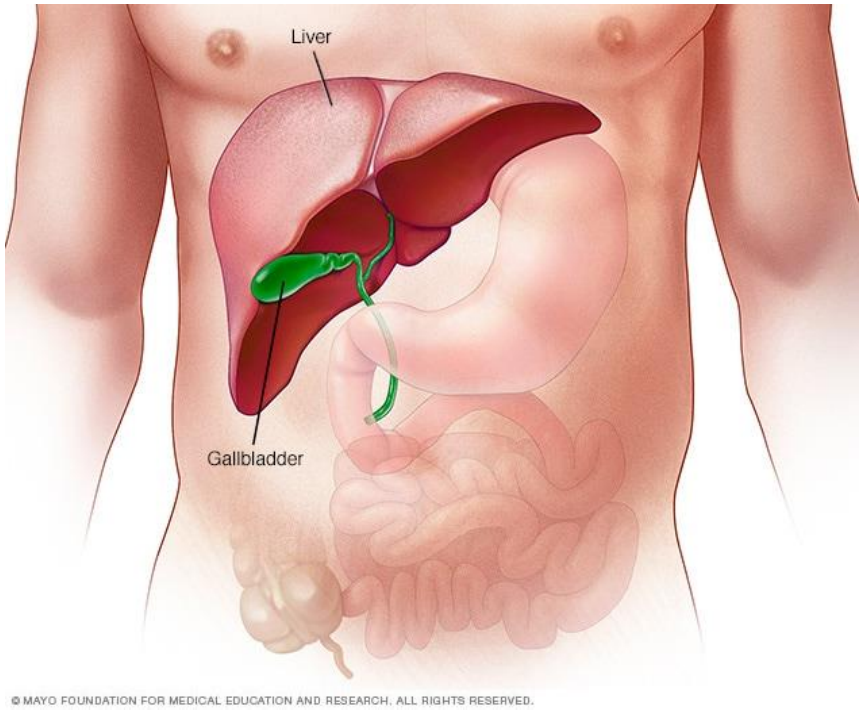
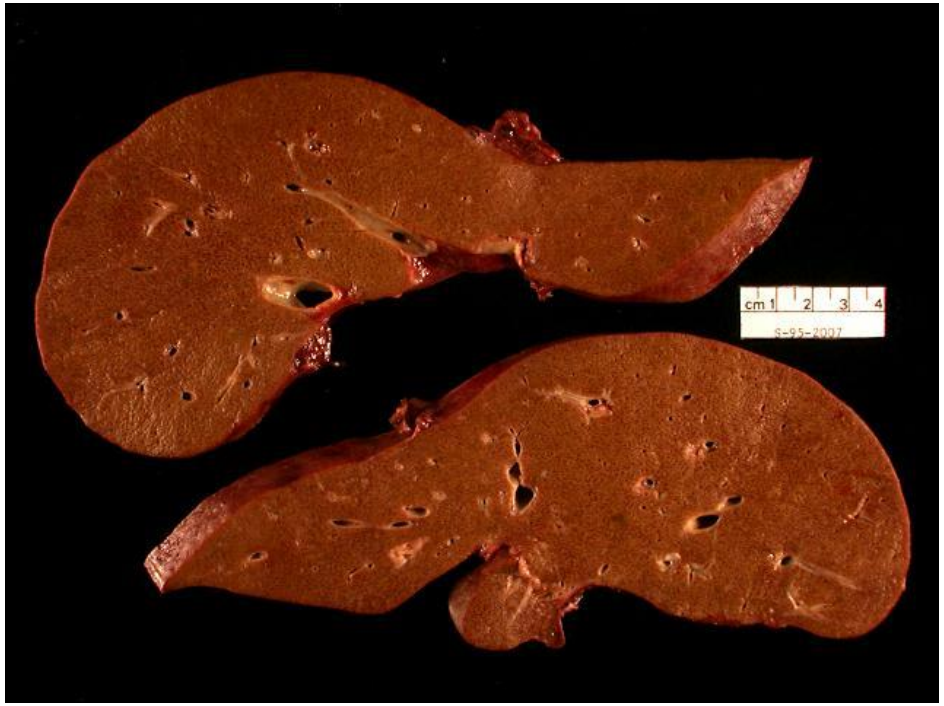
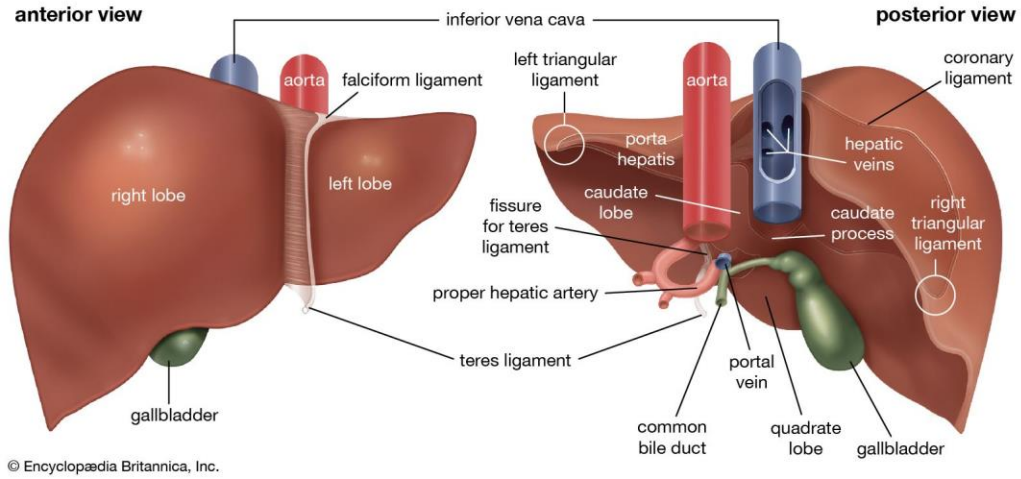
CIRRHOSIS AND CHOLESTASIS



