine pouch is the deepest fold of parietal peritoneum located between the vagina and rectum
  - can be used to surgically access the abdomen via the posterior fornix of the vagina
- Blood supply via vaginal artery and vein
  - comes off of anterior trunk of internal iliac
- Innervation:
  - upper 2/3 visceral sensory
  - lower 1/3 somatosensory
- Transverse vaginal septum is a result of incomplete fusion of the urogenital sinus and Mullerian ducts

☐ Cervix
- Made of non-muscular, collagenous tissue
- External os, internal os, and cervical canal
- Contains glands that may form Nabothian cysts (usually self-resolving)