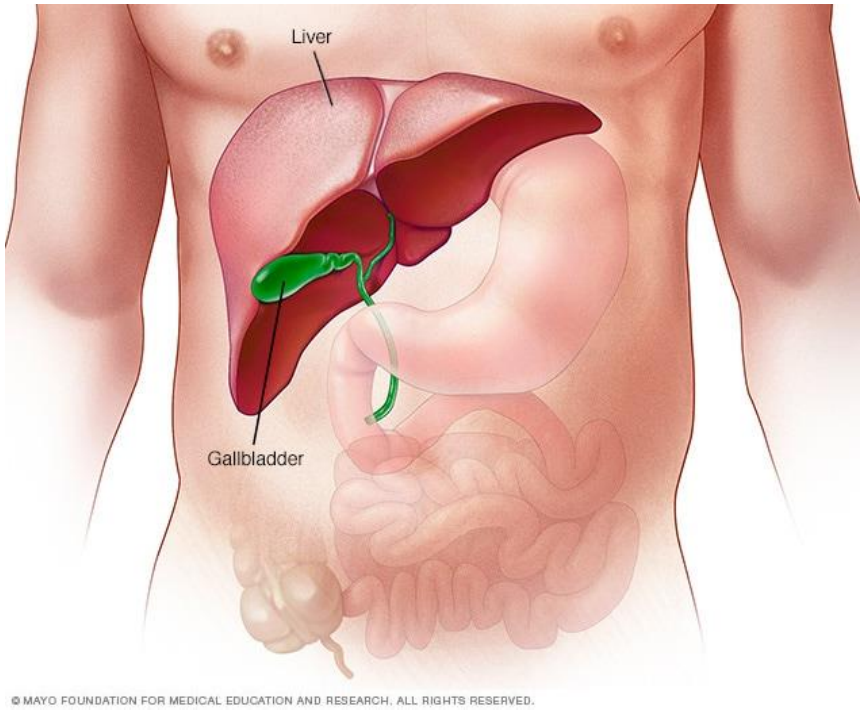
Cirrhosis and cholestasis

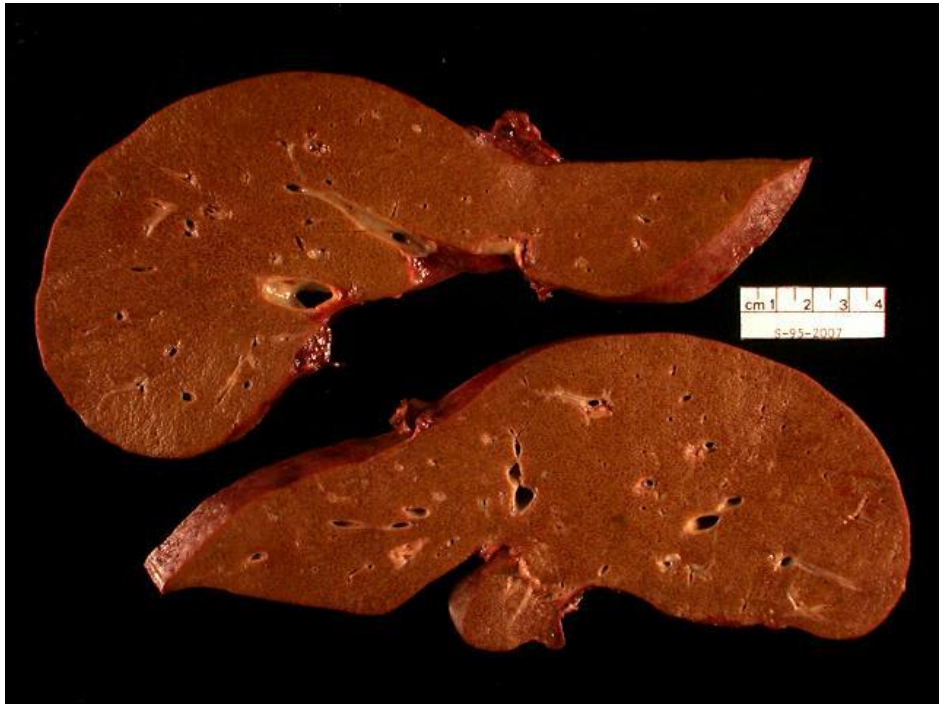


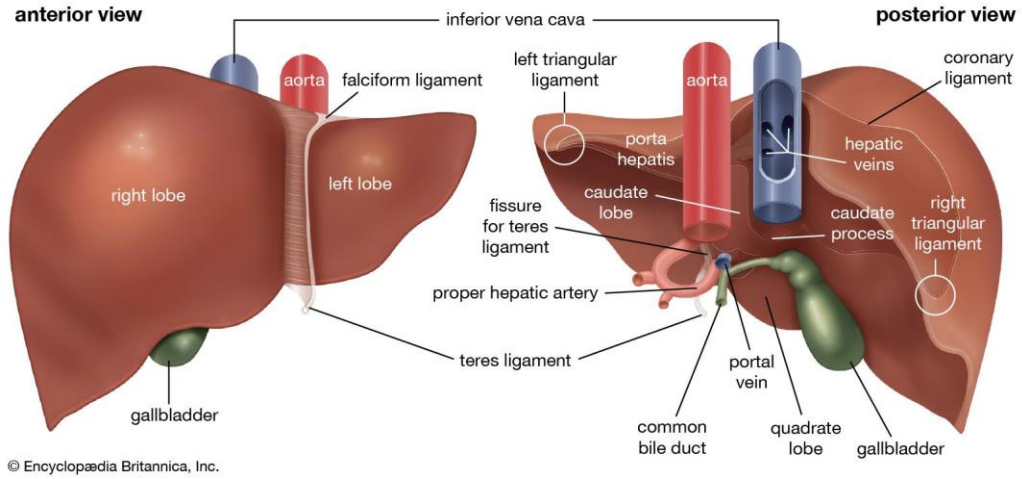
Dr.eman Krieshan,m.d.

7-4-2024.

