Biliary Disease

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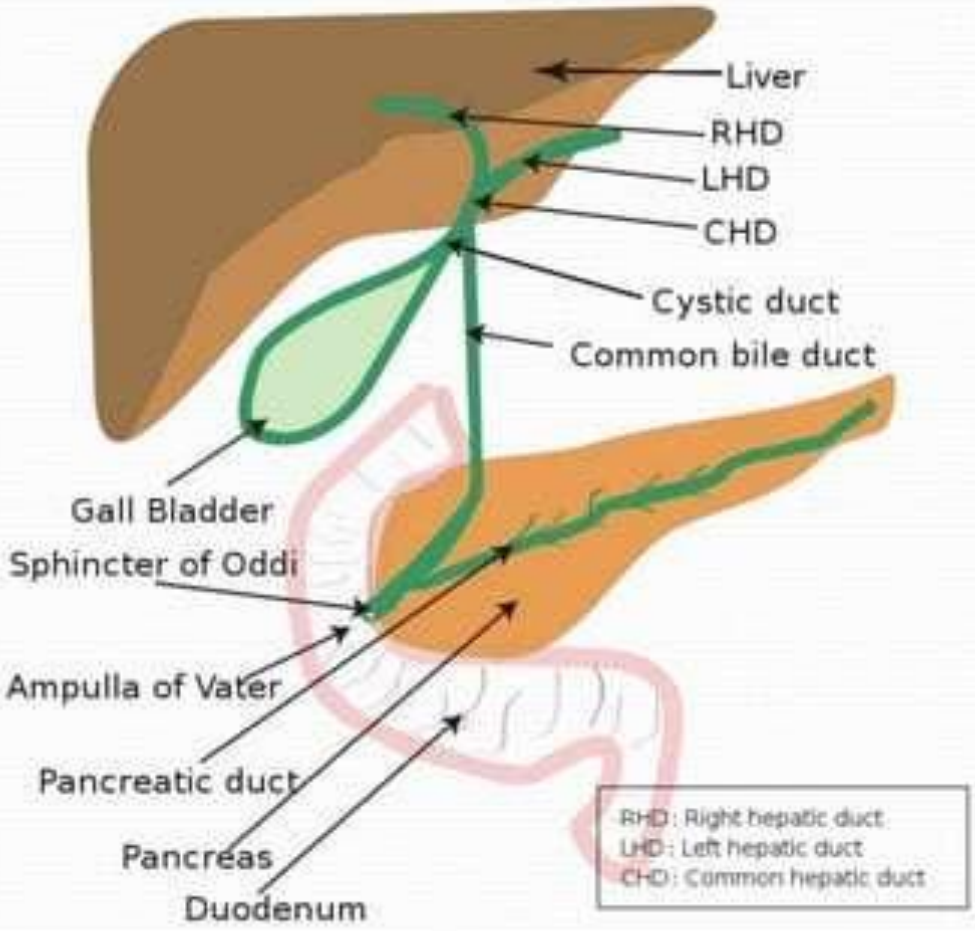
Objectives

- Define bile, bile salts, and bile acids, and state the function of each.
- Indicate which bile salts are the "primary" bile salts.
- Describe bile acid metabolism and the enterohepatic circulation.
- Define cholestasis.
- Describe the diagnostic approach to the patient with cholestasis.
- Describe the causes of cholestasis.
- Define gallstone.
- Describe the pathophysiology of gallstone formation.
- Describe the clinical features of gallstones.
- Discuss the clinical features, lab tests and imaging studies useful in the diagnosis of gallstone disease.
- Discuss the treatment of gallstone disease.
- Define cholesterolosis.
- Define biliary dyskinesia.