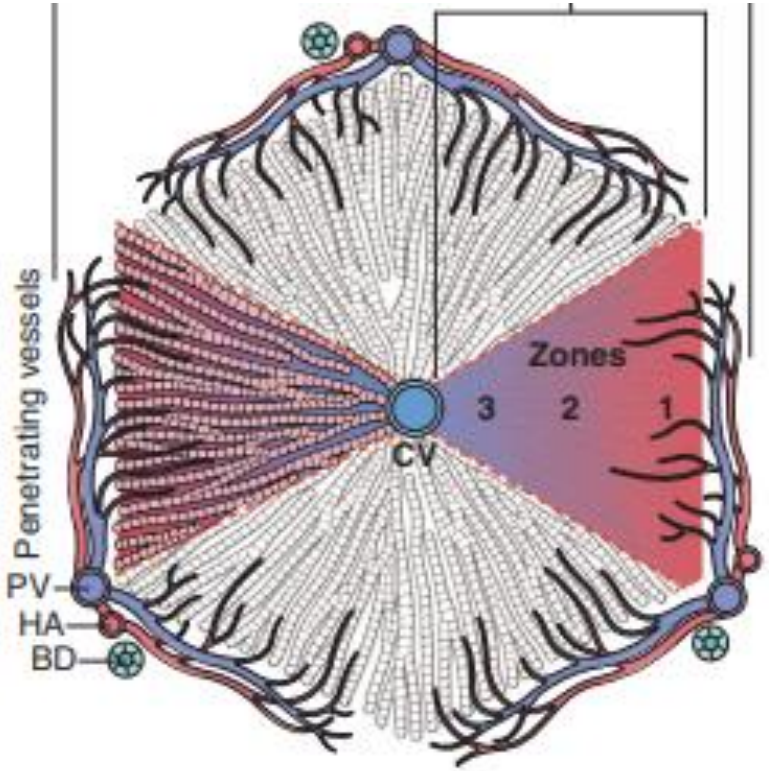
- The normal adult liver weighs 1400 to 1600 gm. It has a dual blood supply, with the portal vein providing 60% to 70% of hepatic blood flow and the hepatic artery supplying the remaining 30% to 40%.

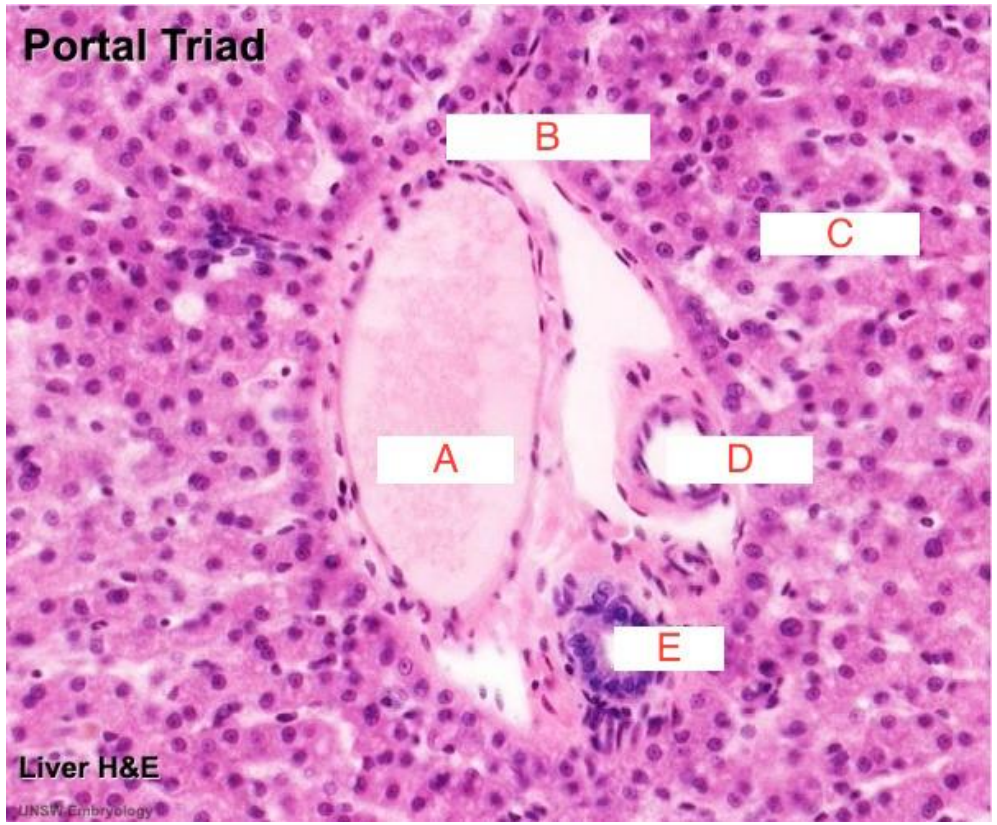
- Portal tract?