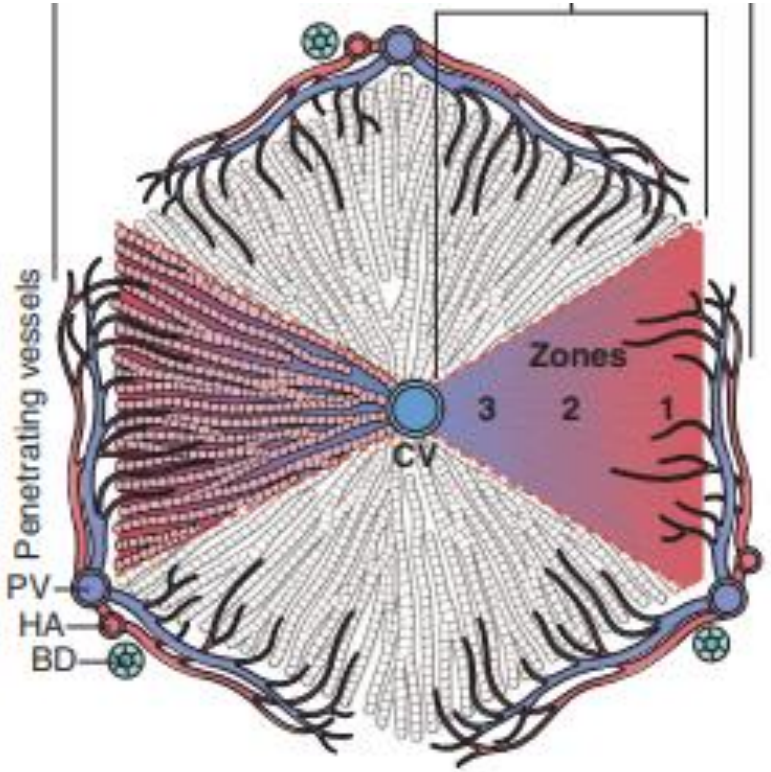
- The normal adult liver weighs 1400 to 1600 gm. It has a dual blood supply, with the portal vein providing 60% to 70% of hepatic blood flow and the hepatic artery supplying the remaining 30% to 40%.

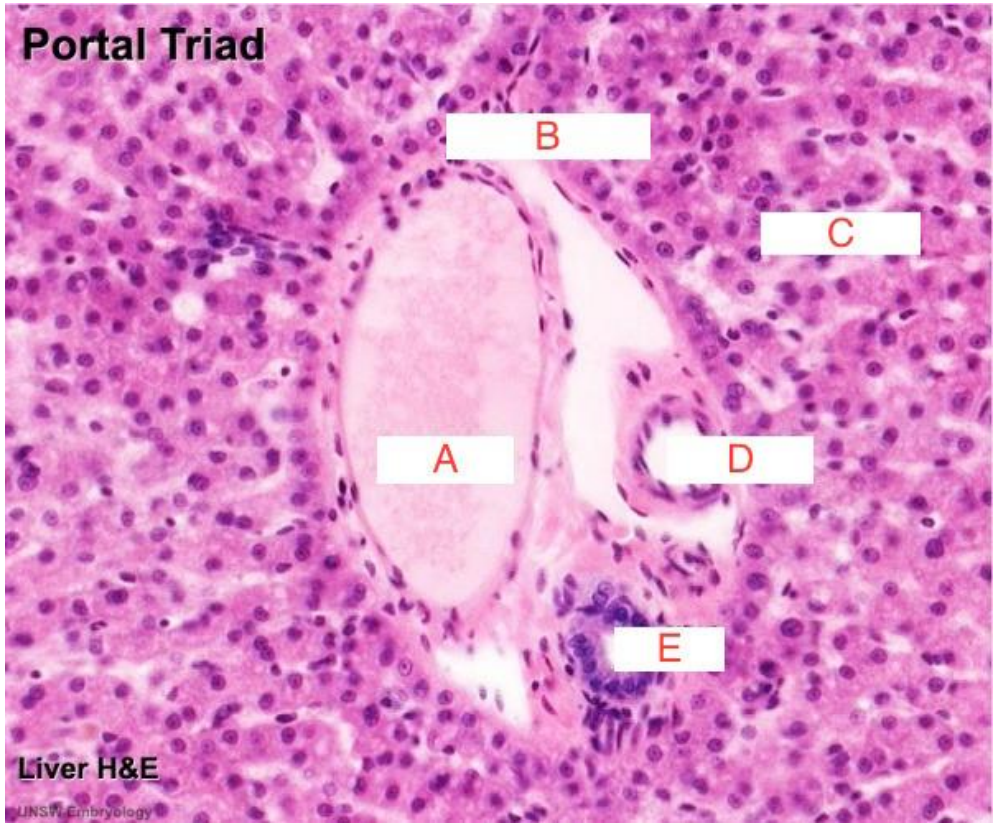
- Portal tract?





