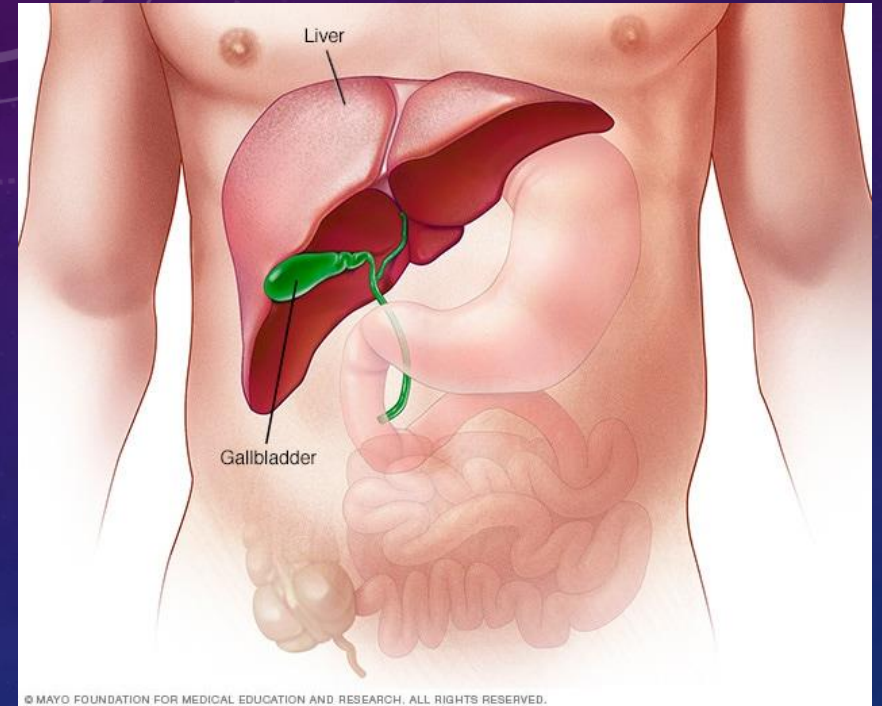
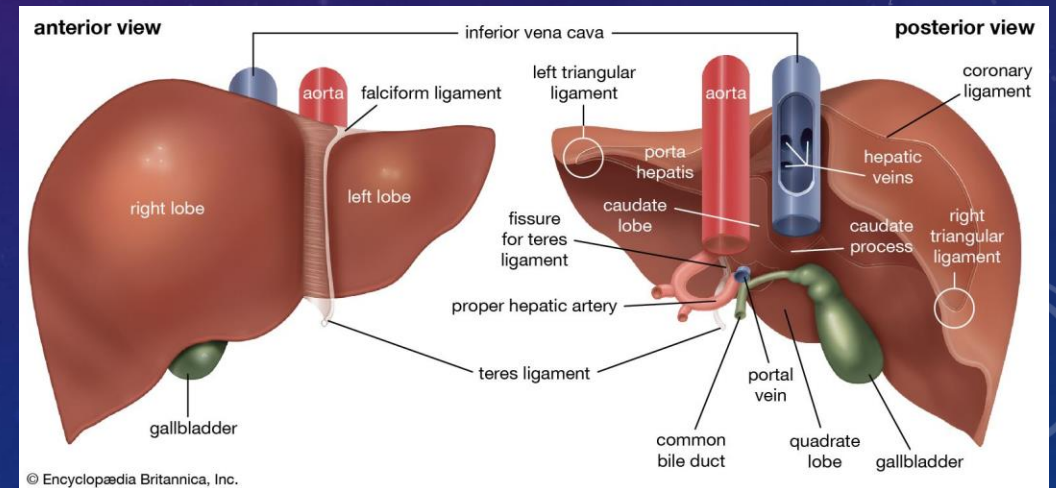


