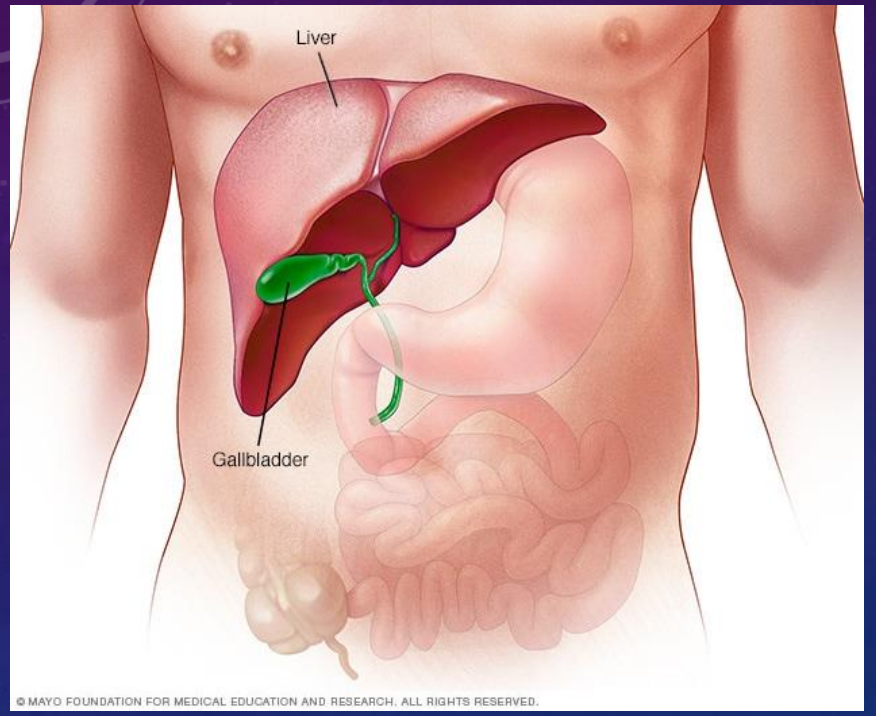
CIRRHOSIS AND CHOLESTASIS



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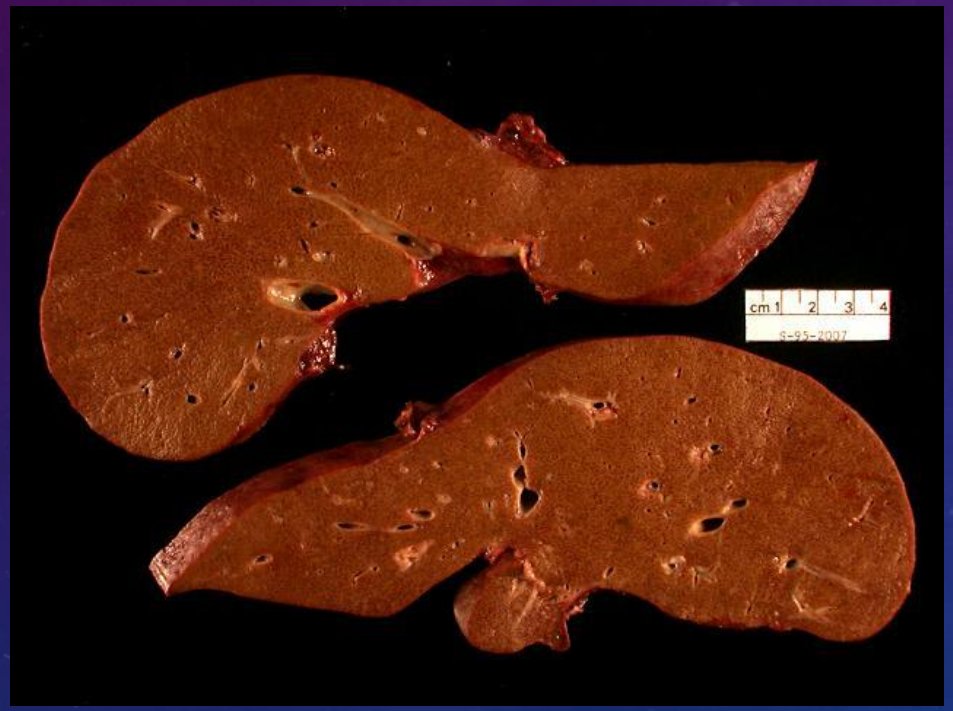
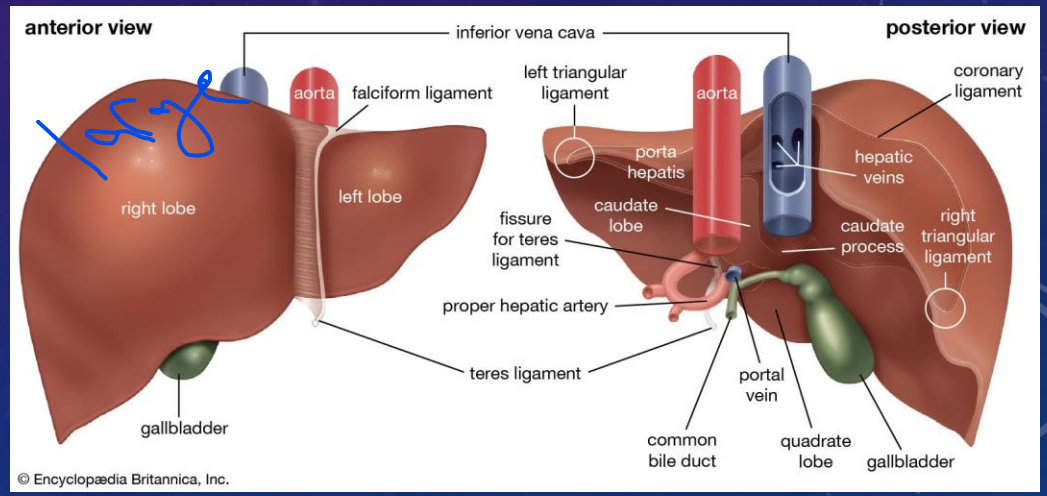
normal liver: the liver is a major metabolic organ in our body, it has many synthetic and detoxification roles

- 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?