Models of liver anatomy





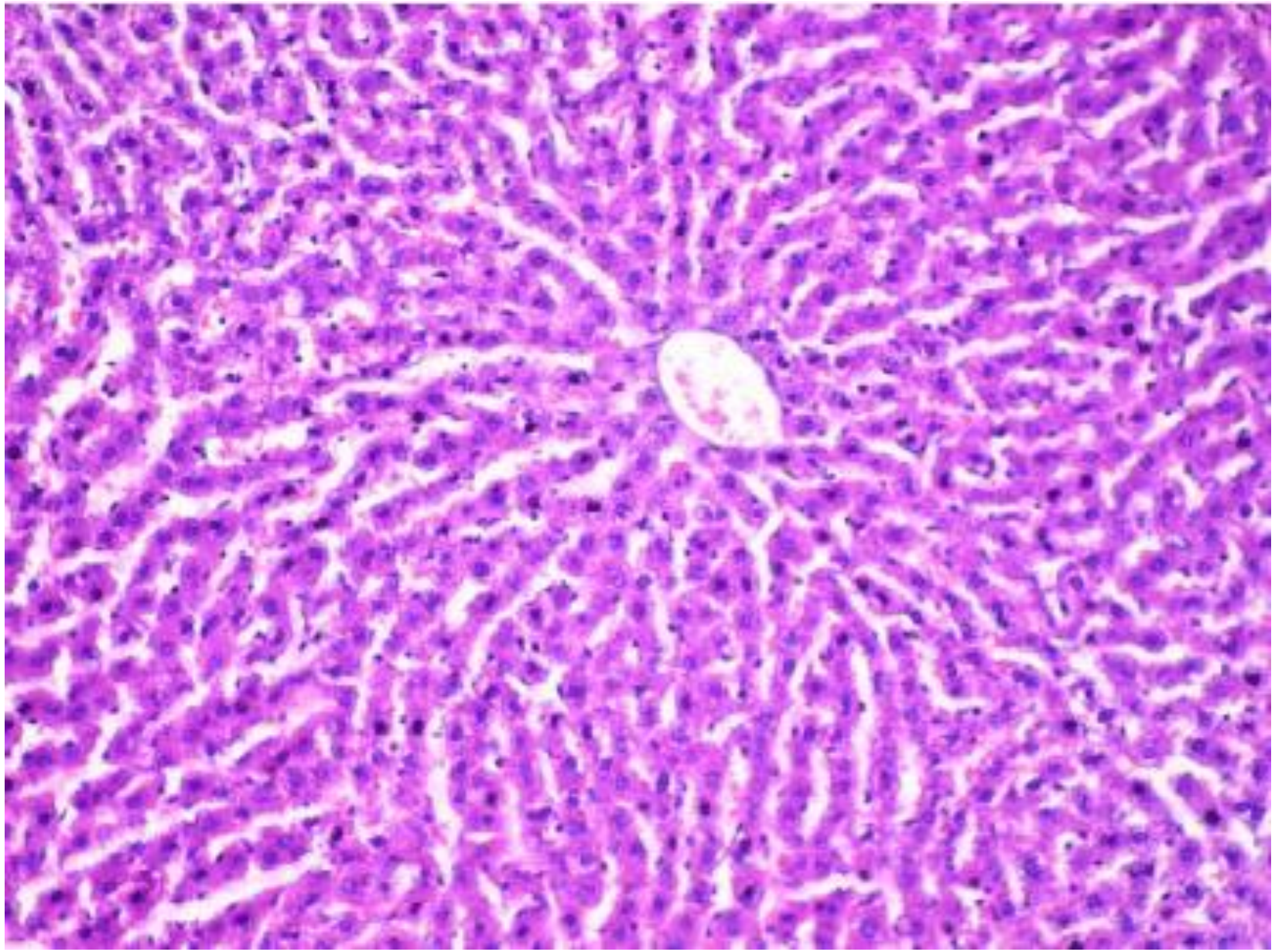


Table 16.1 Laboratory Evaluation of Liver Disease

Test Category	Blood Measurement*
Hepatocyte integrity	Cytosolic hepatocellular enzymes† *Serum aspartate aminotransferase* (AST) *Serum alanine aminotransferase* (ALT) Serum lactate dehydrogenase (LDH)
Biliary excretory function	Substances normally secreted in bile† *Serum bilirubin* *Total*: unconjugated plus conjugated *Direct*: conjugated only Urine bilirubin Serum bile acids Plasma membrane enzymes (from damage to bile canaliculus)† *Serum alkaline phosphatase* *Serum γ-glutamyl transpeptidase (GGT)*
Hepatocyte function	Proteins secreted into the blood *Serum albumin*‡ *Prothrombin time (PT)*† *Partial thromboplastin time (PTT)*† Hepatocyte metabolism Serum ammonia‡ Aminopyrine breath test (hepatic demethylation)‡

- The major hepatic diseases can be classified as:

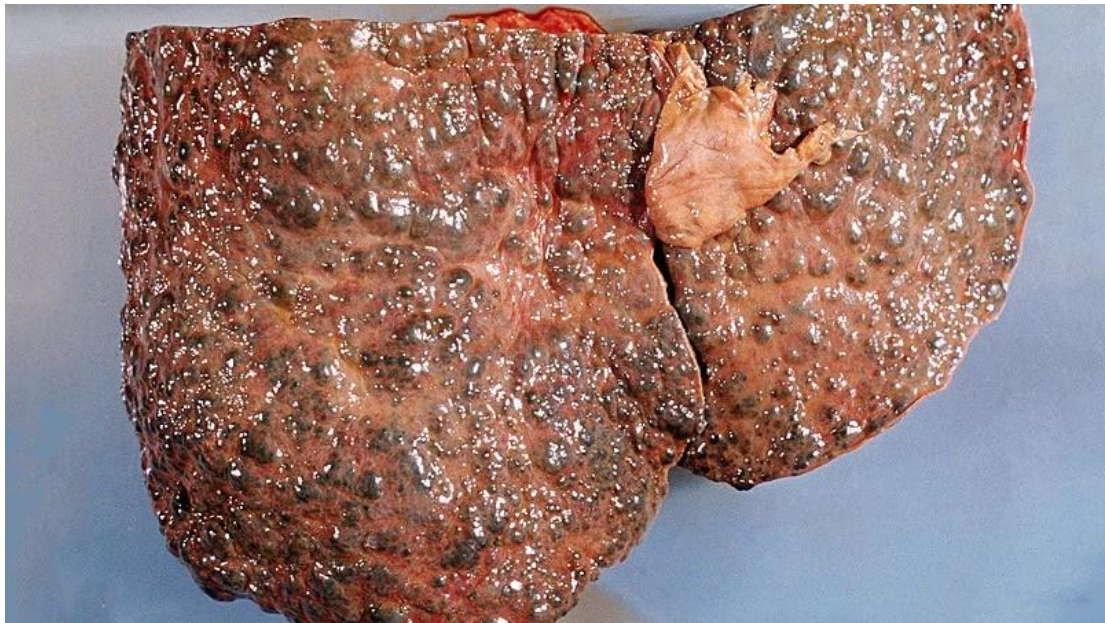
- 1. primary:
- viral hepatitis.
- alcoholic liver disease.
- nonalcoholic fatty liver disease (NAFLD).
- Cirrhosis.
- hepatocellular carcinoma (HCC).

- 2. secondary:
- cardiac disease.
- disseminated cancer.
- extrahepatic infections

cirrhosis

- Cirrhosis is the morphologic change most often associated with chronic liver disease; it refers to the diffuse transformation of the liver into regenerative parenchymal nodules surrounded by fibrous bands.

- The leading causes include:
  - chronic hepatitis B, C.
  - non-alcoholic fatty liver disease (NAFLD).
  - alcoholic liver disease
  - Drug induced liver injury
  - Cryptogenic (idiopathic) cirrhosis