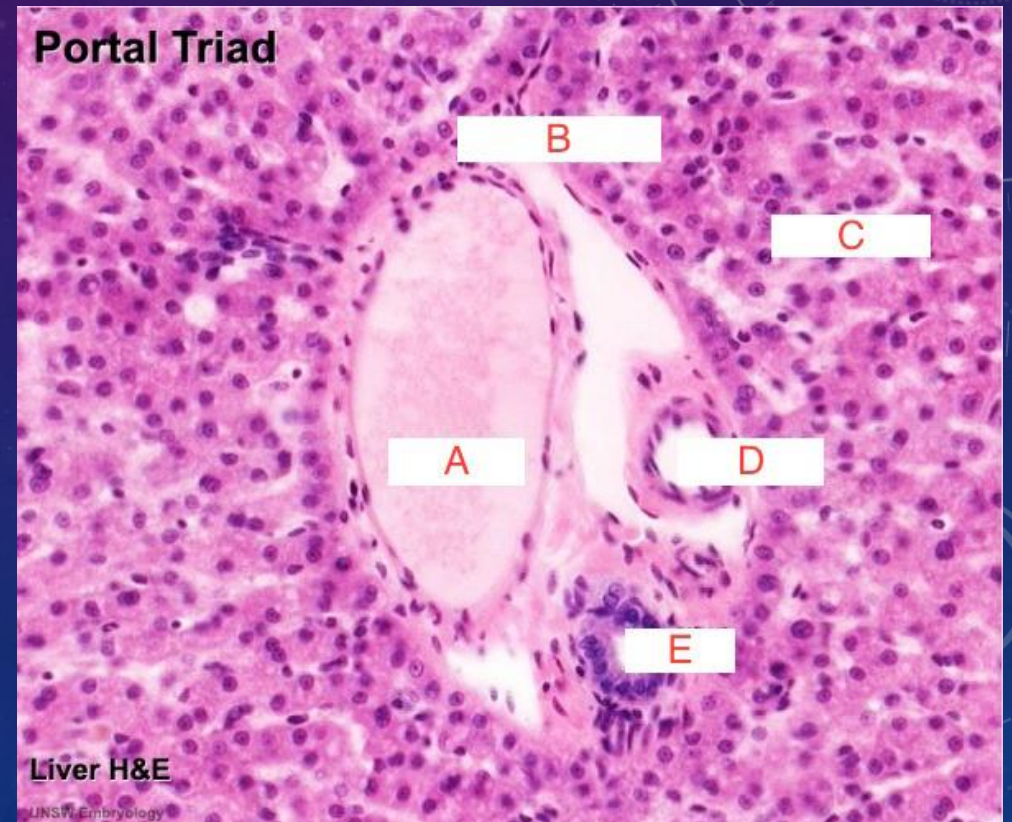
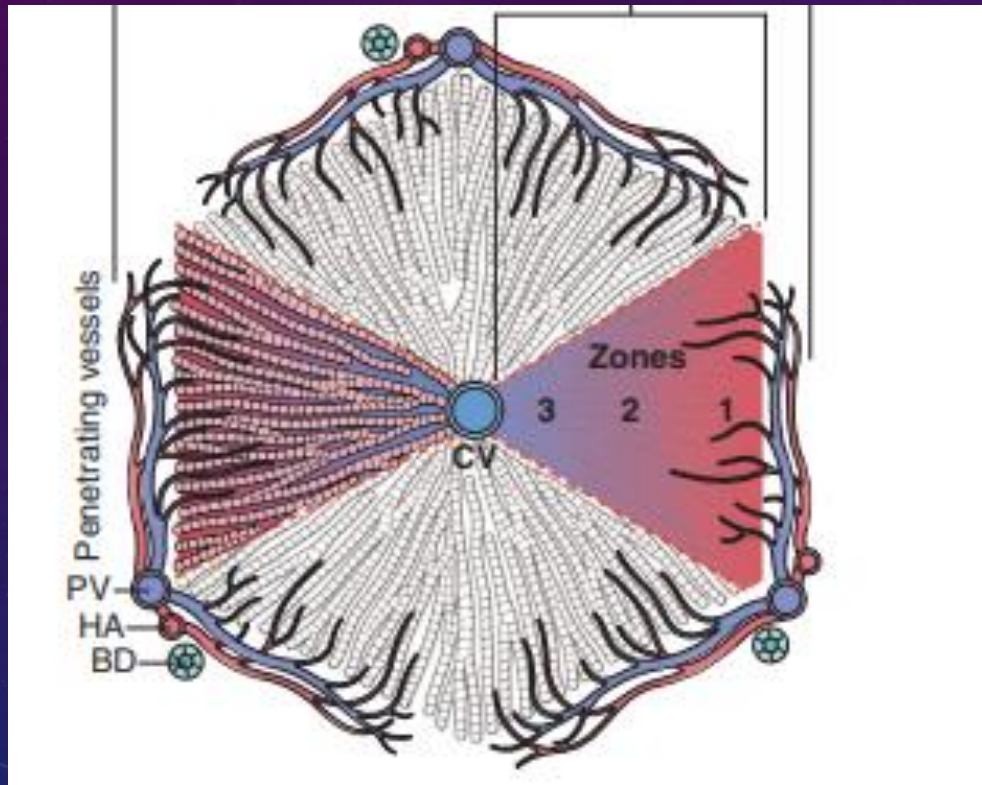
CIRRHOSIS AND CHOLESTASIS