wedge shaped organ, it has a smooth surface

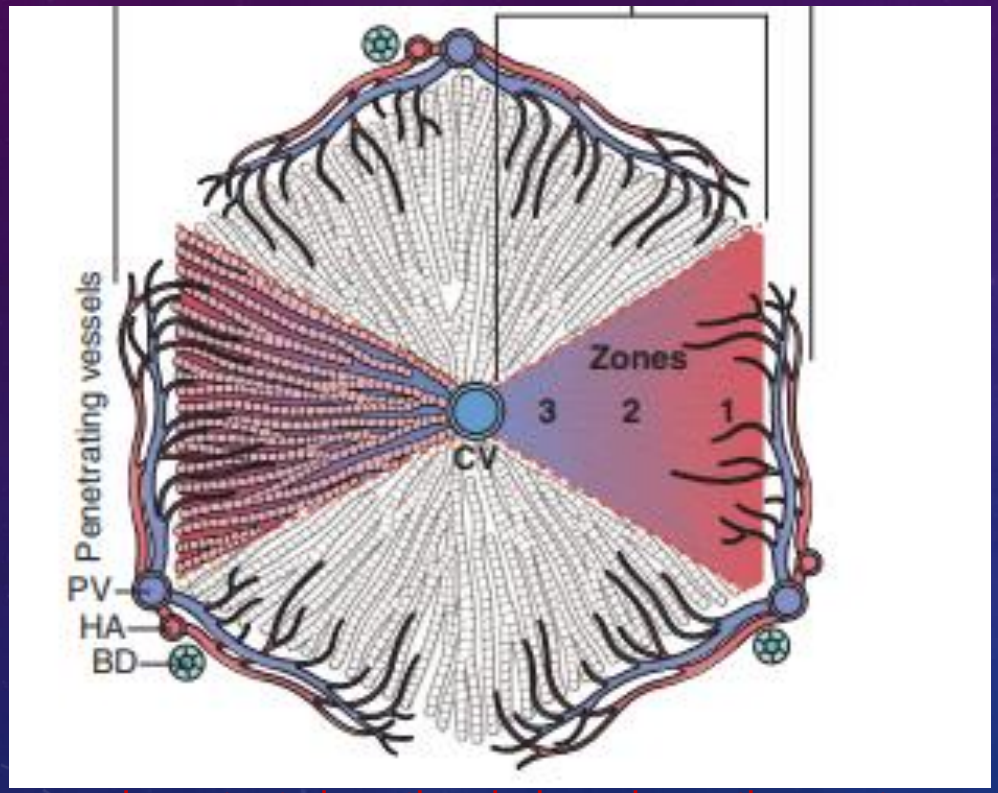


it has 2 lobules of unequal size

it characterizes by basic structure unit of hexagonal structure. on the sides there is the portal triad and in the center there is a center vein

Models of liver anatomy

it has millions of hepatocytes arranged as plates
sinusoids are attached to these plates so the blood flow can move freely. the hepatic lobules are subdivided into 3 zones: zone 1 is the closest to the artery

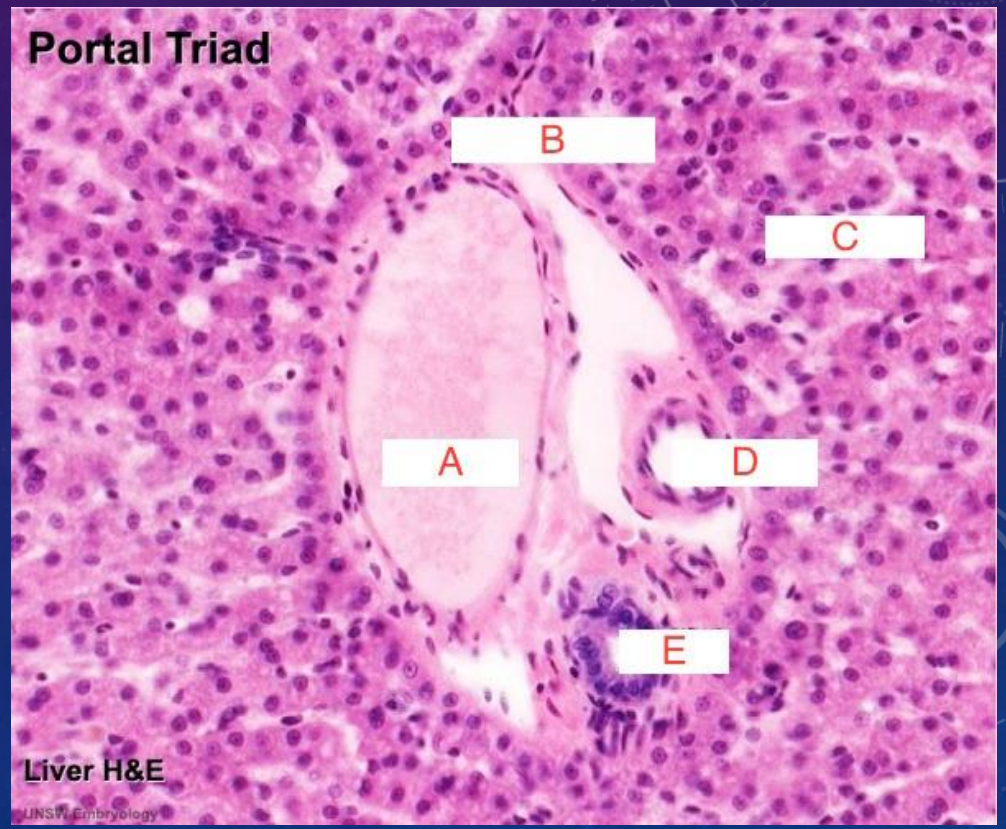


these zones are important since they help us know the most susceptible areas that can be affected by ischemia, any ischemic insult will affect the areas that are far away from the hepatic artery and more closer to the CV which is zone 3

the poral triad contains 3 major components: the hepatic artery, the portal vein and bile duct