Pathophysiology

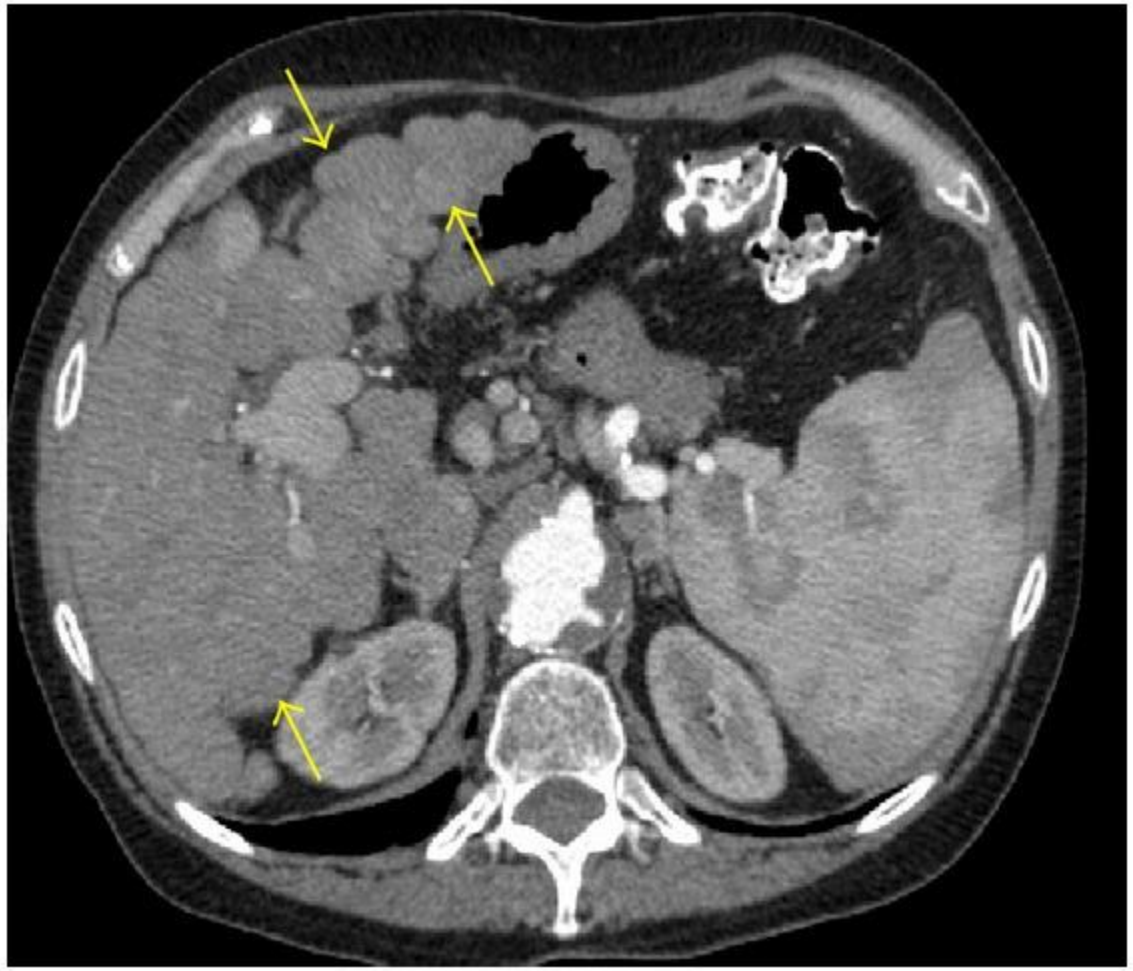
- Combination of processes :

- Fibrosis: excessive production of collagen type I / III by hepatic stellate cells

- Regeneration of hepatocytes through proliferation of progenitor cells of the ductular reaction

diagnosis

- 1. Liver function test.
- 2. Radiology.
- 3. Biopsy

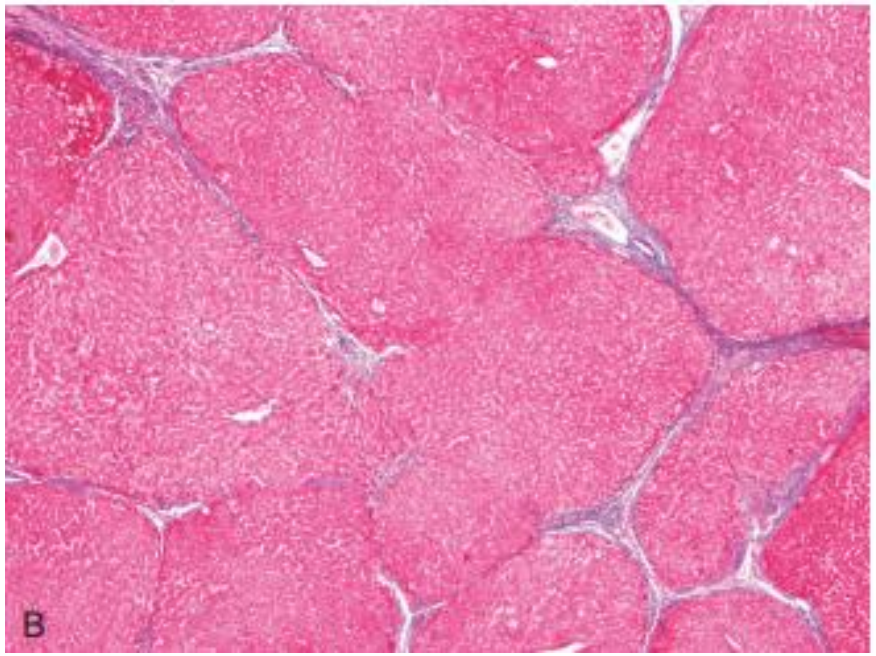


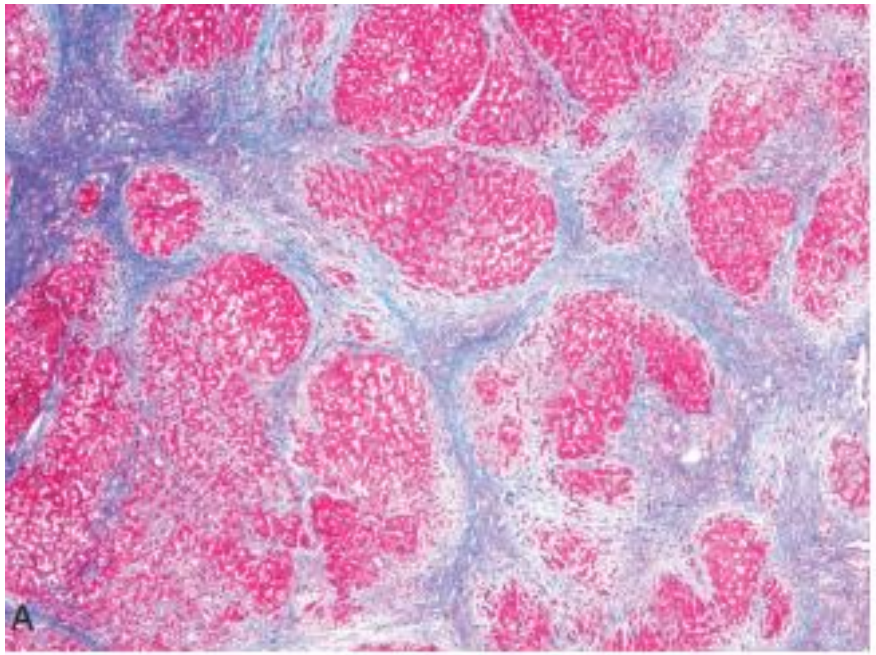
histopathology

*diffuse transformation of the entire liver into regenerative parenchymal nodules surrounded by fibrous bands.

* ductular reactions.