- 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



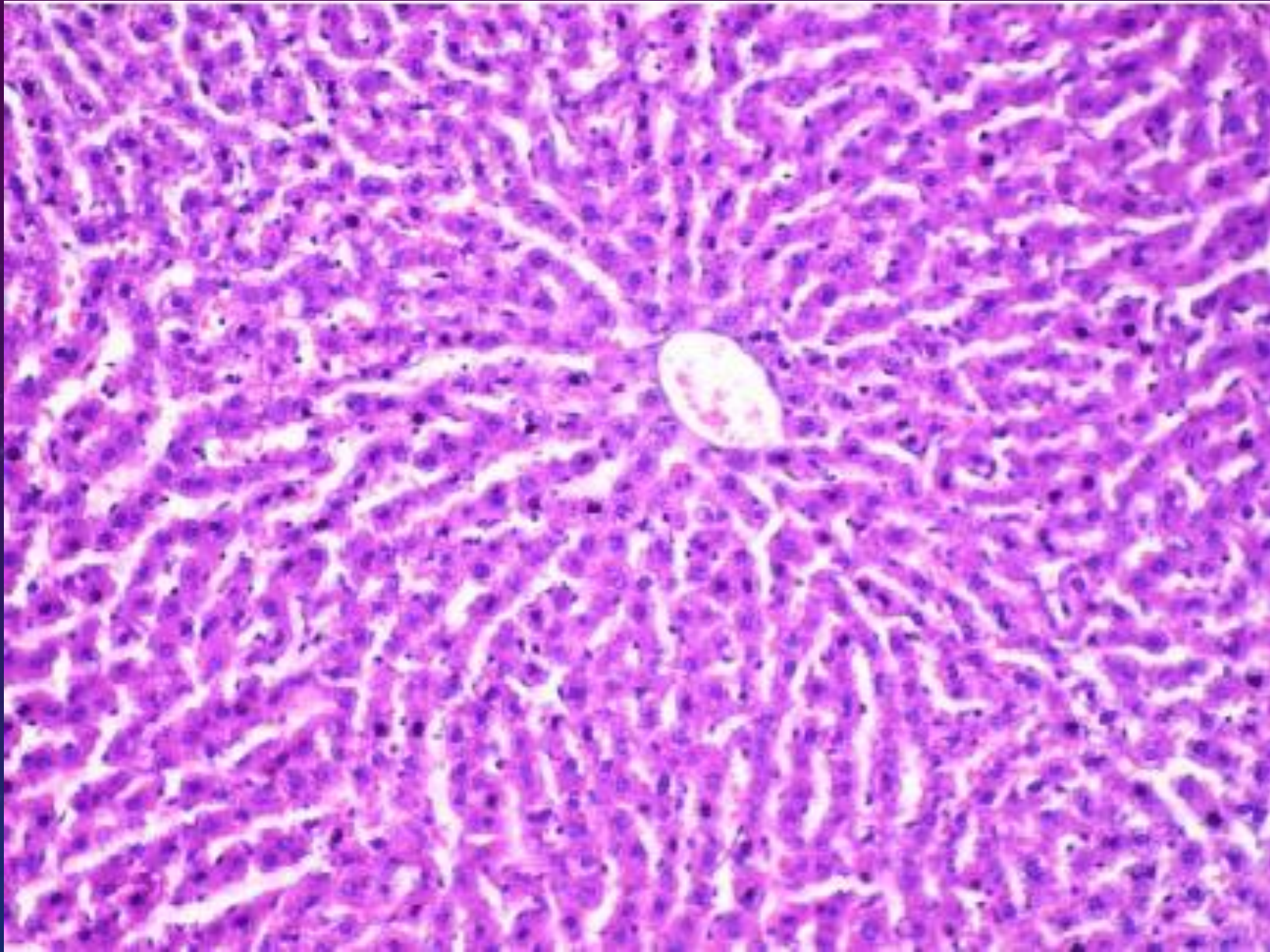


Table 16.1 Laboratory Evaluation of Liver Disease

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