Biliary System

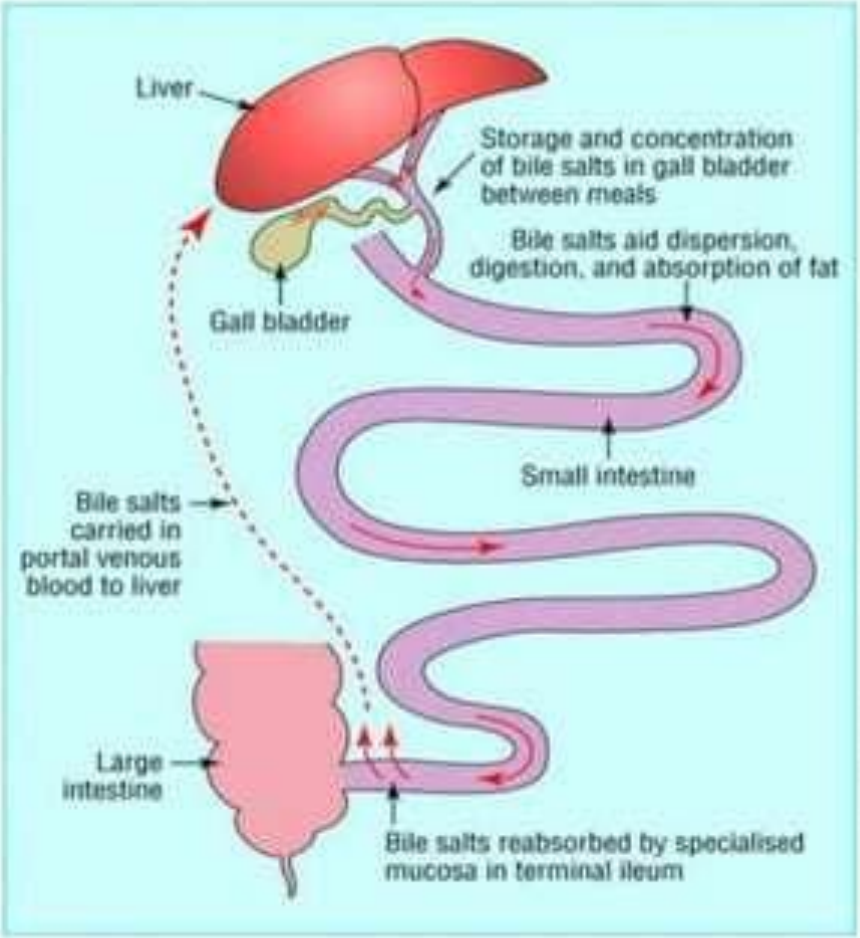


What is Bile? Why do we need salts and acids?

- Bile= bile acids + phospholipids + cholesterol
- Primary Bile Acids= (cholic acid and chenodeoxycholic) acid which are formed by cholesterol from the liver along with amino acids
- Secondary Bile Acids= bacterial metabolites (deoxycholate and lithocholate) of primary bile acids formed in the colon
- What do they do? They help excrete cholesterol, aid in fat digestion and absorption of fat, cholesterol and fat-soluble vitamins in the intestines
- Bile forms micelles (bound to cholesterol and fat) and aids in their absorption through micellar transport mechanism

Enterohepatic Circulation

- Bile acids are stored in the gallbladder
- During digestion bile acids are absorbed through the gut mostly uncongugated (some congugated)
- In the terminal ileum the bile salts are reabsorbed and carried through the portal blood circulation to be reconjugated and secreted back into bile

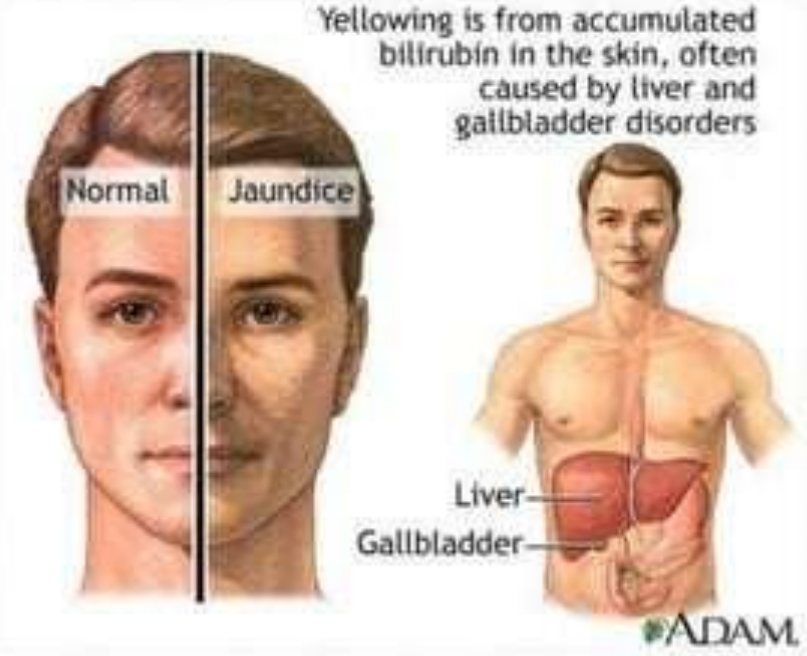


Cholestasis

- Chole= gallbladder or its ducts
- Stasis= stuck!
- Cholestasis is the obstruction of the secretion of bile
- Different forms of Cholestasis: Cholelithiasis (gallstones), Choledocholithiasis (gallstones in the common bile duct)
- What else can cause Cholestasis?
  Tumors, cysts, pancreatic problems blocking the duct (pancreatitis), liver disease

Patient with Cholestasis

- RUQ pain may be intermittent if blockage is intermittent
- Jaundice
- Dark urine
- Light stools
- Weight loss



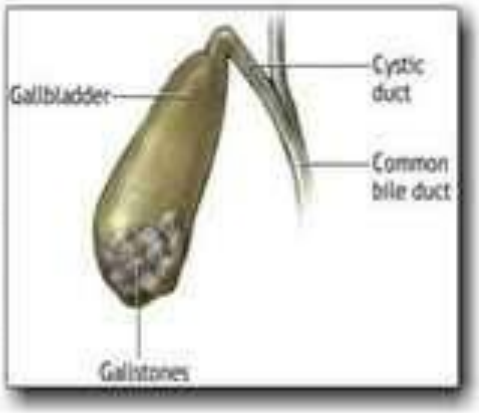
Cholestasis

Labs and Imaging

- ASL and ALT may be elevated
- Blood in stool suggests cancer etiology
- Alkaline Phosphatase will be elevated
- Ultrasound needed to look for stones or tumors
- CT may be needed to clarify obstruction
- MRI can be used to further evaluate liver disease