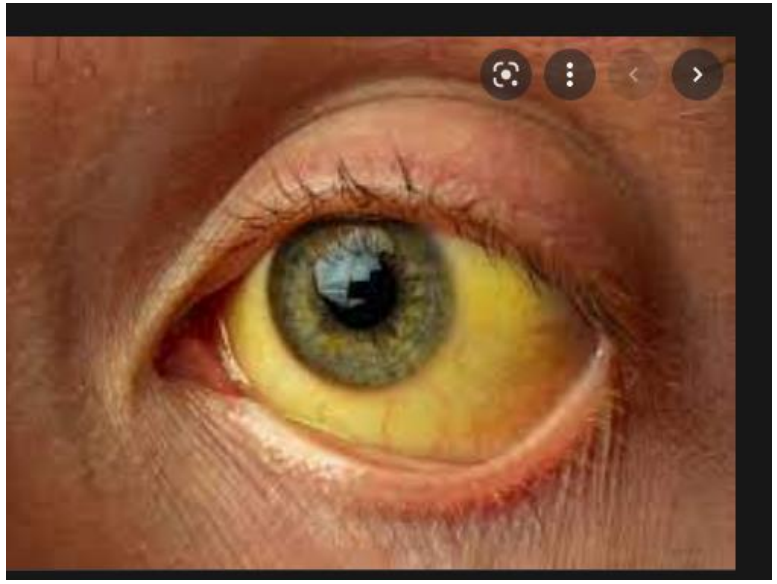
* (Masson trichrome stain) highlights these fibrous septa.

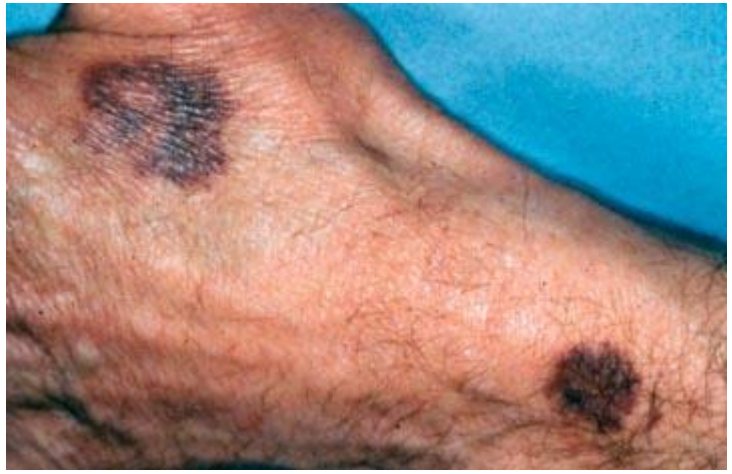


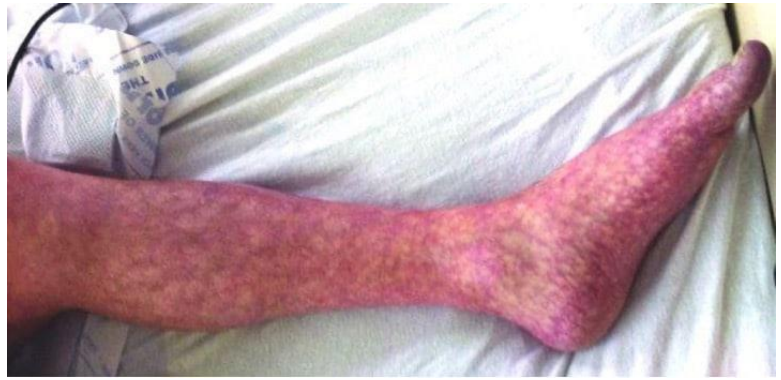


Clinical features

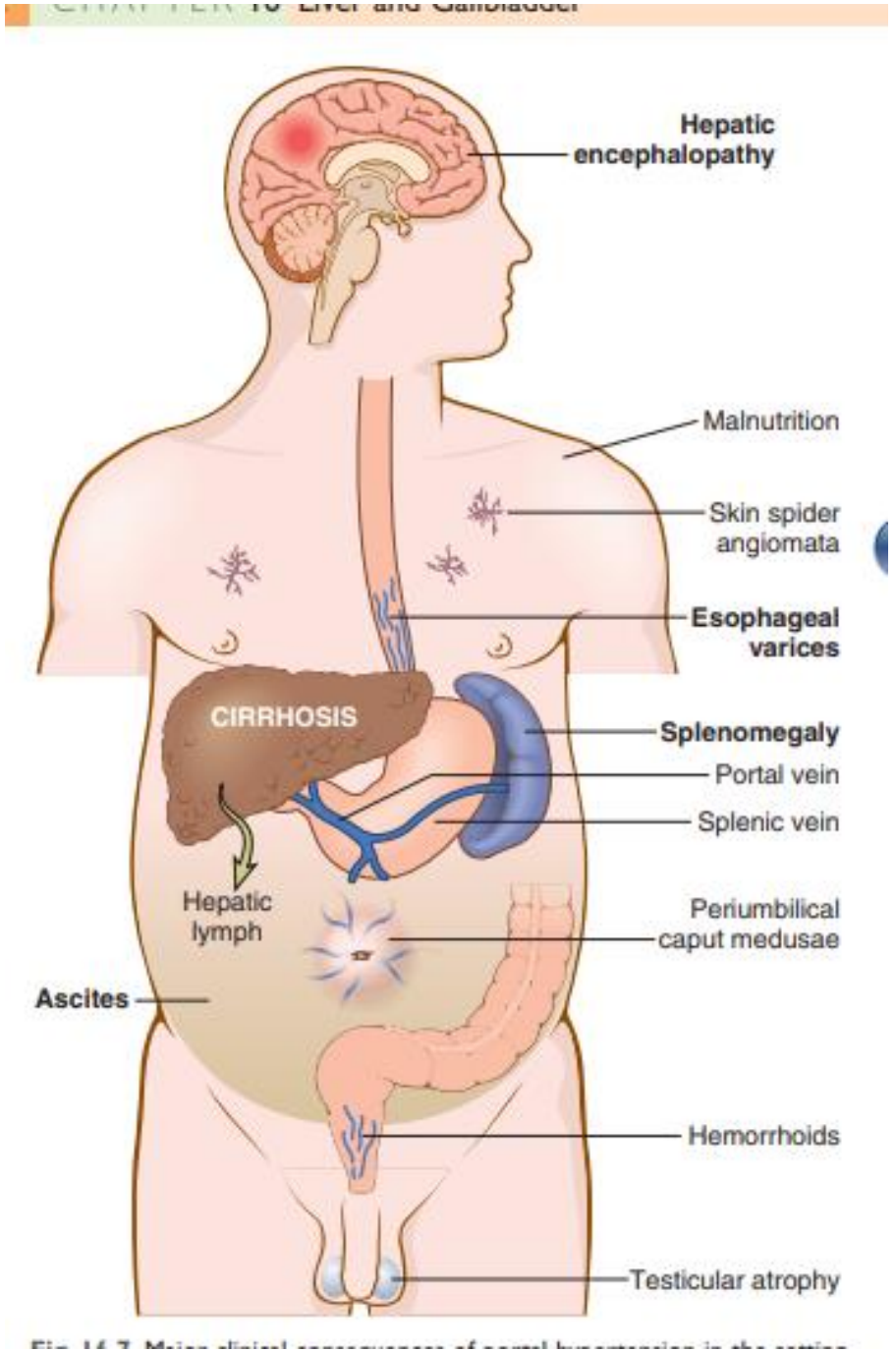
- 1. 40% of individuals with cirrhosis are asymptomatic until the most advanced stages of the disease.
- 2. Non specific symptoms such as anorexia, weight loss, weakness.
- 3. signs and symptoms of liver failure e.g Jaundice, encephalopathy, and coagulopathy.
- 4. Pruritus, portal hypertention (intrahepatic vascular resistance).