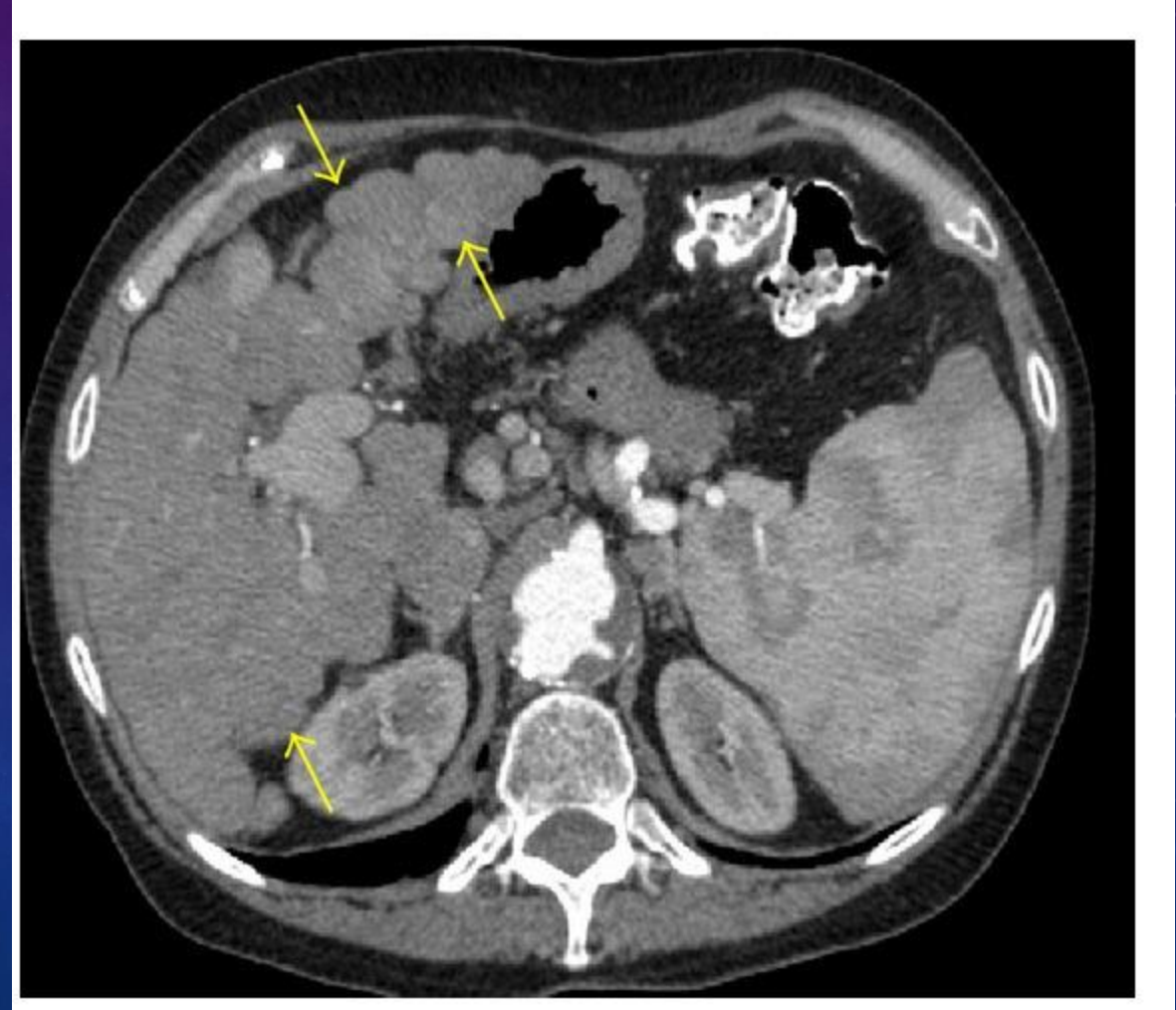


PATHOPHYSIOLOGY

- 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

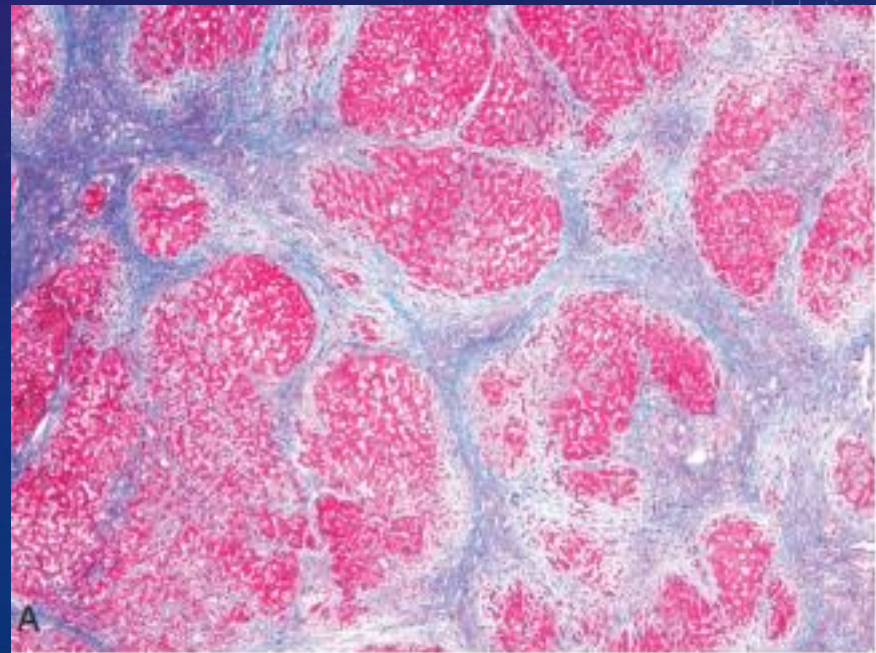
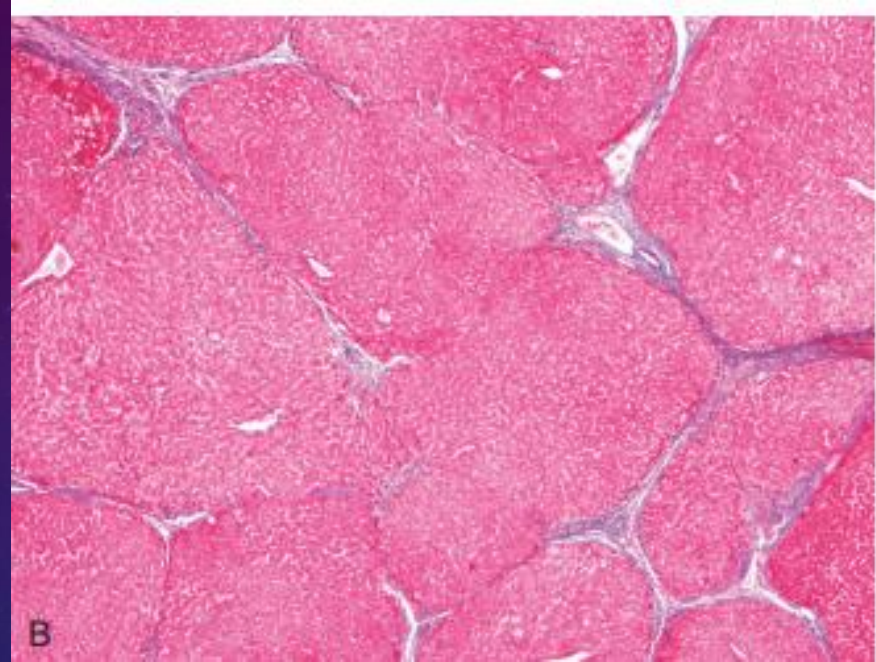


