GALL BLADDER

Cholelithiasis (Gallstones)

- Gallstones afflict 10-20% of adult populations in northern hemisphere Western countries.
- Adult prevalence rates are higher in Latin American countries (20-40%)
- low in Asian countries (3%-4%).
- In the United States there are about 1 million new cases of gallstones diagnosed annually, and two-thirds of these individuals undergo surgery.

- **There are two main types of gallstones.**
- **1- *cholesterol stones* (*80%)***
- ***crystalline cholesterol monohydrate.***
- **2-*pigment stones.***
- **bilirubin calcium salts**

Risk Factors for Gallstones

- **Cholesterol Stones**
- Demography: Northern Europeans, North and South Americans,
- Americans, Mexican Americans.
- Advancing age
- Female sex hormones
- Female gender
- Oral contraceptives
- Pregnancy
- Obesity
- Rapid weight reduction
- Gallbladder stasis
- Inborn disorders of bile acid metabolism
- Hyperlipidemia syndromes

Pathogenesis and Risk Factors

- Bile is the only significant pathway for elimination of excess cholesterol from the body, either as free cholesterol or as bile salts.
- Cholesterol is water insoluble and is rendered water soluble by aggregation with bile salts and lecithins secreted into bile.
- When cholesterol concentrations exceed the solubilizing capacity of bile (supersaturation), cholesterol can no longer remain dispersed and nucleates into solid cholesterol monohydrate crystals.

- **Cholesterol gallstone formation involves :**
- **1-Supersaturation of the bile with cholesterol**
- **2-Establishment of nucleation sites by microprecipitates of calcium salts**
- **3-Hypomobility of the gallbladder (stasis), which promotes nucleation**
- **4-Mucus hypersecretion to trap the crystals, enhancing their aggregation into stones.**

- The pathogenesis of pigment stones is also complex.
- The presence of unconjugated bilirubin in the biliary tree increases the likelihood of pigment stone formation, as occurs in :
- 1-hemolytic anemias.
- 2-infections of the biliary tract.

- **Pigment Stones**
- Demography: Asian more than Western, rural more than urban
- Chronic hemolytic syndromes
- Biliary infection
- Gastrointestinal disorders: ileal disease (e.g., Crohn disease), ileal resection or bypass, cystic fibrosis with pancreatic insufficiency

- ***Age and gender.***
- The prevalence of gallstones increases throughout life.
- In the United States, less than 5-6% of the population younger than age 40 has stones.
- 25-30% of those older than 80 years.
- F:M 2:1

- ***Ethnic and geographic***.
- Gallstones are more prevalent in Western industrialized societies and uncommon in developing societies.
- Cholesterol gallstone prevalence approaches 75% in Native American populations-the Pima, Hopi, and Navajos
- Pigment stones are rare.
- The prevalence seems to be related to biliary cholesterol hypersecretion.

- ***Heredity.***
- Family history alone imparts increased risk, as do a variety of inborn errors of metabolism such as those associated with impaired bile salt synthesis and secretion.
- ***Environment.***
- Estrogenic influences, including oral contraceptives and pregnancy, increase hepatic cholesterol uptake and synthesis, leading to excess biliary secretion of cholesterol.
- Obesity, rapid weight loss, and treatment with the hypocholesterolemic agent clofibrate are also strongly associated with increased biliary cholesterol secretion.

- ***Acquired disorders***.
- Any condition in which gallbladder motility is reduced predisposes to gallstones.
- E.g pregnancy

  rapid weight loss

  spinal cord injury

Cholesterol stones

- arise exclusively in the gallbladder
- consist of 50-100% cholesterol.
- **Pure cholesterol stones** are pale yellow; increasing proportions of calcium carbonate, phosphates, and bilirubin impart gray-white to black discoloration
- Single – several
- **Most cholesterol stones are radiolucent, although as many as 20% may have sufficient calcium carbonate to render them radiopaque.**

Cholesterol gallstones. Mechanical manipulation during laparoscopic cholecystectomy has caused fragmentation of several cholesterol gallstones, revealing interiors that are

pigmented because of entrapped bile pigments

Pigment stones

- may arise anywhere in the biliary tree and are trivially classified as black or brown.
- black pigment stones are found in sterile gallbladder bile, while brown stones are found in infected intrahepatic or extrahepatic ducts.
- The stones contain calcium salts of unconjugated bilirubin and lesser amounts of other calcium salts, mucin glycoproteins, and cholesterol.

- Black stones are usually small and present in large quantities and crumble easily.
- Brown stones tend to be single or few in number and are soft with a greasy, soaplike consistency that results from the presence of retained fatty acid salts released by the action of bacterial phospholipases on biliary lecithins.

- **50-75% of black stones are radiopaque.** because of calcium carbonates and phosphates content.
- Brown stones are radiolucent.

Clinical features

- 70-80% remain asymptomatic throughout life
- 20-30% become symptomatic at the rate of 1-3% per year.
- pain tends to be excruciating, either constant or "colicky" (spasmodic) from an obstructed gallbladder or when small gallstones move down-stream and lodge in the biliary tree.
- Inflammation of the gallbladder, in association with stones, also generates pain.