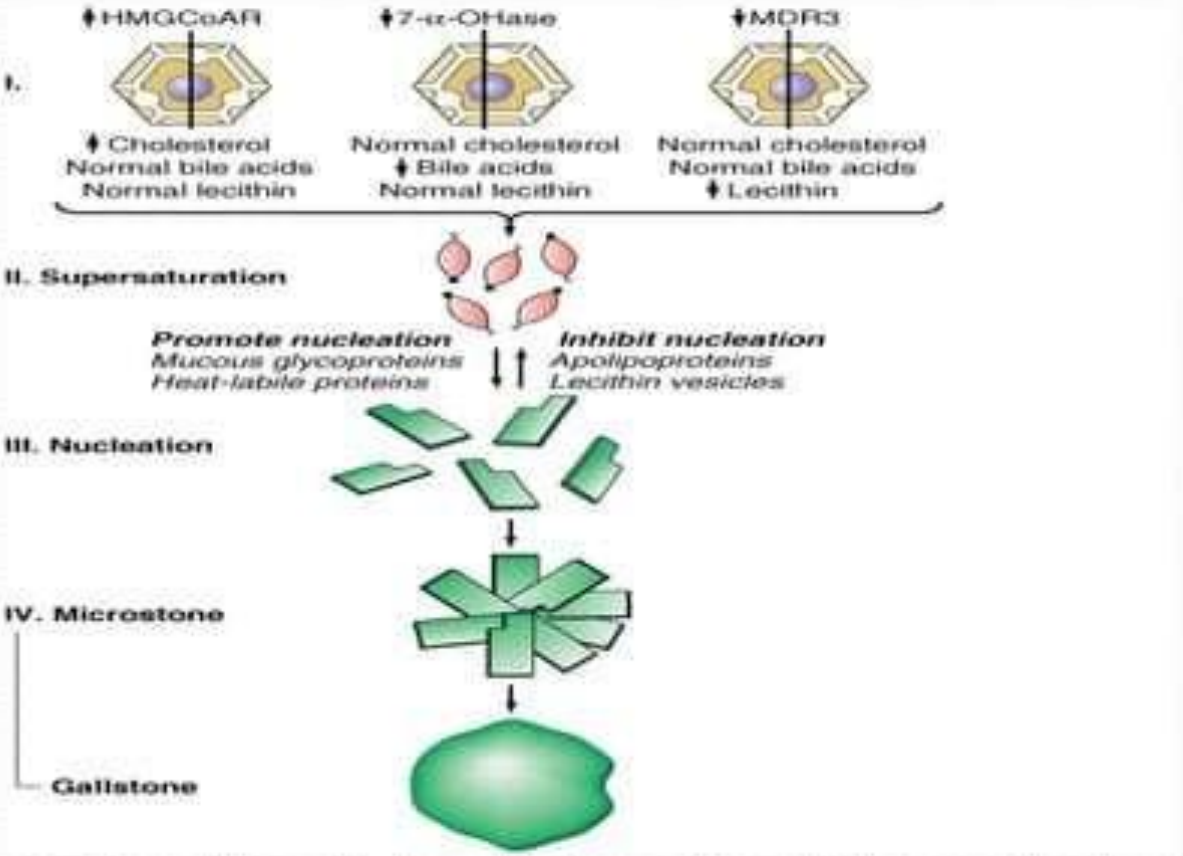
Cholelithiasis

Cholelithiasis



- Chole= gallbladder
- Lithiasis= stone
- Pathophysiology of gallstone formation
  - Form secondary to abnormal bile constituents
  - Mechanisms of gallstone formation
    - Increased biliary secretion of cholesterol
    - Cholesterol crystals precipitate and form a "stone"
    - Gallbladder hypomotility
  - Types of Gallstones
    - Cholesterol 80% of stones
    - Calcium bilirubinate (pigment) <20% of stones
  - Biliary sludge
    - Mucus like (supersaturation of bile with either cholesterol or calcium bilirubinate)
    - Likely a precursor to stones

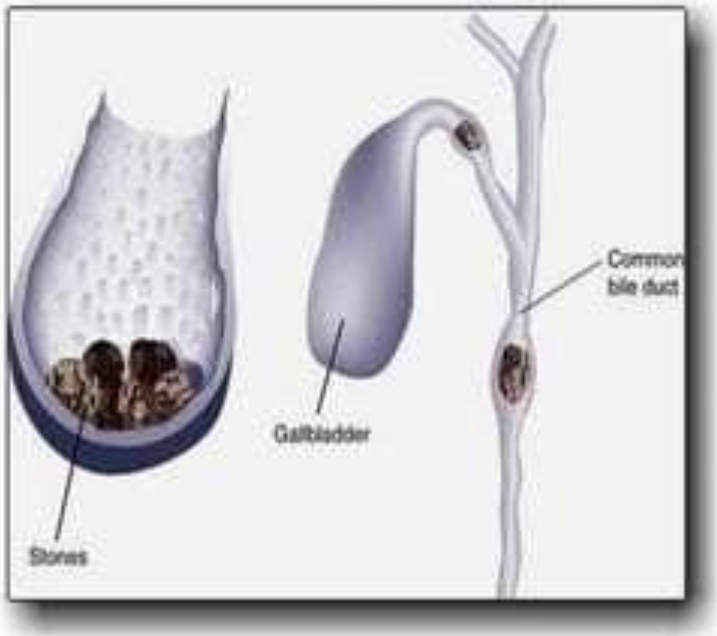
Cholesterol Gallstones



Source: Fauci AS, Kasper DL, Braunwald E, Hauser SL, Longo DL, Jameson JL, Loscalzo J: *Harrison's Principles of Internal Medicine*, 17th Edition: http://www.accessmedicine.com