HISTOPATHOLOGY

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

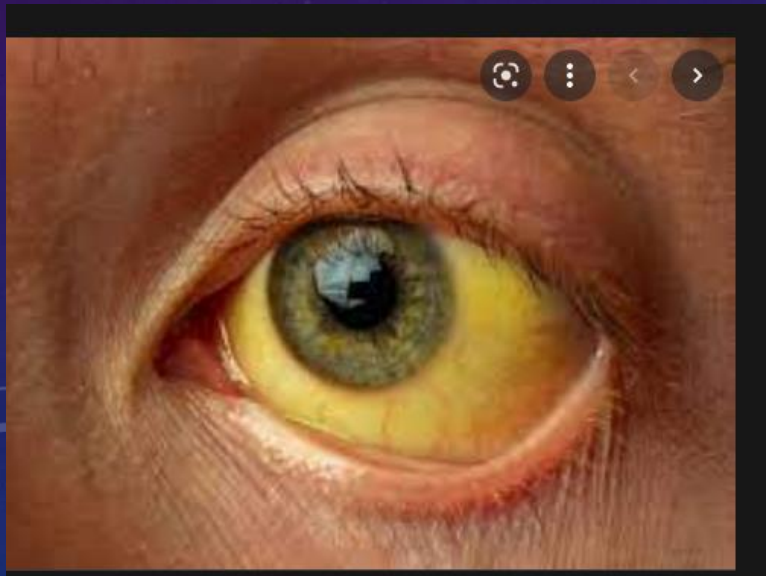
* ductular reactions.

* (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.