- **<u>Complications include:</u>**
- 1- empyema
- 2- perforation
- 3- fistulae
- 4- inflammation of the biliary tree
- 5- obstructive cholestasis or pancreatitis.
  6- intestinal obstruction ("gallstone ileus").

Cholecystitis

- **1-Acute**
- Acute calculous cholecystitis
- Acute non-calculous cholecystitis
- **2-Chronic**
- **3-Acute superimposed on chronic**
- Almost always occurs in association with gallstones

Acute calculous cholecystitis

- **Acute inflammation of a gallbladder that contains stones is termed acute calculous cholecystitis.**
- **It is precipitated by obstruction of the gallbladder neck or cystic duct.**
- **It is the most common major complication of gallstones and the most common reason for emergency cholecystectomy.**

- Symptoms may be mild and resolve without medical intervention-emergency.
- Acute calculous cholecystitis is initially the result of chemical irritation and inflammation of the gallbladder wall in the setting of obstruction to bile outflow.
- The action of phospholipases derived from the mucosa hydrolyzes biliary lecithin to lysolecithin which is toxic to the mucosa.
- The normally protective glycoprotein mucous layer is disrupted exposing the mucosal epithelium to the direct detergent action of bile salts.

- PGs released within the wall of the distended gallbladder contribute to mucosal and mural inflammation.
- Distention and increased intraluminal pressure may also compromise blood flow to the mucosa.

Acute Non-Calculous Cholecystitis

- 5-12% of gallbladders removed for acute cholecystitis contain no gallstones.
- Most of these cases occur in seriously ill patients:
- (1) the postoperative state after major, nonbiliary surgery
- (2) severe trauma (e.g., motor vehicle accidents)
- (3) severe burns
- (4) sepsis

- **Mechanism:**
- 1-dehydration
- 2-gallbladder stasis
- 3-sludging
- 4-vascular compromise
- 5-bacterial contamination.

Chronic Cholecystitis

- It is due to repeated bouts of acute cholecystitis, but in most instances it develops without any history of acute attacks.
- It is almost always associated with gallstones.
- Gallstones do not seem to have a direct role in the initiation of inflammation or the development of pain, because chronic acalculous cholecystitis causes symptoms and morphologic alterations similar to those seen in the calculous form.

- Supersaturation of bile predisposes to both chronic inflammation and stone formation.
- *Escherichia coli* and enterococci, can be cultured from the bile in only about one-third of cases.
- Unlike acute calculous cholecystitis, stone obstruction of gallbladder outflow in chronic cholecystitis is not a requisite.

- The symptoms of chronic cholecystitis are similar to those of the acute form and range from biliary colic to indolent right upper quadrant pain and epigastric distress.

Complications:

- **1-Bacterial superinfection with cholangitis or sepsis**
- **2-Gallbladder perforation and local abscess formation**
- **3-Gallbladder rupture with diffuse peritonitis**
- **4-Biliary enteric (cholecystenteric) fistula, with drainage of bile into adjacent organs, entry of air and bacteria into the biliary tree, and potentially gallstone-induced intestinal obstruction (ileus)**
- **5-Aggravation of preexisting medical illness, with cardiac, pulmonary, renal, or liver decompensation**

Carcinoma of the Gallbladder

- Carcinoma originating from the epithelial lining of the organ, is the most frequent malignant tumor of the biliary tract.
- F>M
- 7^{th} decade of life
- It is more frequent in Mexico and Chile.
- In USA is highest in Hispanics and Native Americans.
- The mean 5-year survival has remained at a dismal 5% rate.

Risk Factors

- Gallstones are present in 60-90% of cases.
- In Asia, where pyogenic and parasitic diseases of the biliary tree are more common, gallstones are less important.
- Gallbladders containing stones or infectious agents develop cancer as a result of recurrent trauma and chronic inflammation.
- The presence of a abnormal choledochopancreatic duct junction is considered to be a risk factor.

- **Exophytic** or **infiltrating** tumors
- **Most carcinomas of the gallbladder are adenocarcinomas.**
- They may be papillary, poorly differentiated, or undifferentiated infiltrating tumors.
- About 5% are squamous cell carcinomas or have adenosquamous differentiation.
- A minority are carcinoid tumors.

- By the time gallbladder cancers are discovered, **most have invaded the liver directly** and many have extended to the cystic duct and adjacent bile ducts and portal hepatic lymph nodes.
- The peritoneum, GIT, and lungs are less common sites of seeding.

Clinical Features

- Preoperative diagnosis of carcinoma of the gallbladder is the exception, occurring in fewer than 20% of patients.
- Presenting symptoms are insidious and typically indistinguishable from those associated with cholelithiasis: abdominal pain, jaundice, anorexia, and nausea and vomiting.
- The fortunate person develops early obstruction and acute cholecystitis before extension of the tumor into adjacent structures or undergoes cholecystectomy for coexistent symptomatic gallstones.