Cholelithiasis

- Epidemiology
  - Women > Men
  - Increases with age
  - Native Americans
- Risk factors (4 F's)
  - Obesity
  - Rapid weight loss (bariatric surgery)
  - Increasing age
  - High calorie (specifically fat) diet
  - Pregnancy/ OCP
  - Primary Biliary cirrhosis
  - Clofibrate, octreotide, ceftriaxone therapy
  - Chronic Hemolysis (sickle cell andemia)
  - Chronic biliary tract infection - men(hepatitis)
  - Diabetes and insulin resistance
  - Crohn's diesase

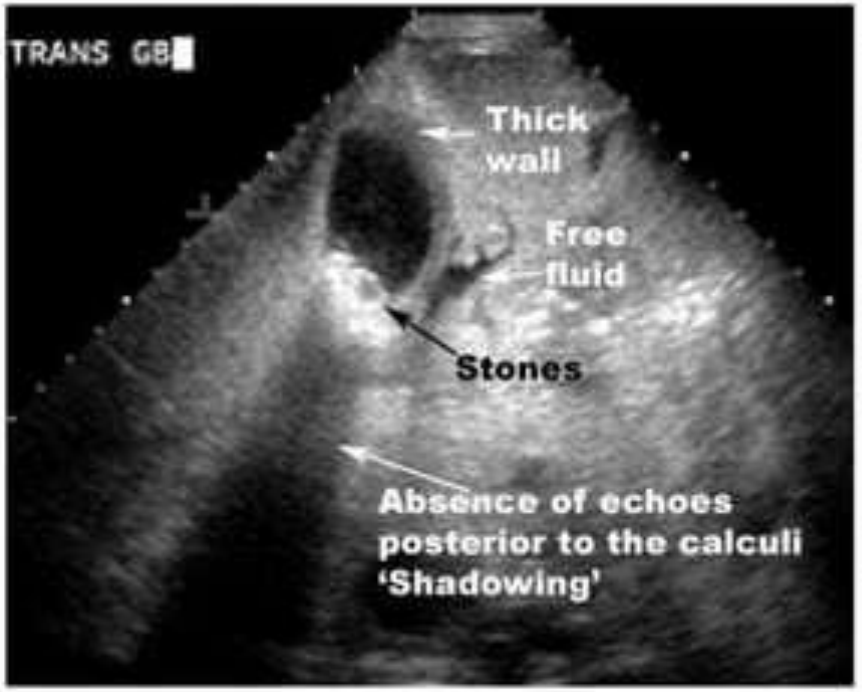


Cholelithiasis

- Clinical presentation
  - Many times asymptomatic
  - Gallbladder pain presents as intermittent severe RUQ pain radiation to the scapula (biliary colic)
    - Pain happens in 15-25% of gallstones
  - Can be epigastric pain radiating to the RUQ
    - Onset of pain is generally sudden and can last from 30 min to 5 hours.
    - N/v generally accompany pain
    - Tend to be postprandial, especially a high fat meal
    - More common at night

Cholelithiasis

- Diagnosis
  - Ultrasound
    - Very accurate even for small stones (2mm and up)
    - Can assess the emptying function of the gallbladder
  - Plain film x-ray
    - May detect 10-15% of cholesterol stones if they have enough calcium and up to 50% of pigment stones
  - HIDA
    - Looks more at the functioning and emptying of the gallbladder
    - Determines cystic duct obstruction



Cholelithiasis

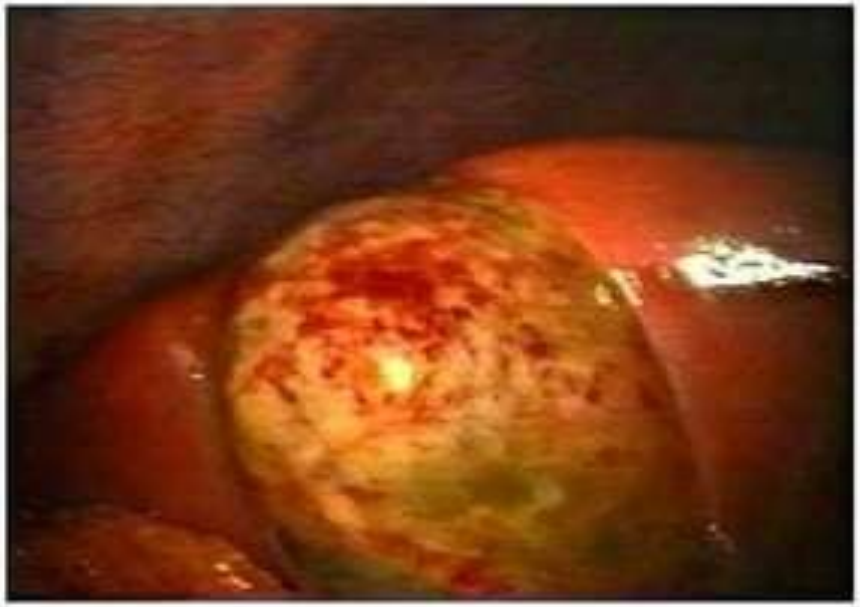
- Treatment of gallstones
  - ONLY FOR SYMPTOMATIC PATIENTS
  - Laparoscopic cholecystectomy
    - Generally outpt surgery with quick recovery (generally <1 week)
  - Lithotripsy
    - In combo with bile salt therapy for a single radiolucent stone (<20mm)
    - Infrequently used in the US anymore
  - Chenodeoxycholic and Ursodeoxycholic Acid (7mg/kg/day of each or just UCSA 8-13mg/kg/day in divided doses)
    - Bile salts that can be given orally to dissolve stones over 2 year period of time
    - For patients who refuse surgery and have a functioning gallbladder (visualized by oral cholecystography)
    - Most gallstones recur within 5 years
    - Few patients are candidates for this