Models of liver anatomy





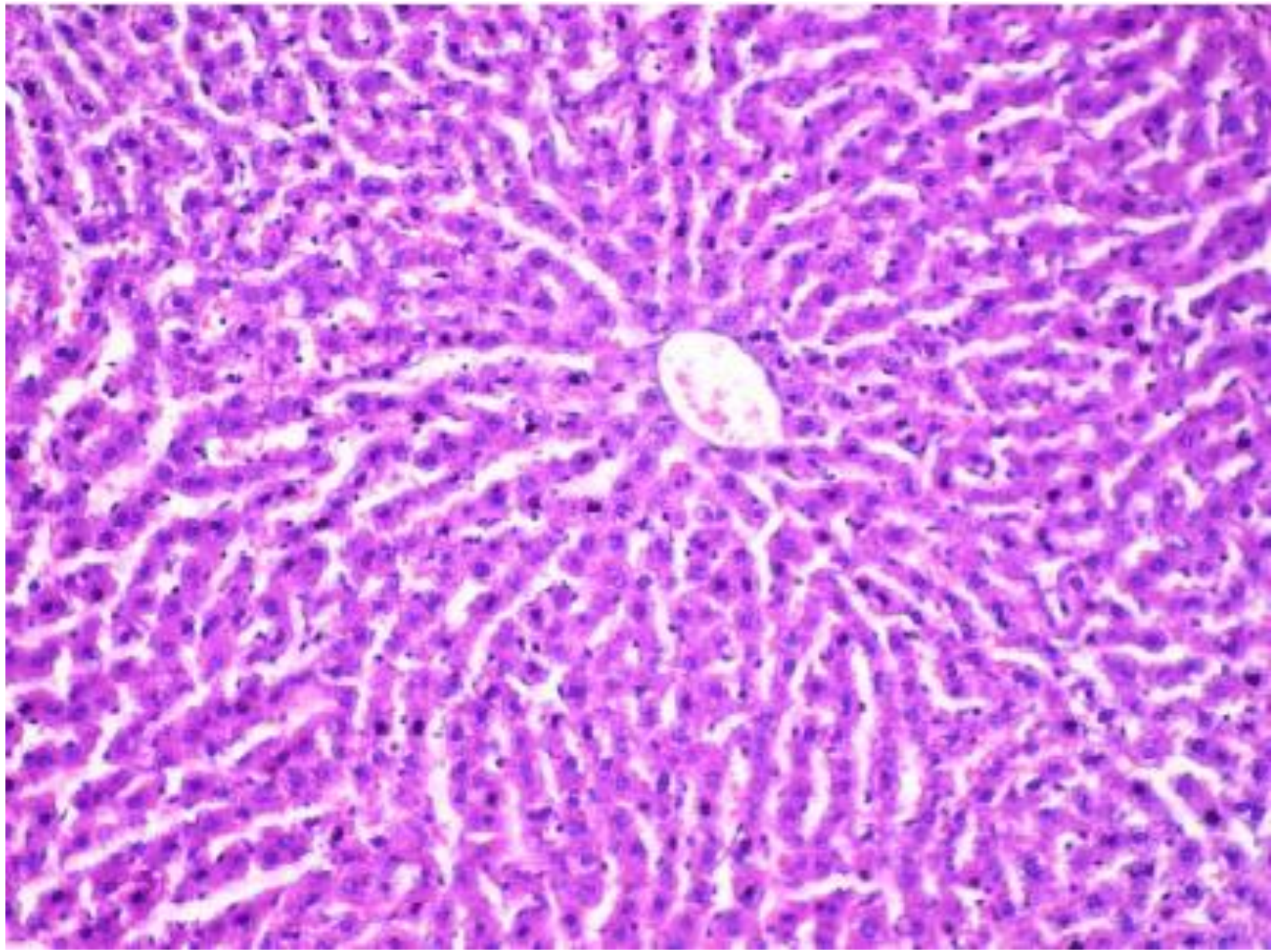


Table 16.1 Laboratory Evaluation of Liver Disease

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:

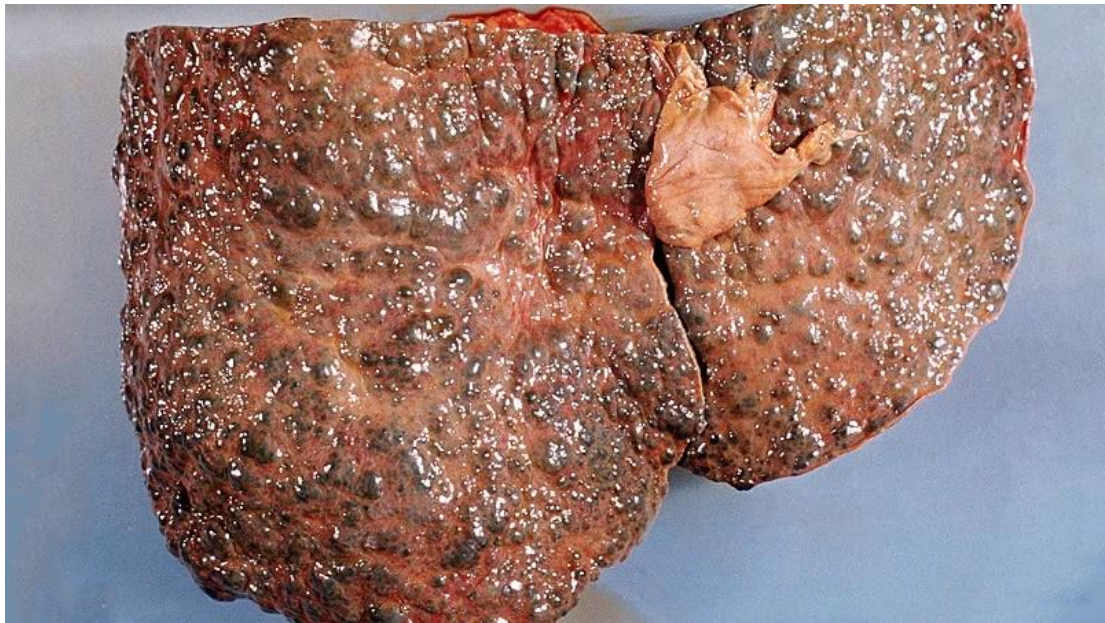
chronic hepatitis B, C.

non-alcoholic fatty liver disease (NAFLD).