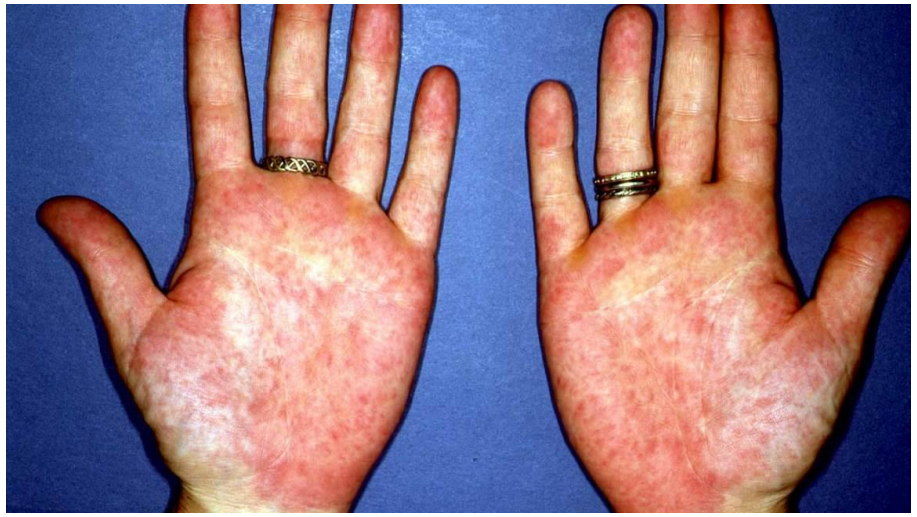


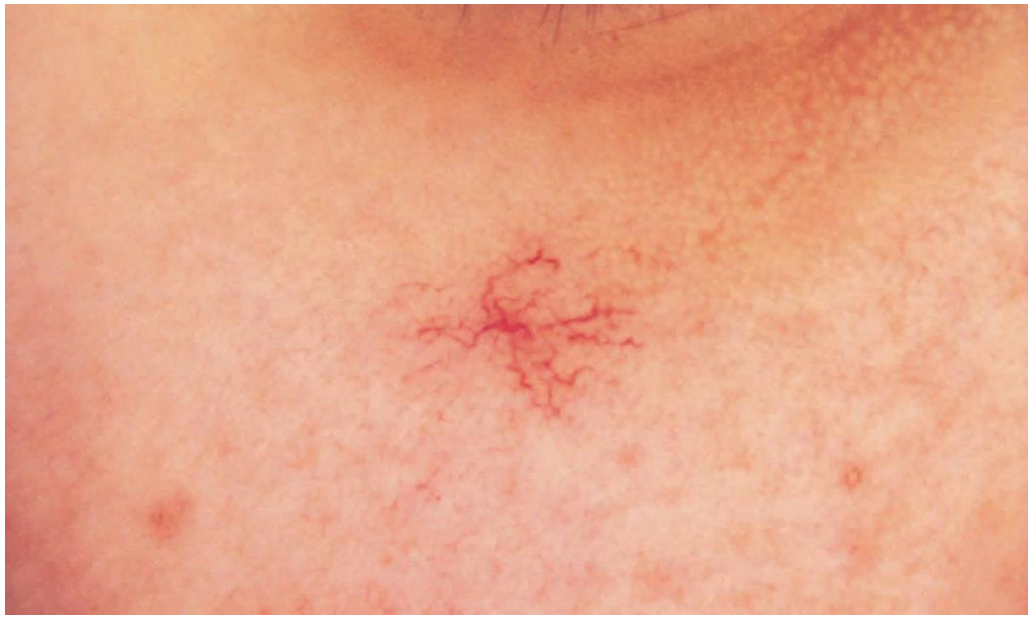


Major clinical consequences of portal hypertension in the setting of cirrhosis.



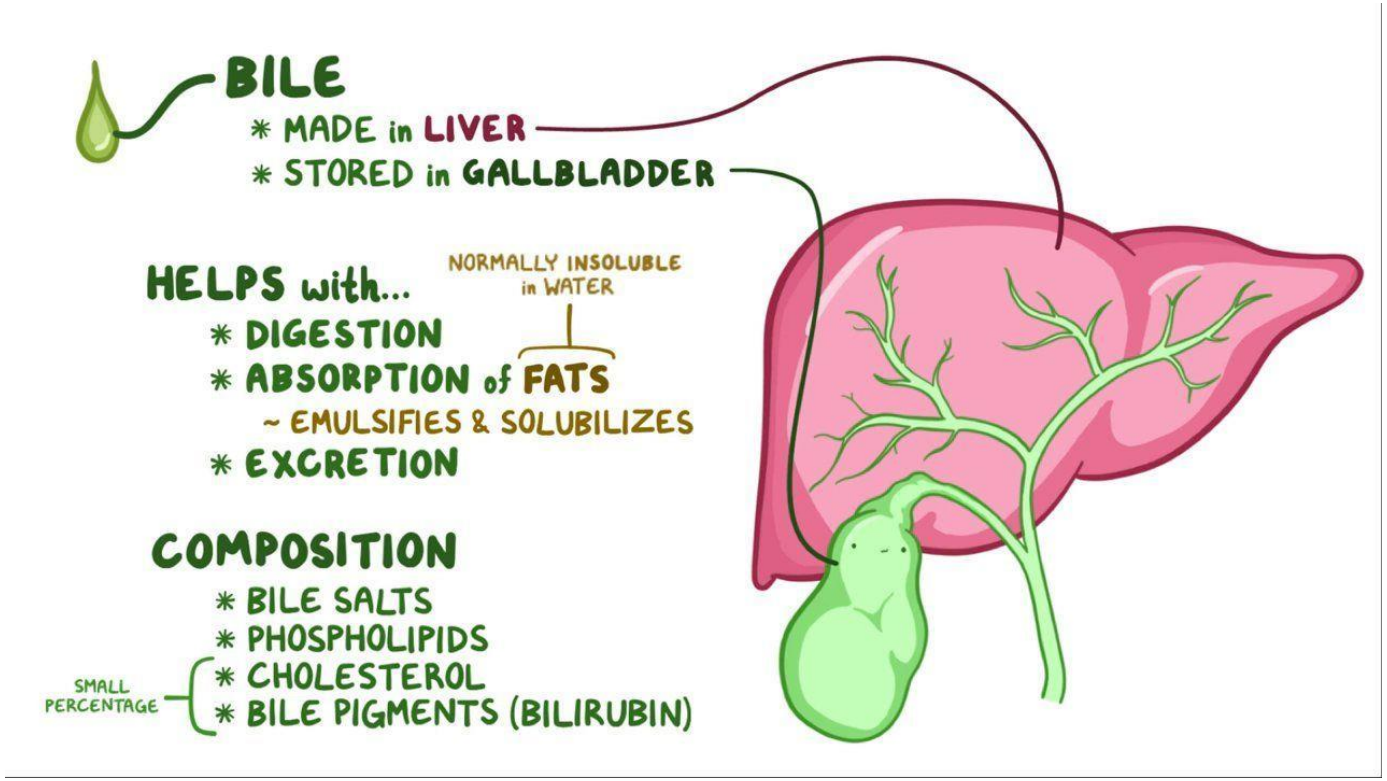
- 5. Hyperestrogenemia:
- due to impaired estrogen metabolism in male patients with chronic liver failure can give rise to palmar erythema (a reflection of local vasodilatation) and spider angiomas of the skin.
- Such male hyperestrogenemia also leads to hypogonadism and gynecomastia.
- 6. hepatocellular carcinoma (HCC).