Acute Cholecystitis

- Chole=gallbladder
- Cystitis= inflammation of the cyst wall
- Caused by gallstone obstruction 90% of the time
  - Biliary pain that progressively worsens
  - Most patients (>50%) have experienced attacks before that resolved spontaneously

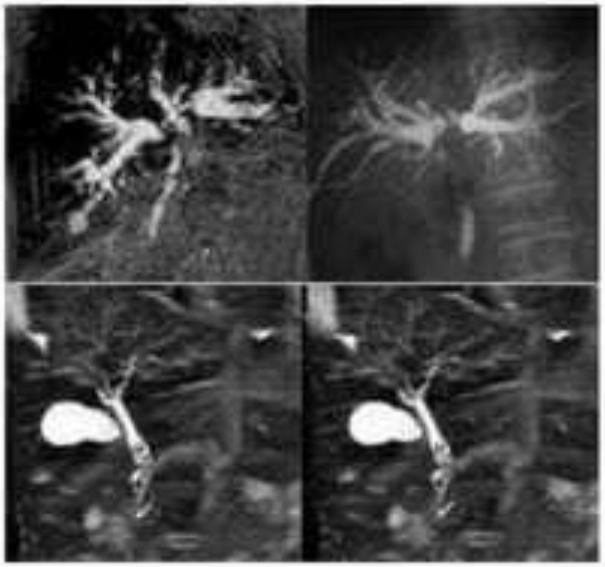
Acute Cholecystitis

- Persistant severe RUQ pain
- Generally after a fatty meal
- Fever
- N/V
- Anorexia
- RUQ TTP with +Murphy's sign
- Guarding/rebound
- Enlarged gallbladder palpable in 15% of patients
- Distended abdomen with hypoactive bowel sounds
- Jaundice in 25% of patients



Acute Cholecystitis

- Labs
  - Elevated WBC (12,000-15,000)
  - Elevated bili possible
  - AST/ALT often elevated
  - Alkaline phosphatase can be high especially in ascending cholangitis
  - Amylase can be high
- Imaging
  - Plain film x-ray show stones in 15% of cases
  - HIDA shows cystic duct obstruction (most common cause of acute cholecystitis)
  - RUQ U/s shows stones, but does not as good at showing acute cholecystitis.
    - Usually done first to show stones and then progress to HIDA



Acute Cholecystitis

- Differential Diagnosis
  - PUD
  - Pancreatitis
  - Appendicitis
  - Perforated colonic carcinoma or diverticulum
  - Liver abscess
  - Hepatitis
  - Pneumonia
  - Rarely myocardial ischemia

Acute Cholecystitis

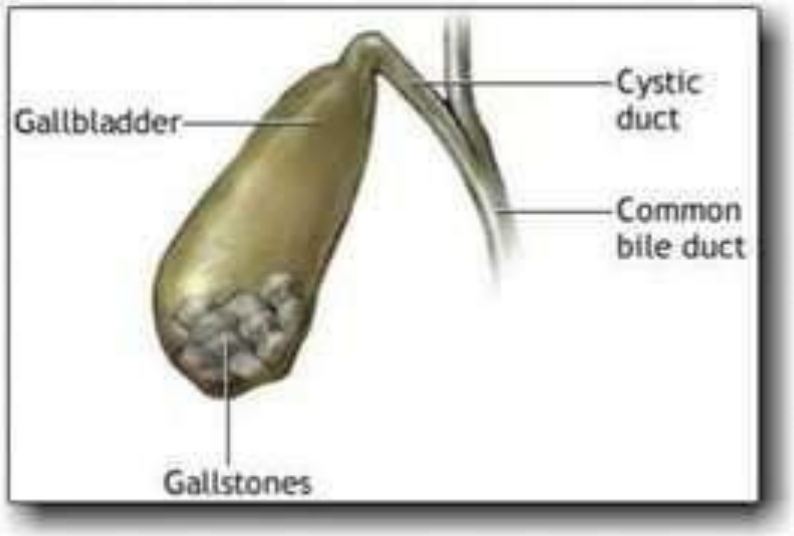
- Complications
  - Gangrene
    - Leading to perforation and possible abscess
  - Emphasematous cholecystitis
  - Empyema
  - Chronic Cholecystitis
    - Repeated acute cholecystitis
    - Cholesterolosis- gallbladderpolypoid enlargement due to cholesterol deposits (AKA strawberry gallbladder)
  - Cholangitis
  - Hydrops
    - Acute cholecystitis resolves but obstruction persists causing mucoid fluid to collect in the gallbladder
  - Poreclain gallbladder
    - Increased risk of ca