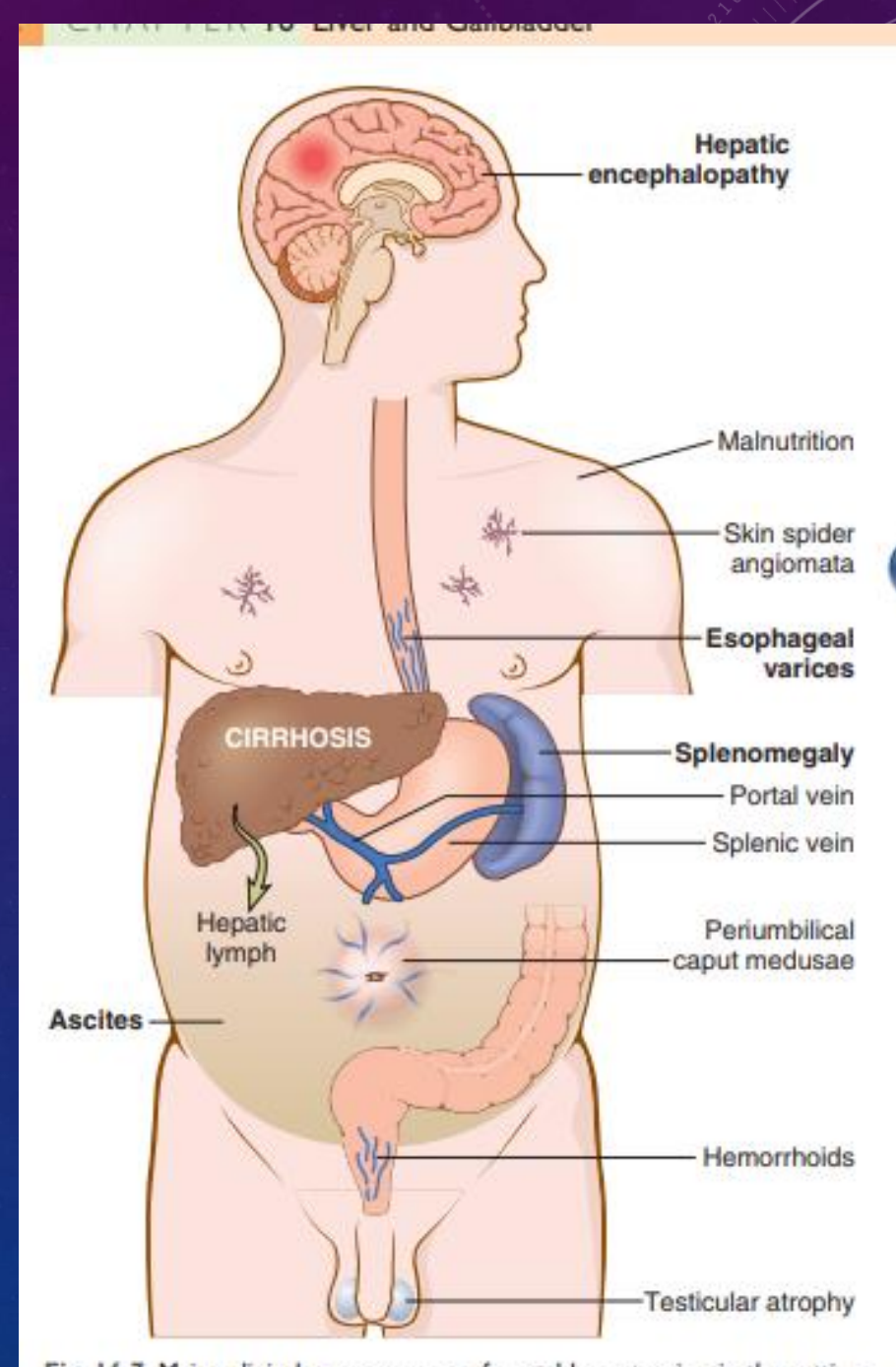


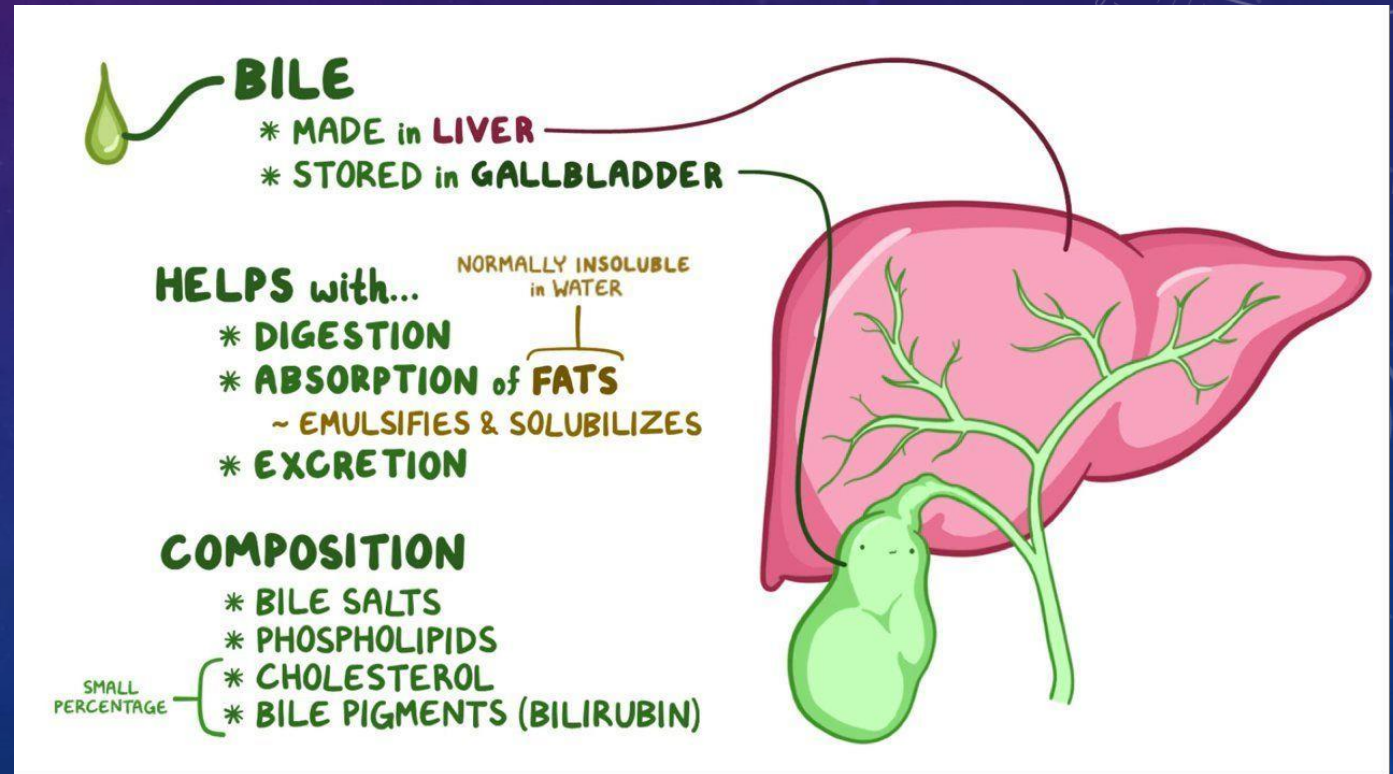
Fig. 14.7. Major clinical consequences of portal hypertension in the setting of cirrhosis.

- 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.