alcoholic liver disease

Drug induced liver injury

Cryptogenic (idiopathic) cirrhosis



PATHOPHYSIOLOGY

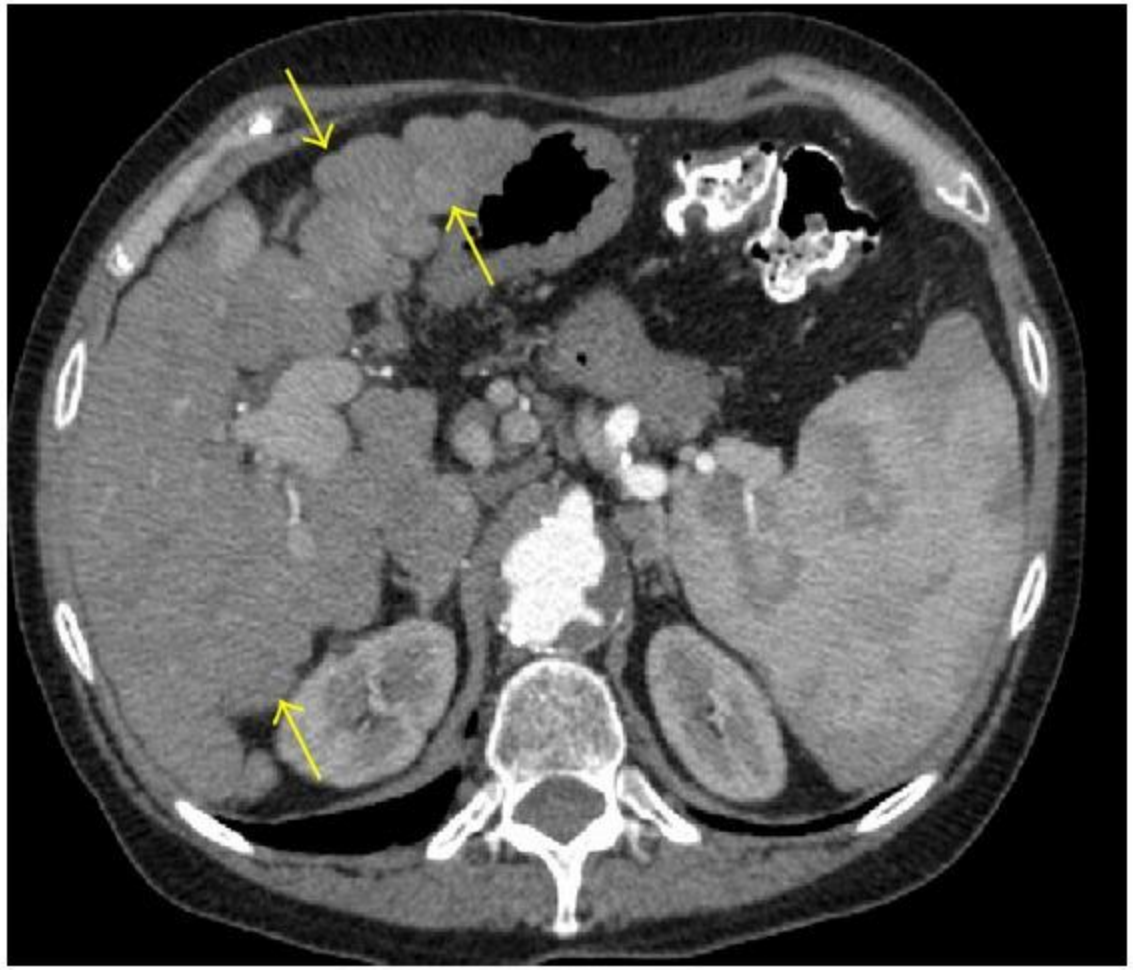
Combination of processes :

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

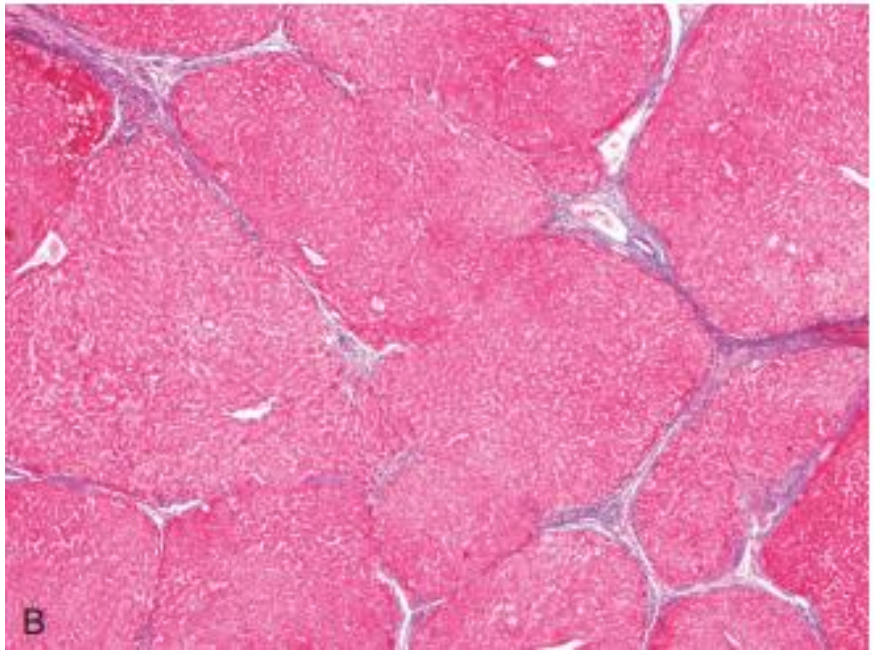


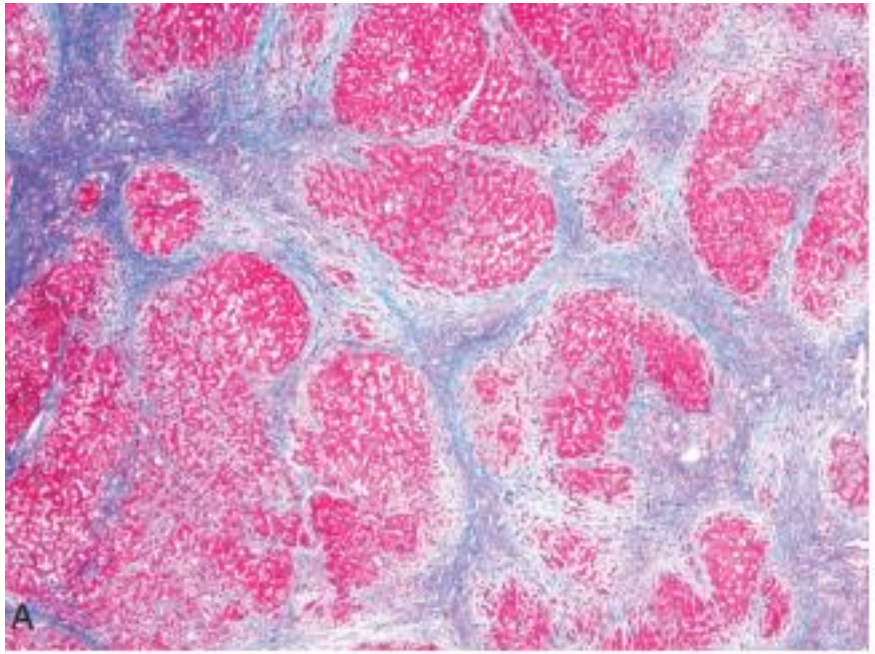
HISTOPATHOLOGY

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

* ductular reactions.