Acute Cholecystitis

- Treatment
  - Lap Cholecystectomy
  - Conservative treatment (not able to have surgery or waiting for stabilization before surgery)
    - NPO, IV fluids, analgesia, IV Abx (3rd gen cephalosporin + Flagyl, severe cases may need Fluoroquinolone + Flagyl
    - 75% will see remission of sx in 2-7 days
    - Many recurrences
    - Meperidine (Demerol) for pain control. Morphine can cause spasm of the sphincter of Oddi and increase pain
- Prognosis
  - Low mortality rate (<0.2%)
  - Surgery consistent with resolution of sx

Choledocolithiasis and Cholangitis

- Chole= gallbladder
- Doco= duct
- Lithiasis= stone
  - Common bile duct
  - Stones generally form in the gallbladder
  - Can form spontaneously in the duct (pigment stones) even after cholecytectomy
  - Same risk factors and epidemiology as cholelithiasis
  - Increases with age
- Cholangitis= inflammation of bile duct
  - Complication of choledocolithiasis



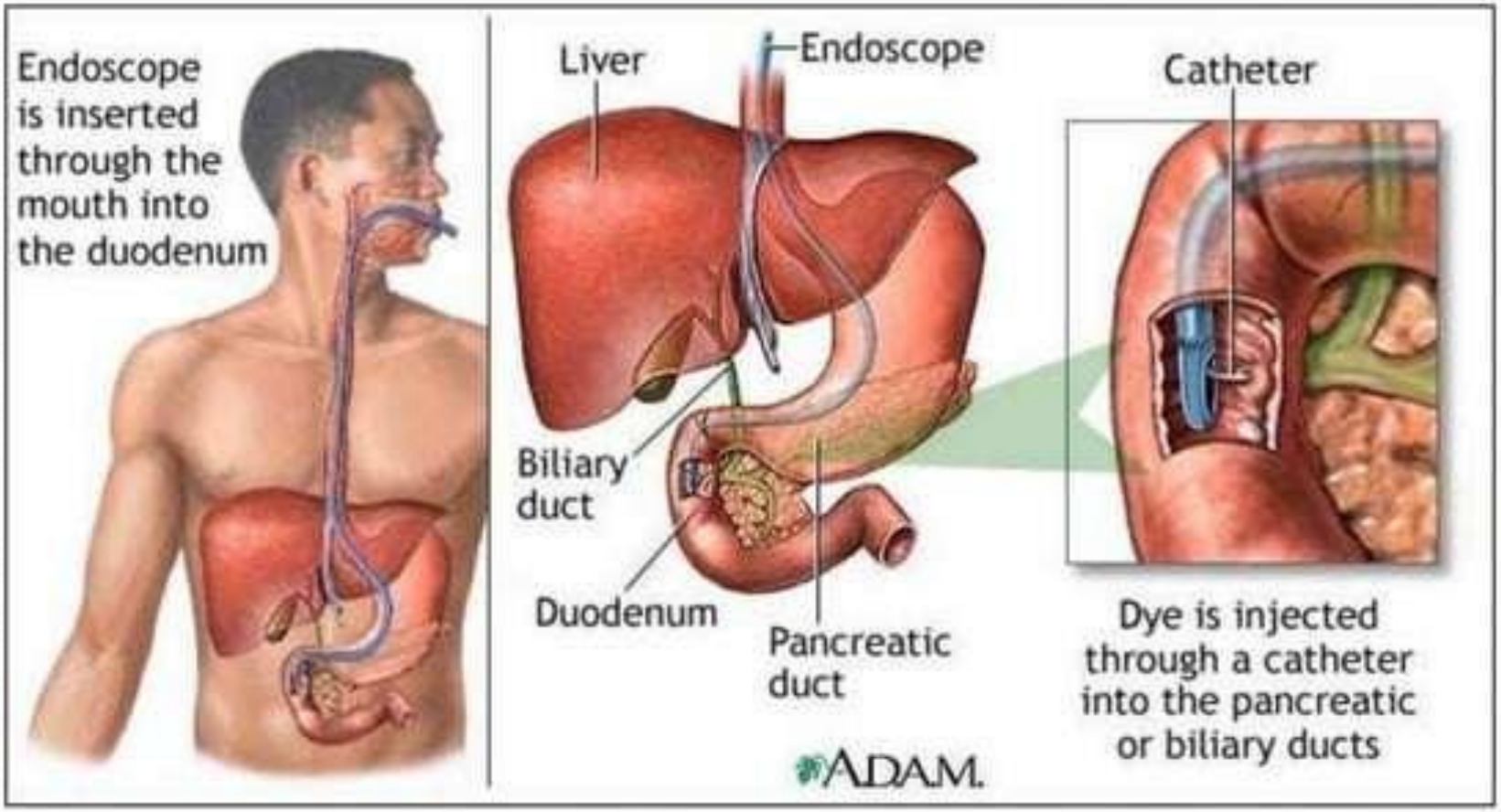
Choledocolithiasis and Cholangitis

- Signs and symptoms of Cholangitis
  - CHARCOT'S TRIAD- fever jaundice, severe RUQ pain
  - Pruritis
  - Dark urine
  - Acholic stools (light colored)
- Signs and symptoms of Acute Supportive Cholangitis
  - REYNOLD PENTAD- Charcot's Triad + AMS +hypotension
  - ENDOSCOPIC EMERGENCY