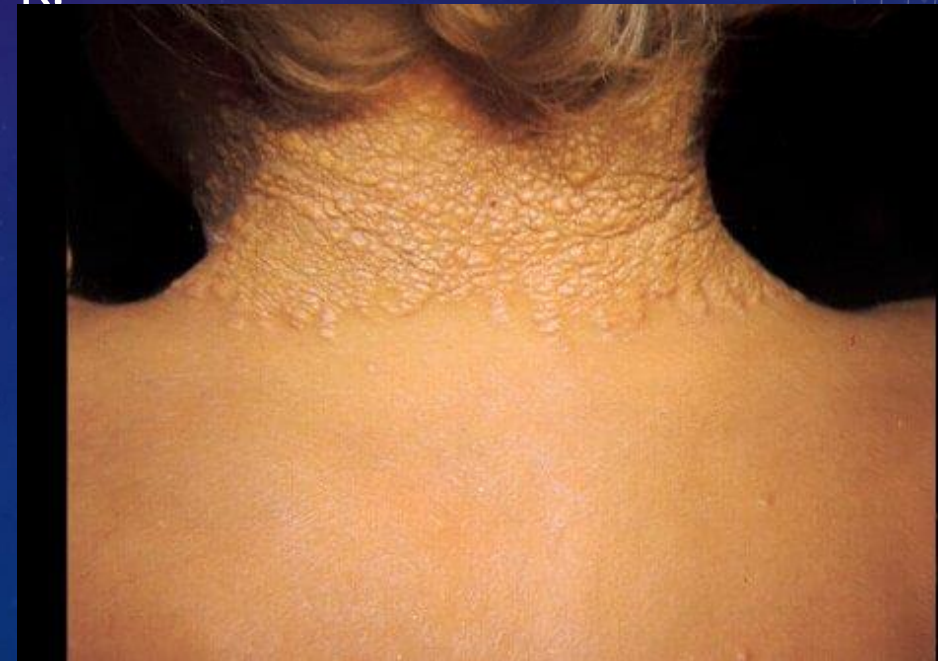
- skin xanthomas (focal accumulation of cholesterol).

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

Lab:

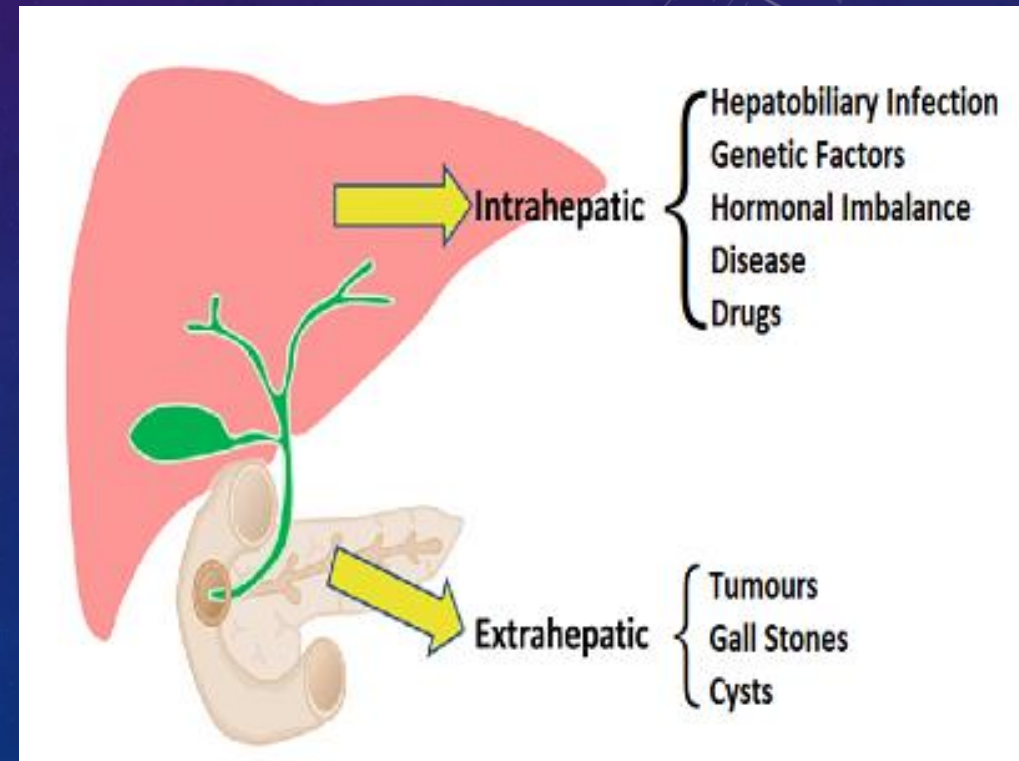
elevated serum alkaline phosphatase and

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

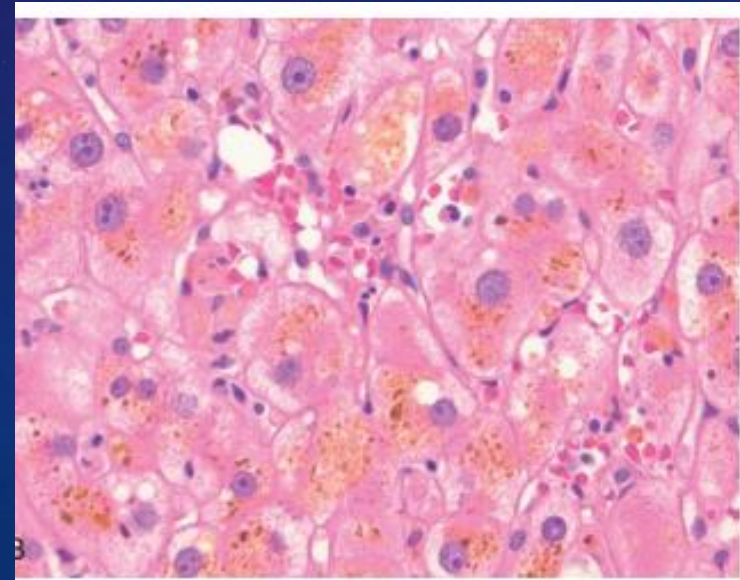


PATHOPHYSIOLOGY

- 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

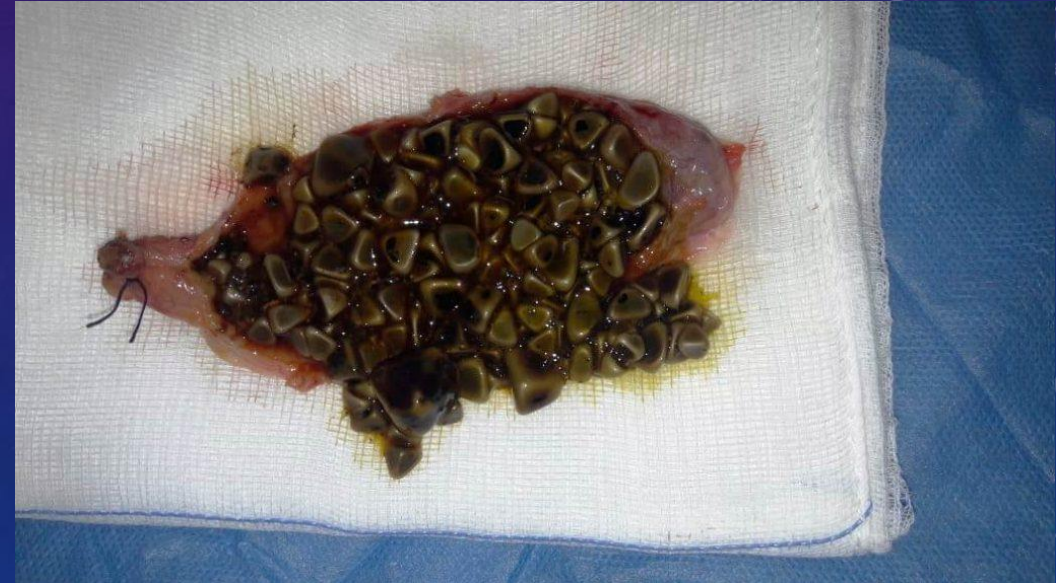
HISTOPATHOLOGY

- 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

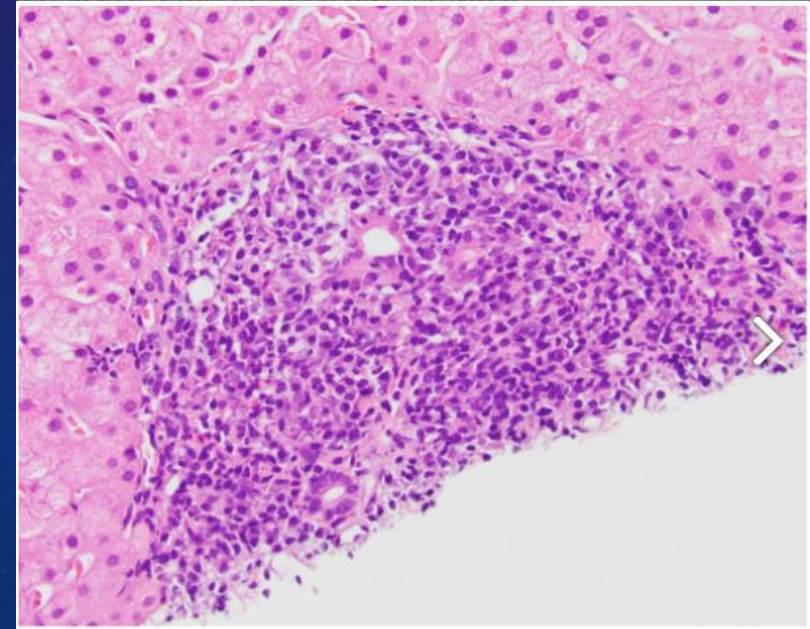


B. NEONATAL CHOLESTASIS

- 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 granulomatous destruction and loss of medium sized interlobular bile ducts, focal 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