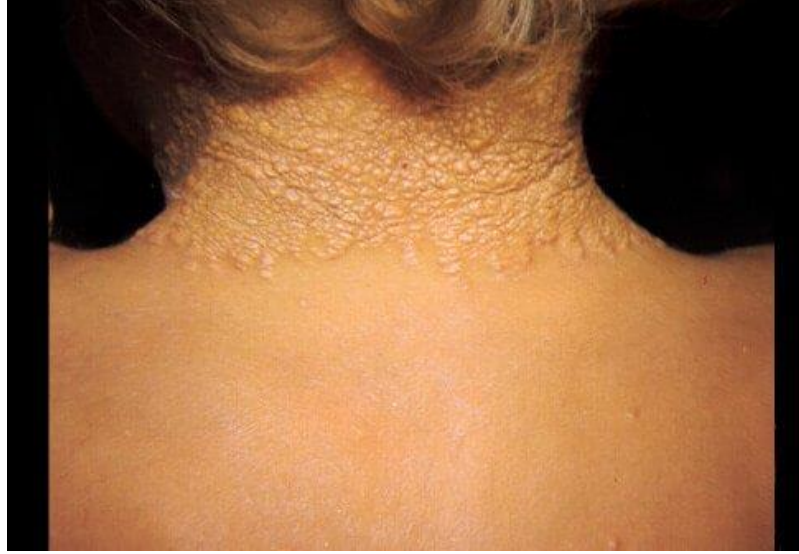




cholestasis

- Cholestasis is a condition caused by extrahepatic or intrahepatic obstruction of bile channels or by defects in hepatocyte bile secretion.





- Patients may have :

➢Jaundice.

➢Pruritus.

➢skin xanthomas (focal accumulation of cholesterol).

➢symptoms related to intestinal malabsorption, including nutritional deficiencies of the fat-soluble vitamins A, D, or K.

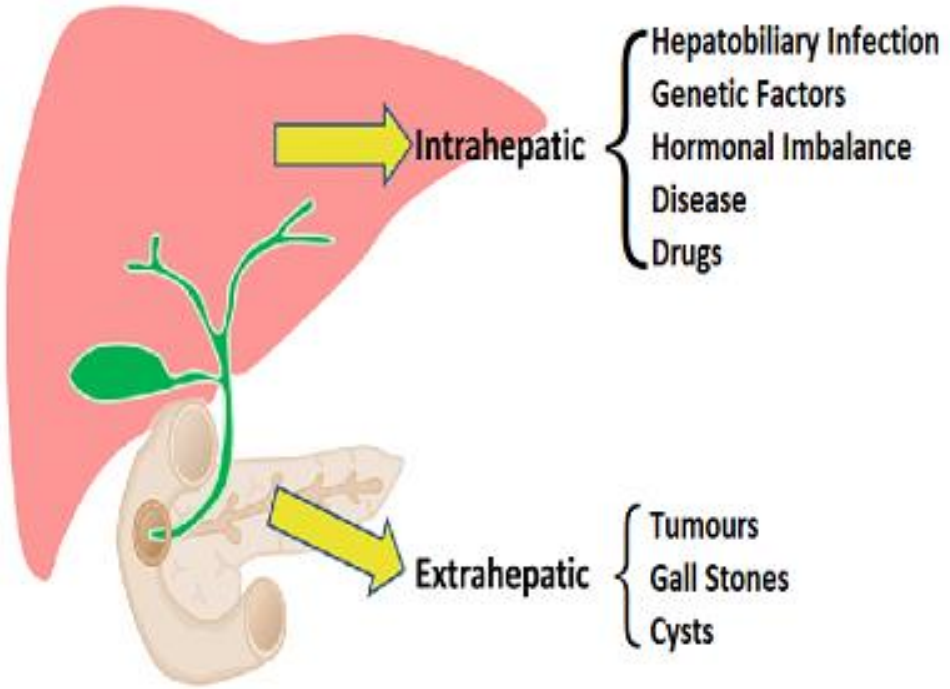
Lab:

elevated serum alkaline phosphatase and

γ-glutamyl transpeptidase (GGT),

causes

- Most typically seen in biliary disease (primary sclerosing cholangitis, primary biliary cirrhosis) .
- drug induced liver injury.
- pregnancy.
- benign familial recurrent cholestasis