Choledocolithiasis and Cholangitis

- Labs
  - Very elevated ALT/AST from obstruction (often >1000)
  - Elevated Bili
  - Alk phos rises slowly
  - Amylase can be elevated when comorbid pancreatitis
  - Elevated WBC in cholangitis
- Imaging
  - U/s and CT show dilitation of ducts
  - Endoscopic U/s, helical CT and MRI used if low suspicion
  - **ERCP is gold standard**
    - Therapeutic as well- can do sphincterotomy with stone extraction or stent placement

Endoscopic Retrograde Cholangiopancreatography (ERCP)

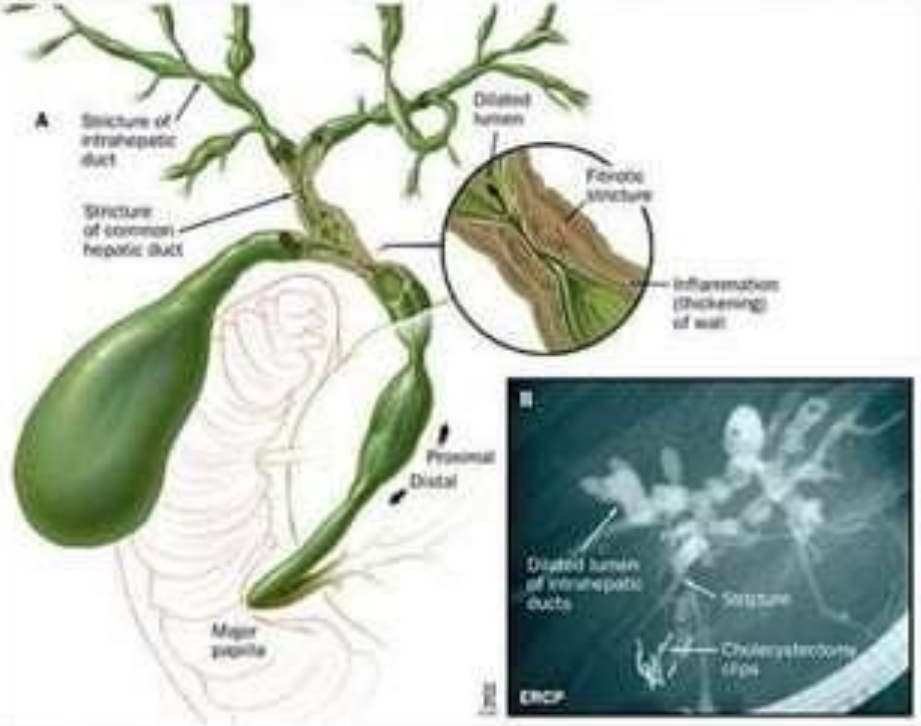


Choledocolithiasis and Cholangitis

- Differential Diagnosis
  - Cancer- pancreas, ampulla of Vater, bile duct, gallbladder
  - Compression from metastatic ca (GI tract of breast)
  - Chronic liver disease
    - Primary biliary cirrhosis
    - Sclerosing cholangitis
    - Drug-induced liver disease
- Treatment
  - Endoscopic sphincterotomy and stone extraction (usually by ERCP)
  - Lap chole usually follows this
  - Antibiotics if bile cultures or blood cultures are positive
    - Ampicillin+ Gentamicin+ Cipro or Flagyl

Primary Sclerosing Cholangitis

- Chronic diffuse inflammation of the biliary system
- Leads to fibrosis and strictures
- VERY RARE



Primary Sclerosing Cholangitis

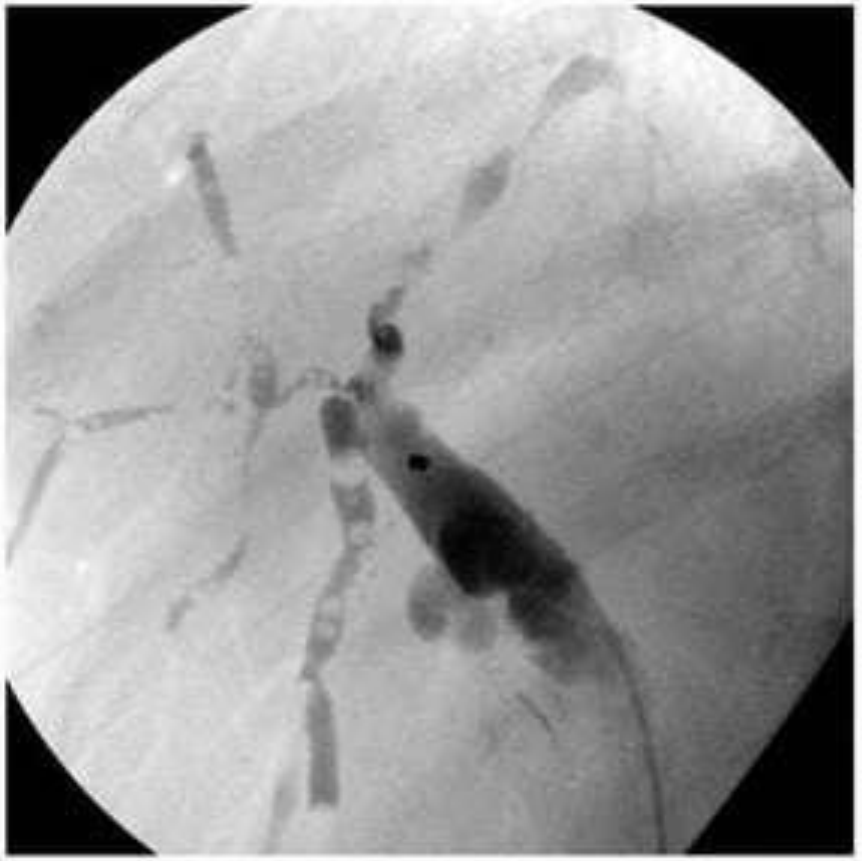
- Epidemiology
  - Men>women
  - Ages 20-50
- Risk Factors
  - Ulcerative Colitis significantly increases risk
  - Crohn's some increased risk
  - HLA- B8, DR-3, DR-4
  - 1st degree family member