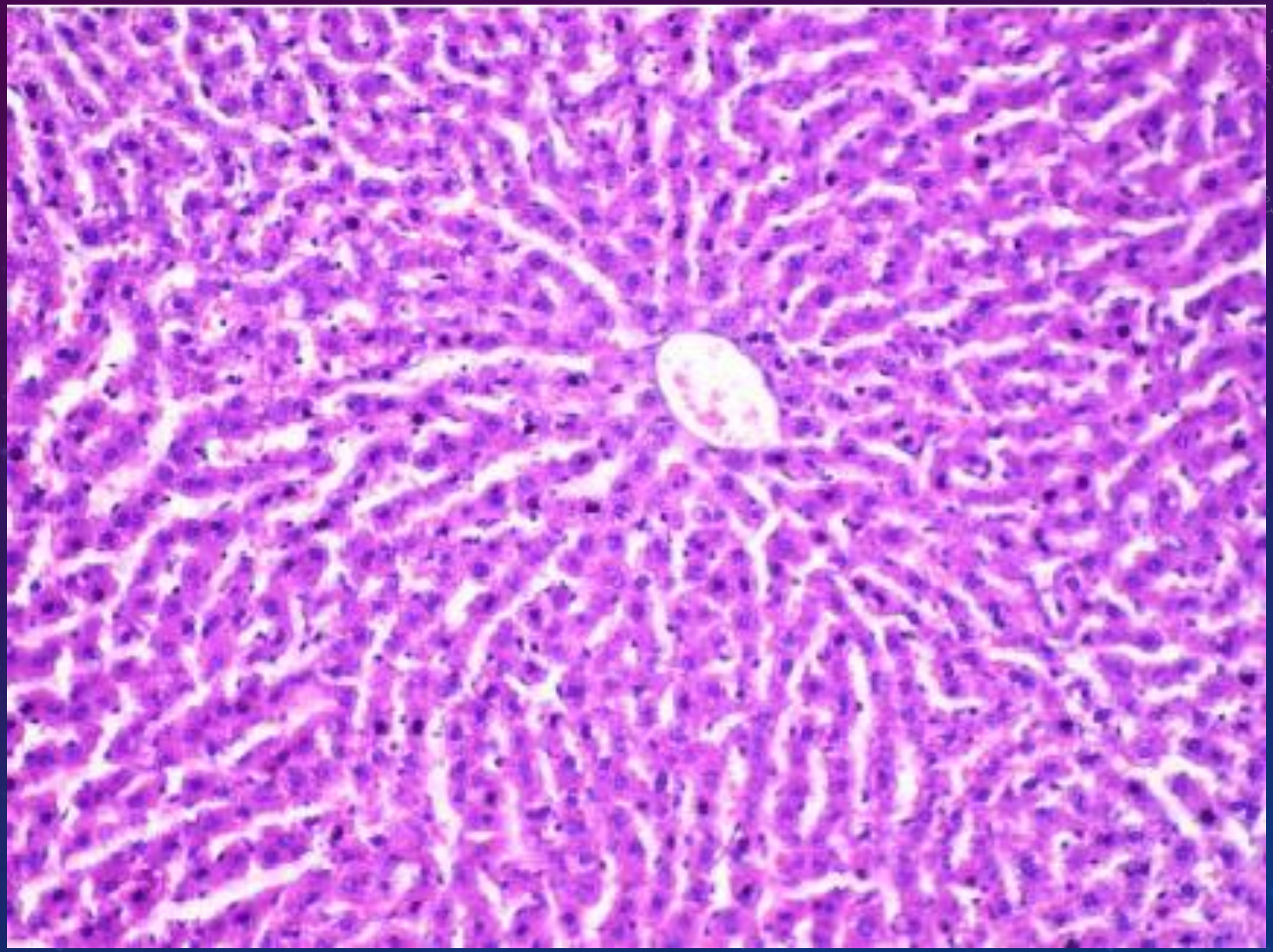
vein is A i think : lacks smooth muscle

D: artery which has muscular wall to compress



E: bile duct which is lined by bile epithelium

huge numbers of hepatocytes arranges as cords , the whitish areas are sinusoids



liver function tests are divided to 3 major headlines

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)‡

synthetic function

clotting factors

major toxin to get rid of

if ammonia builds up in the body it can reach the brain and cause certain neurological manifestations

- The major hepatic diseases can be classified as:

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

- 2. secondary: the liver involvement is part of systemic manifestations
- cardiac disease. exp: a patient with heart failure the heart is mainly effected but there can be hepatic manifestations