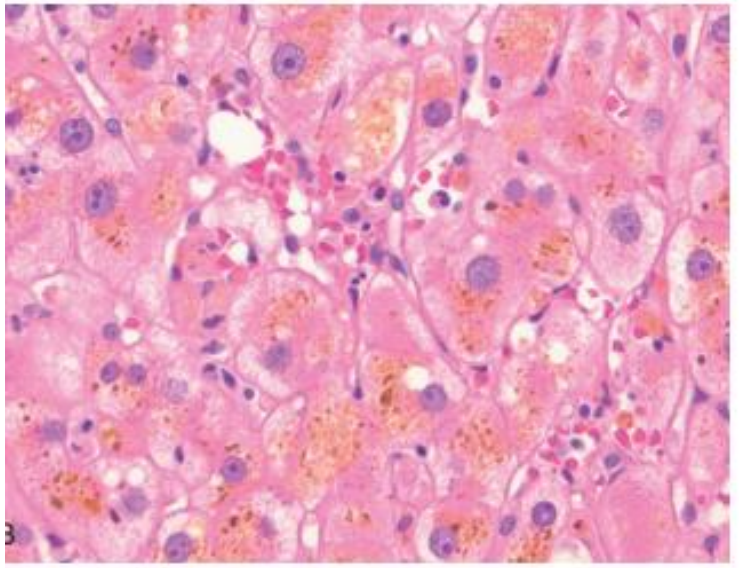


Pathophysiology

- Bile is produced in hepatocytes and flows as follows:
- hepatocyte canaliculi → canals of Hering → bile ductules → interlobular bile ducts → larger bile ducts → duodenum
- Injury or obstruction at any point along biliary flow can lead to cholestasis

histopathology

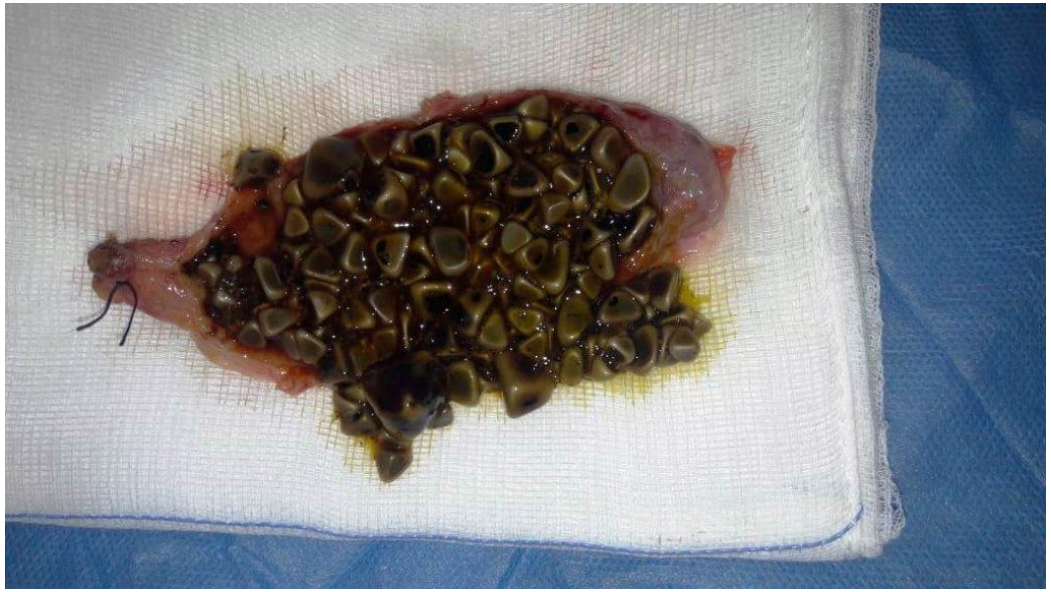
- accumulation of bile pigment within the hepatic parenchyma.
- Rupture of canaliculi leads to extravasation of bile, which is quickly phagocytosed by Kupffer cells.
- feathery degeneration:
- Droplets of bile pigment accumulate within hepatocytes, give them foamy appearance



Causes: a. Bile Duct Obstruction.

- The most common cause of bile duct obstruction in adults is:
  - extrahepatic cholelithiasis.
  - malignant obstructions.
  - postsurgical strictures.

- Obstructive conditions in children include :
  - biliary atresia.
  - cystic fibrosis.
  - choledochal cysts



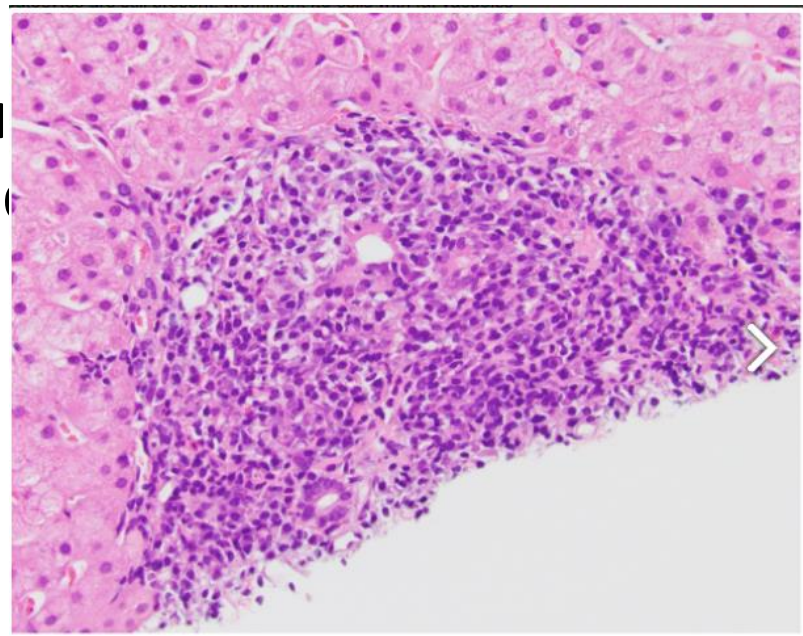
b. Neonatal Cholestasis

- Prolonged conjugated hyperbilirubinemia in the neonate, termed neonatal cholestasis.

- The major conditions causing it are:
- (1) cholangiopathies, primarily biliary atresia .(complete or partial obstruction of the extrahepatic biliary tree that occurs within the first 3 months of life.)
- (2) a variety of disorders causing conjugated hyperbilirubinemia in the neonate, collectively referred to as neonatal hepatitis

C. Primary Biliary Cholangitis.

- autoimmune disease (Anti-mitochondrial antibodies) whose primary feature is nonsuppurative, inflammatory destruction of small- and medium-sized intrahepatic bile ducts.
- **Occur in** middle-age women, with a female-to-male ratio of 6:1. Its peak incidence is between 40 and 50 years of age.
- **Histology:**
- Dense lymphocytic infiltrate in portal tracts with granu
  destruction and loss of medium sized interlobular bile
  and variable within the liver



d. Primary Sclerosing Cholangitis

- Primary sclerosing cholangitis (PSC) is characterized by inflammation and obliterative fibrosis of intrahepatic and extrahepatic bile ducts, leading to dilation of preserved segments.

- Classic finding is "onion skin" fibrosis around affected bile ducts