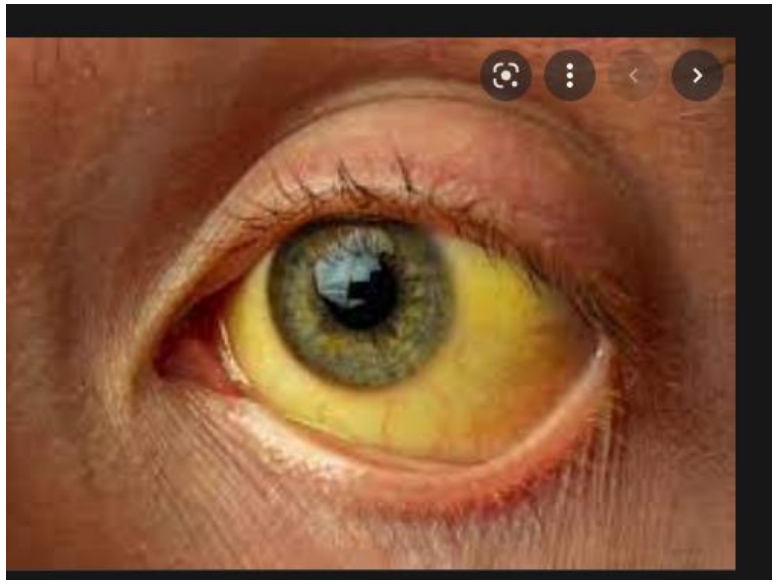
* (Masson trichrome stain) highlights these fibrous septa.

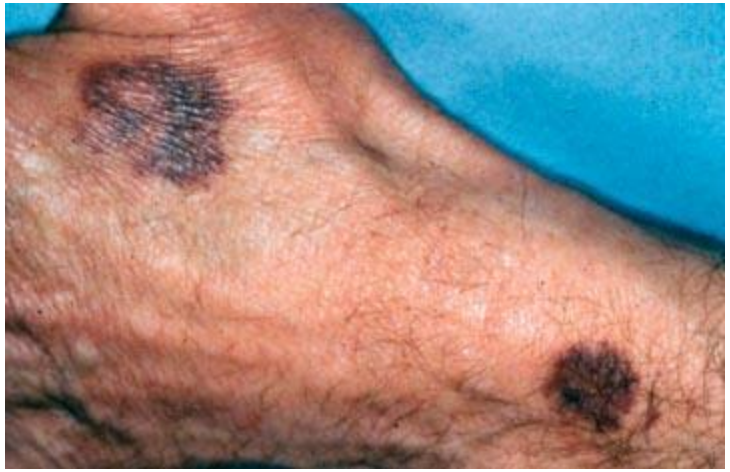


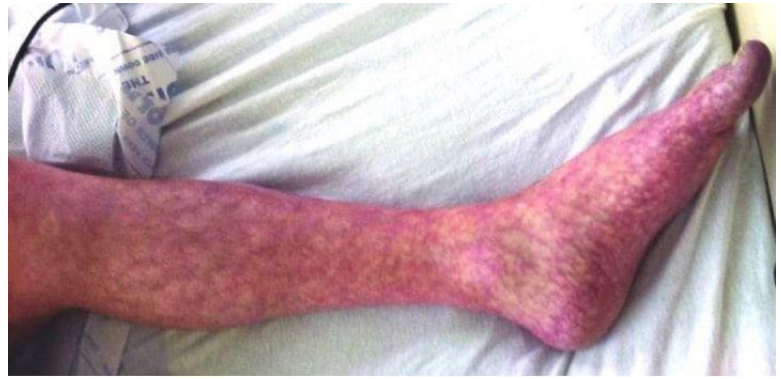


CLINICAL FEATURES

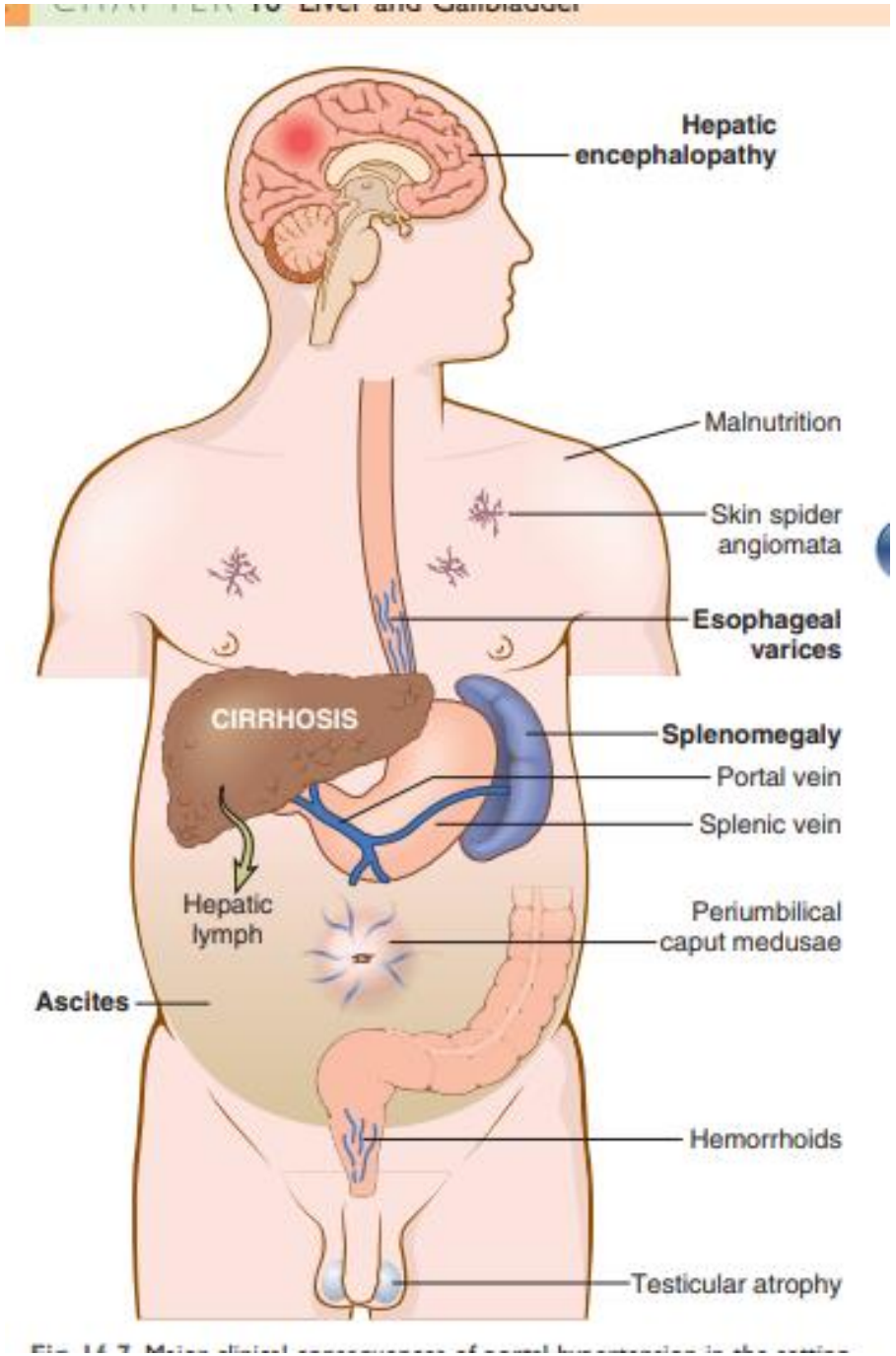
1. 40% of individuals with cirrhosis are asymptomatic until the most advanced stages of the disease.
2. Non specific symptoms such as anorexia, weight loss, weakness.
3. signs and symptoms of liver failure e.g Jaundice, encephalopathy, and coagulopathy.
4. Pruritus, portal hypertention.