Primary Sclerosing Chloangitis

- Clinical Presentation
  - Progressive obstructive jaundice
  - Fatigue
  - Pruritis
  - Anorexia
  - indigestion
- Labs
  - Elevated Alk phos
  - Low serum albumin (secondary to malabsorption)
  - Possibly low platelet count

Primary Sclerosing Cholangitis

- Diagnostics
  - Imaging
    - ERCP
    - MRI
  - Liver biopsy
    - Shows characteristic periductal fibrosis ("onion-skinning")
    - histology and antibody studies needed for autoimmune diseases



Primary Sclerosing Cholangitis

- Complications
  - Cholangiocarcinoma in 20% of cases
    - Check CA 19-9
    - Annual imaging with U/s, CT or MRI with MRCP
  - Gallstones
  - Cholecystitis
  - Gallbladder polyps
  - Gallbladder carcinoma

Primary Sclerosing Cholangitis

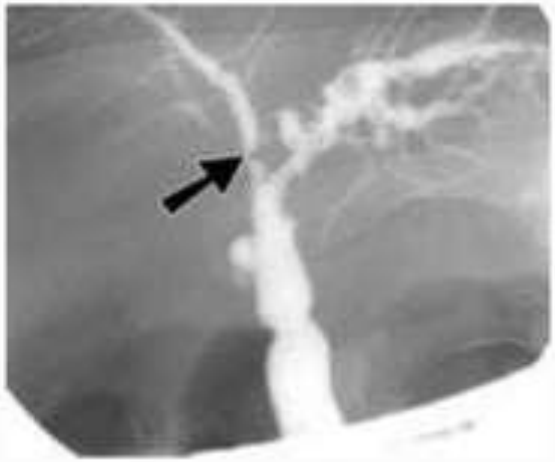
- Treatment
  - Acute bacterial
    - Cipro 750mg bid
  - Chronic
    - Balloon dilitation or stenting
      - May increase risk of complications or cholangitis
    - Resection of dominant bile duct stricture
      - May lead to longer survival and decreased risk of cholangiocarcinoma
    - In pt with UC, colorectal surveillance is necessary to reduce colorectal ca
      - Ursodeoxycholic acid could reduce colorectal dysplasia
    - For pt with cirrhosis and primary sclerosing cholangitis liver transplantation will likely be needed

Primary Sclerosing Cholangitis

- Prognosis
  - Survival 12-17 years
  - Liver transplant increases survival if before cholangiocarcinoma
  - Adverse prognostic factors
    - Older age at dx
    - Higher bilirubin/ AST
    - Lower albumin
    - Variceal bleeding
    - Dominant bile duct stricture
    - Extrahepatic changes

Biliary Stricture

- 95% of the time are secondary surgery (anastomosis or injury)
- Other causes:
  - Blunt trauma to the abdomen
  - Pancreatitis
  - Erosion of the duct by gallstone
  - Prior endoscopic sphincterotomy



Biliary Stricture

- Unless complete obstruction, may not be apparent immediately after surgery
- Erosion causes Biloma (collection of bile) which leads to infection and likely fibrous stricture
- Most common complication is Cholangitis
- Needs ERCP for repair, stent or dilitation

Biliary Dyskinesia

- Gallbladder dysfunction (AKA chronic acalculous cholecystitis)
- Most common in women <50 years of age
- Clinical presentation
  - Episodic RUQ pain
  - Intolerance to fatty foods
  - Mild nausea
- Imaging
  - Pt have already had U/s, x-ray, EGD, upper GI without findings
  - ERCP diagnostic with <35% ejection fraction at 20 minutes
    - ERCP with injection of sincalide reproduces RUQ pain
- Treatment
  - Lap Cholecystectomy cures 85-90% of patients
  - Pathology report shows chronic cholecystitis

THE END!

QUESTIONS?????

References

- *Current Medical Diagnosis and Treatment 2010*
- Wikipedia and Google for images
- Harrison's *Principles of Internal Medicine* for content and images
- Images:
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- More images!
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  - Final picture is by my adorable husband, Bill Bunting