

Biliary system

Biliary Atresia

- Complete obstruction of the lumen of the extrahepatic biliary tree within the first 3 months of life
- It occurs in about 1:10000 live births
- It is the cause of neonatal cholestasis in One third of the cases.
- It is the most common cause of death from liver disease in early childhood
- Rapid progress to cirrhosis.

Pathogenesis:

Two types:

1) Fetal form

- 20% of the cases
- Associated with other anomalies as malrotation of abd viscera, interrupted inf. Vena cava, polysplenia, CHD
- Aberrant intrauterine development of extrahepatic biliary tree.

2. Perinatal Form

- Normally developed biliary tree is destroyed after birth
- ? Viral infection as Reovirus and rotavirus
- ? Genetic inheritance.

Morphology of biliary atresia

- Inflammation, edema with narrowing & stricture of the hepatic or common bile ducts.
- Periductular inflammation of intrahepatic bile ducts.
- Progressive destruction of the intrahepatic biliary tree.
- Bile duct proliferation
- Portal tract edema & fibrosis
- Cholestasis → very common feature

Clinical Features:

Neonatal cholestasis

- Normal wt. & postnatal wt. gain
- F > M
- Hyperbilirubinemia
- A cholic stool → pale in color because of the absence of biliary system

Cholelithiasis

- Stone formation within the biliary system
- Common condition; 10-20% of adults in developed countries have GB stones
in Latin America the incidence is higher 20-40%. But in Asia is low 3-4%

Type of stone	Cholesterol stones	Pigment stones
%	80%	20%
Composition	cholesterol monohydrate	bilirubin calcium salts
Risk factors	<ol style="list-style-type: none"> 1- geographical area developed > developing areas 2- advancing age 25-30% in those >80yr 5-6% in those <40yr 3- female sex hormones female gender, oral contraceptives, pregnancy 4- obesity 5- rapid weight reduction 6- GB stasis & hypo motility, obviously seen during: pregnancy, spinal cord injury 7- bile acid metabolism inborn disorders → rare 8- hyperlipidemia syndrome → rare <p>* 80% of the cases have no identifying risk factor other than age & gender → most imp predisposing factors</p>	<ol style="list-style-type: none"> 1- geographical area Asian > western 2- chronic hemolytic anemias characterized by increased unconjugated hyperbilirubinemia 3- biliary infection 4- GI disorders
Pathogenesis	<ul style="list-style-type: none"> - Normally, cholesterol is eliminated from body through bile - As cholesterol is water insoluble, it becomes water soluble through aggregation with bile salts & lecithin - This might be associated with supersaturation of bile by cholesterol which leads to formation of cholesterol monohydrate stones - That's why prerequisites for stone formation are: <ol style="list-style-type: none"> 1- supersaturation of bile with cholesterol 2- nucleation or precipitation of organic & inorganic Ca⁺⁺ salts 3- GB stasis (decrease mobility of GB) 4- mucus hypersecretion to trap the crystal 	<ul style="list-style-type: none"> - composed of insoluble Ca⁺⁺ salts & inorganic Ca⁺⁺ salts of unconjugated bilirubin - this solubility and aggregation and formation of stones is enhanced by: <ol style="list-style-type: none"> 1- infection; usually by bacteria as E.coli, or parasite Ascaris, and these lead to → release of microbial β-glucuronidase which → hydrolyze bilirubin glucuronidases → ↑ unconjugated bilirubin 2- hemolytic anemia
Morphology	<ul style="list-style-type: none"> - exclusively in GB - consists of 50-100% cholesterol - ovoid and firm - usually multiple but can be single - faceted surfaces (have facets on surface) → due to pressure induced by multiple stones present - usually radiolucent if are pure. However, if Ca salts (Ca. carbonate) precipitate within the stones they can appear radiopaque (20%) 	<ul style="list-style-type: none"> - anywhere in biliary tree - black or brown depending on purity - 50-70% are radiopaque due to presence of Ca salts

Clinical features (regardless of the type)	- 70-80% remain asymptomatic for life - 1-3% become symptomatic per year - the main presentation is: pain (constant or colicky) mainly due to presence of inflammation	- Empyema (accumulation of purulent bile within GB) - Perforation of wall - Fistula	- obstructive jaundice if it occurs in the major bile duct - Pancreatitis if pancreatic duct is obstructed - Intestinal obstruction
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Cholecystitis

1. Acute
2. Chronic
3. Acute on top of chronic

*Almost always occurs in association with stones

Clinical features:

Acute calculous cholecystitis

- Steady upper abd. Pain radiating to Rt. Shoulder, colicky pain in nature when stones are present in GB neck.
- Fever, nausea, leukocytosis.
- Obstruction of common bile duct can be associated with severe pain
- Tenderness in Rt subcostal region.
- Mild attacks subside spontaneously in 1-10 days but recurrence is common.
- 25% require surgical intervention.