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

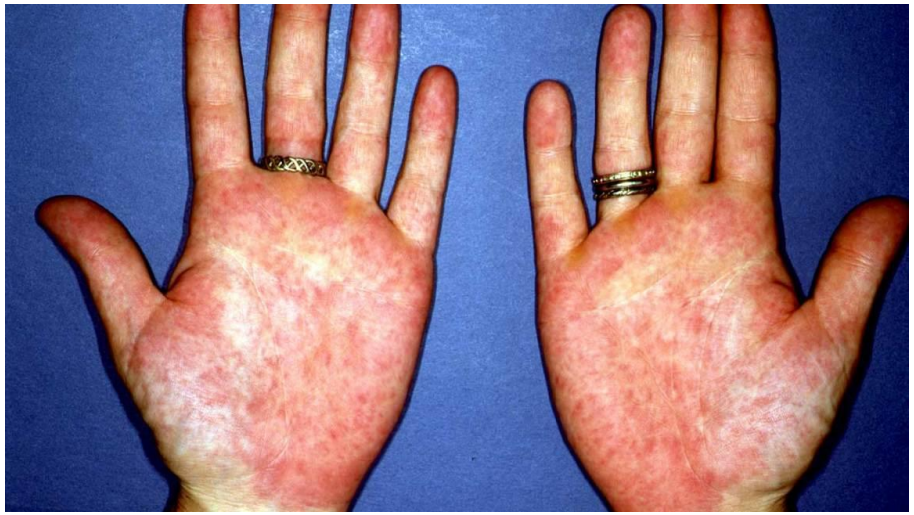


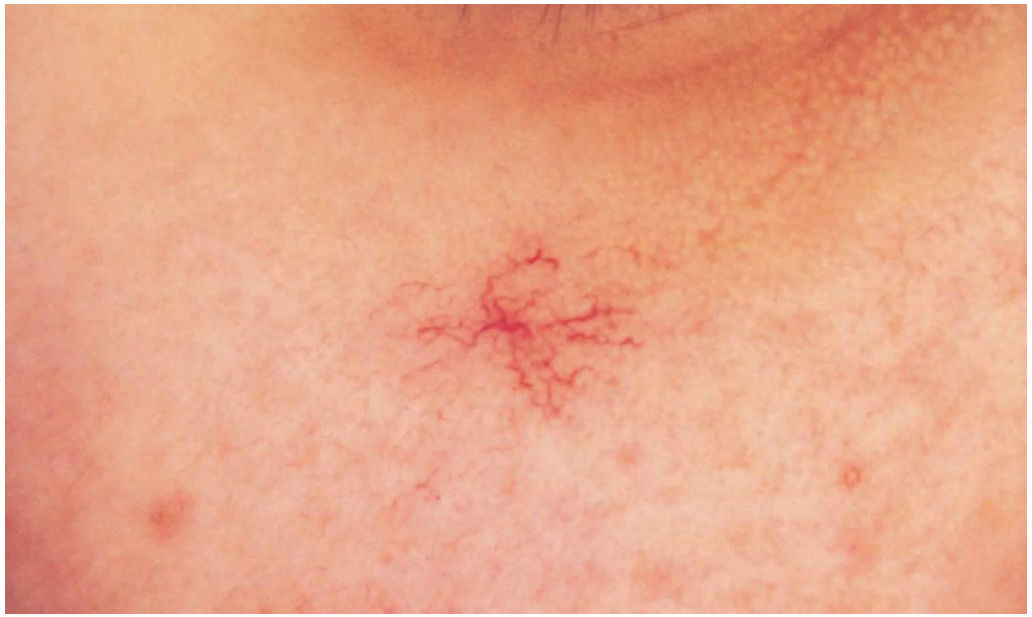
5. Hyperestrogenemia:

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.

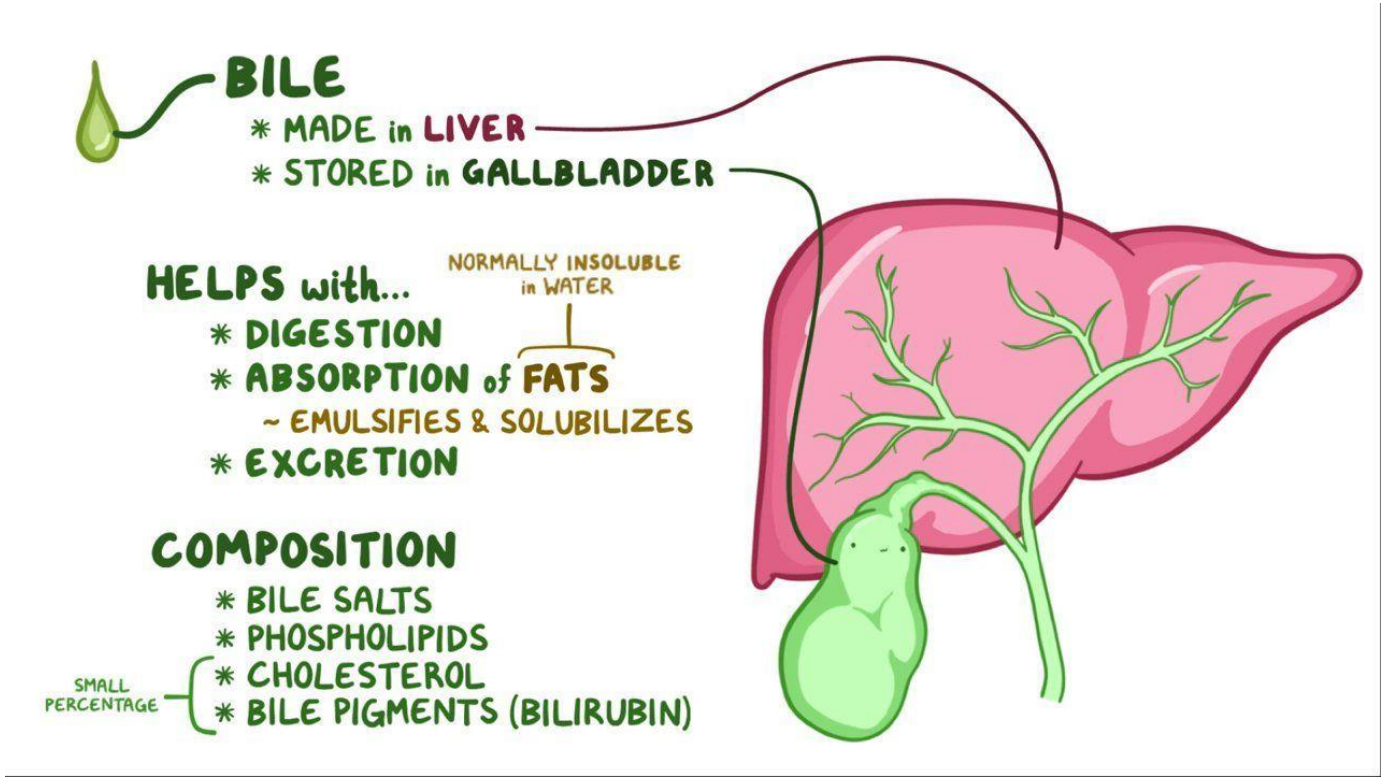
6. hepatocellular carcinoma (HCC).





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.

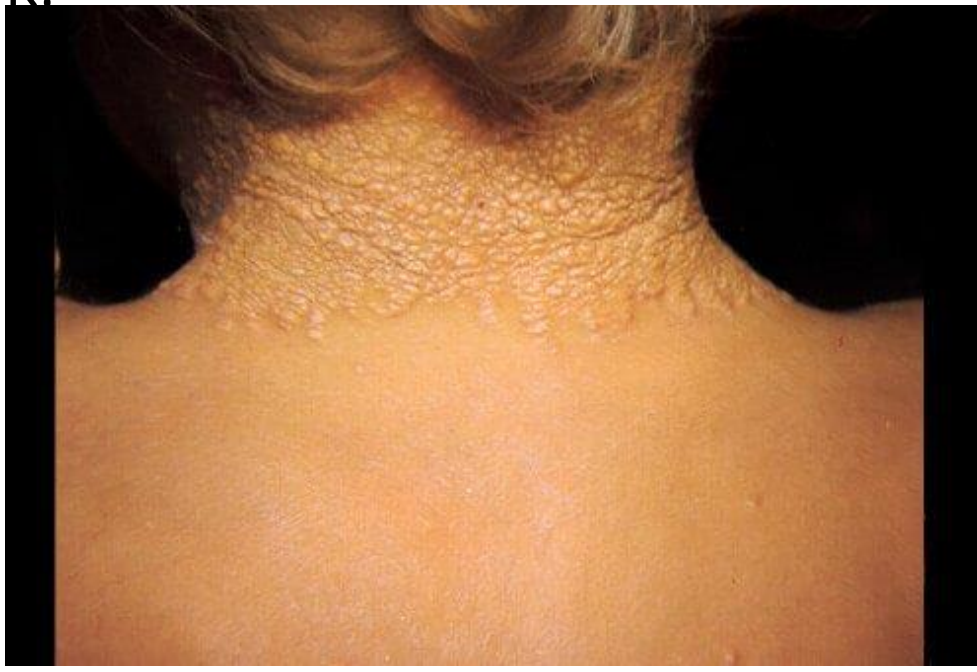
Pruritus.