Acute acalculous cholecystitis

- (5-12%)
 - Symptoms are obscured by the generally severe clinical condition of the pt.
- 1- Post-op state after major non-biliary surgery → the most common predisposing factor
 - 2- Severe trauma & burn
 - 3- Sepsis

Mechanism:

- Dehydration
- GB stasis
- Vascular compromise
- Bacterial contamination.
- Obstruction to bile flow due to stone → can lead to chemical injury of the soft tissue

Morphology

Acute cholecystitis

- enlarged tense GB
- Bright red – Greenblack discoloration

- Subserosal hemorrhages
- Fibrin & suppurative exudate on serosa.
- Stones in 90% of cases in neck of GB or cystic duct.
- Cloudy turbid bile + fibrin, hemorrhage, pus
- **Empyema** = GB filled with pus.
GB wall is thick, edematous, hyperemic
- **Gangrenous GB** = necrosis of wall due to pressure by stones
Histologically GB wall shows features of acute inflammation, edema, leukocytes infiltration congestion etc.

Chronic cholecystitis

- Recurrent attacks of steady or colicky epigastric or RUQ pain.
- Nausea & vomiting,
- Fat intolerance
- Almost always associated with GB stones.

Mechanism:

- super saturation of bile which leads to inflammation or stone formation
- Infection: E. coli & enterococci (1/3 of cases) can be cultured from bile.
- **Obstruction is not a feature** → not like acute cholecystitis

Morphology of chronic cholecystitis

- Changes are variable & might be minimal.
- Presence of stones is sufficient for DX.
- Gall bladder may be normal in size, contracted, or enlarged
- Mucosal ulceration is infrequent
- Submucosal & subserosal fibrosis
- Lymphocytic infiltration of GB wall.

Complications of cholecystitis; Cholangitis = Bacterial infection of the bile ducts and sepsis formation, **perforation** with local abscess formation, **rupture of GB** with diffuse peritonitis, **biliary enteric fistula** → drainage of bile to adjacent organs or allowing air and bacteria to reach biliary tree, if it was due to preexisting medical condition it might lead to aggravation of the medical condition leading to **cardiac, pulmonary, renal decompensation**

Cholangitis:

Causes:

- 1- Stones
- 2- Stent or catheters
- 3- Tumors
- 4- Acute pancreatitis
- 5- Benign stricture
- 6- Fungi, viruses, parasites

- Bacteria enter biliary tract through the sphincter of Oddi.

Carcinoma of the gallbladder

- Mainly in women in 7th decades
- Very bad prognosis; 5yr. Survival about 1%
- Gallstones in 60-90% of cases

Morphology:

- Infiltrating or exophytic
- Infiltrating tumors are commonly scirrhous
- Fundus & neck are the most common sites (lateral walls)
 - Adenocarcinoma → 95%
 - Adenosquamous, squamous ca. → 5%
 - Carcinoid → rarely
 - Mesenchymal → rarely
- Characterized by local extension to liver, cystic duct, lymph nodes
And distant metastasis to: peritoneum, GI, lungs

Clinical Features

- Pre-operative diagnosis in <20% (rarely)
- Nausea, vomiting, pain, jaundice, weight loss, anorexia → totally nonspecific symptoms
- Sometimes they might have symptoms of obstruction which leads to acute cholecystitis.

Cholangiocarcinoma

- Adenocarcinoma that arise from bile ducts within & outside the liver
- Incidence 0.6/100000 in N. USA
- M=F

Predisposing factors:

- Sclerosing cholangitis
- Congenital fibropolycystic disease of biliary system
- Exposure to Thorotrast
- Chronic infection by liver fluke

Morphology

- Adenocarcinoma
- Marked desmoplasia

Metastasis

- Hematogenous: Lung, bones (vertebra), Adrenals, brain (50% of cases)
- Lymphatic: regional LN. (50%)

Clinical presentation:

- Intrahepatic: Detected usually **late** either due to obstruction of bile flow or liver mass.

Prognosis

- 1-2 yrs. Survival rate 13-25%
- Medium survival is 6 months

Carcinoma of the extrahepatic biliary tree

- Uncommon
- Insidious
- Painless jaundice
- M>F, 50-70yr
- Gall stones in about one third of cases (not so common)
- Risk increases with:
 - 1- Biliary tree flukes (clonorchis parasite)
 - 2- Primary sclerosing cholangitis
 - 3- Inflammatory bowel disease
 - 4- Choledochal cyst
 - 5- Thorostat

Ampullary tumors

Morphology

- small tumors at time of diagnosis.
- Arise from ampullary region
- Adenocarcinoma
 - + mucin
 - + Sometimes might show squamous differentiation

Klatskin tumor

Tumors arise from Rt. And Lt. hepatic duct at the liver hilus.

Presentation

- Jaundice, de-coloration of stool
- Nausea, vomiting and weight loss
- ↑liver in 50% (hepatomegaly)
- ↑GB in 25% (enlargement of GB)
- ↑serum alkaline phosphatase and transaminases → indicating malfunction of liver
- ↑prothrombin time
- Dark urine
- Prognosis very bad
- mean survival 6-18 months.