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),



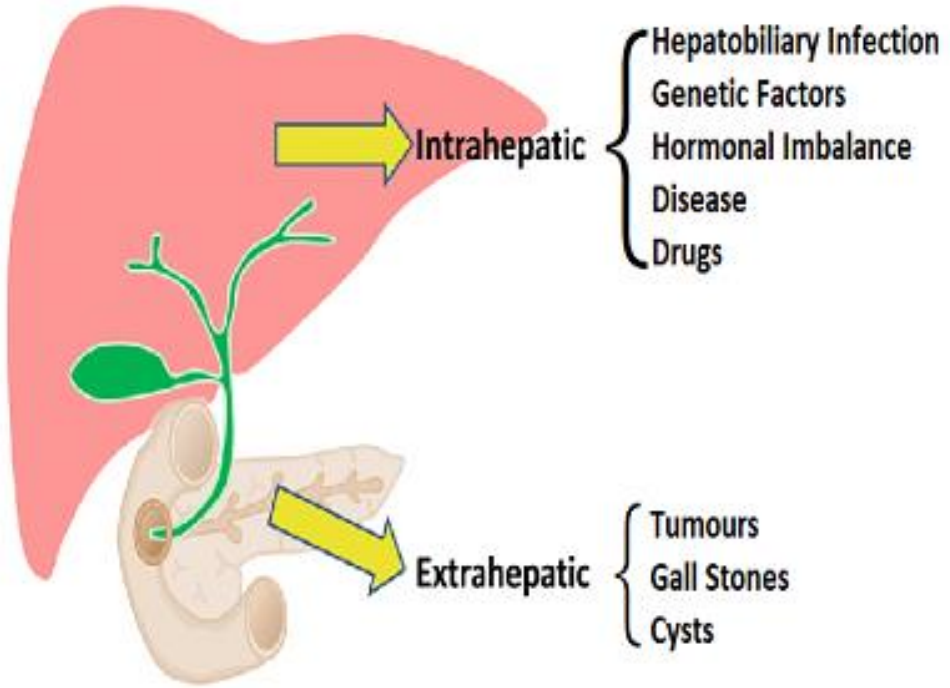
CAUSES

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

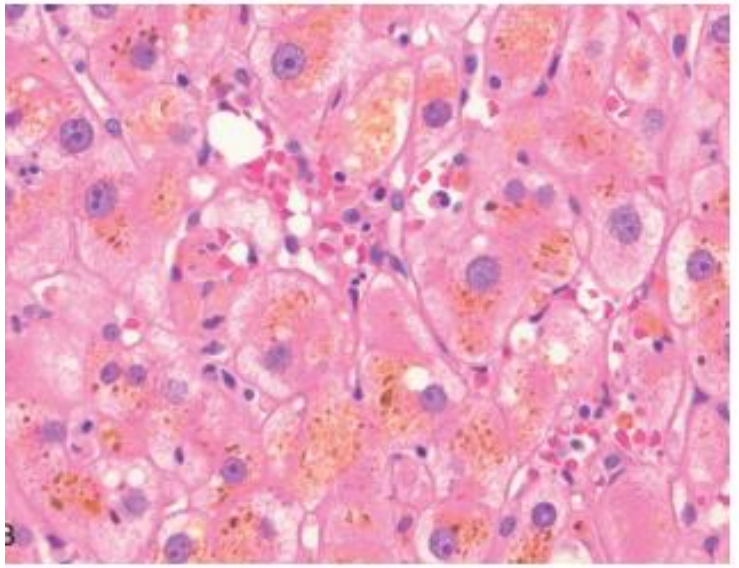
HISTOPATHOLOGY

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



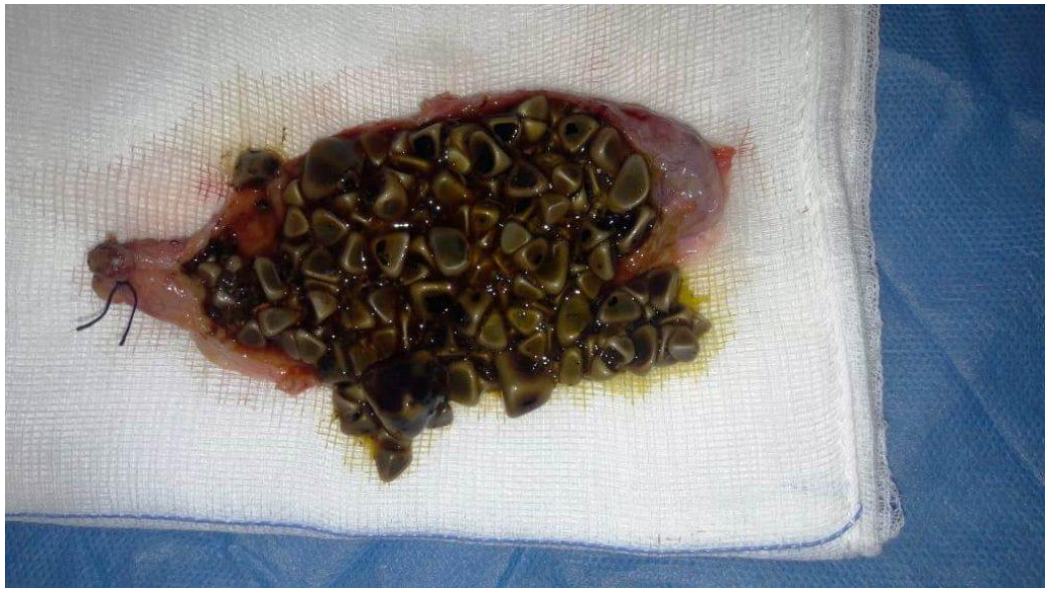
CAUSES: A. BILE DUCT OBSTRUCTION.

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

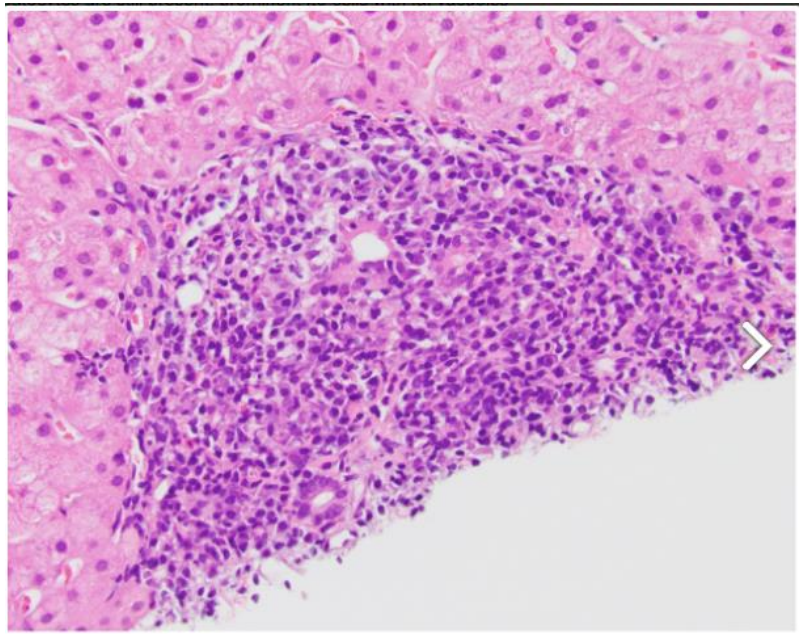
C. PRIMARY BILIARY CHOLANGITIS.

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