- disseminated cancer.
- extrahepatic infections

why is it diffused? in physio we took that the synthetic capacity and regenerative capacity are huge so any insult won't cause liver diseases unless it contained a diffused process

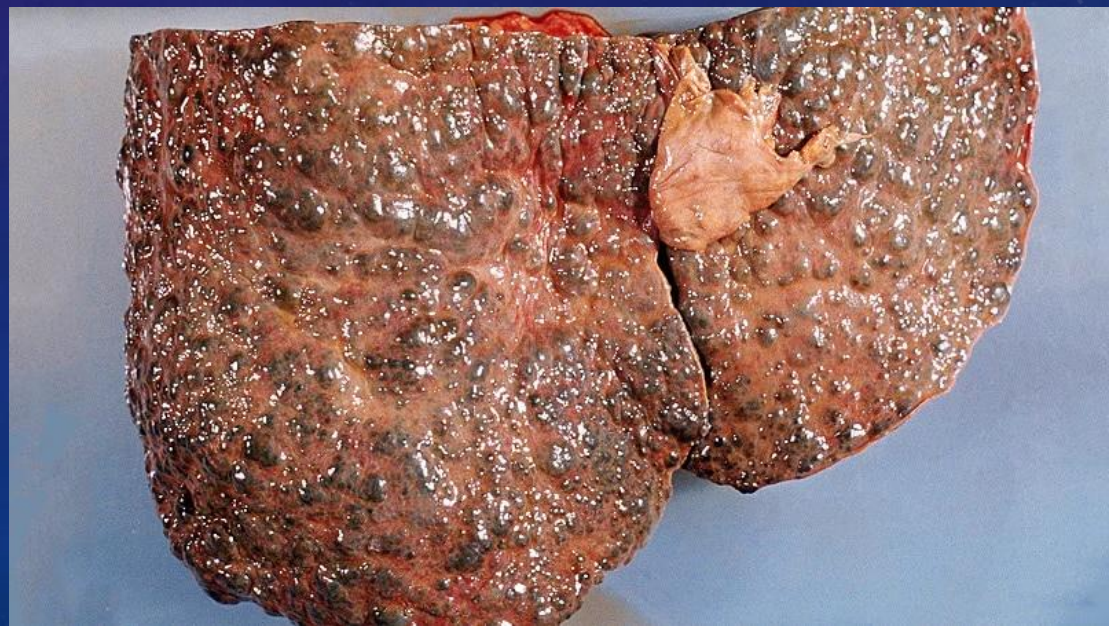
CIRRHOSIS

always linked to chronic problems

- 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

the surface contains multiple polyps and nodules involving the whole liver, around these nodules septa/fibrotic bands are found



any chronic inflammatory process/reaction the body tries to get rid of it which is hard to control; this will lead to 2 pathways/phases: inflammatory phase and regenerative phase (by fibrosis)

PATHOPHYSIOLOGY

- Combination of processes :

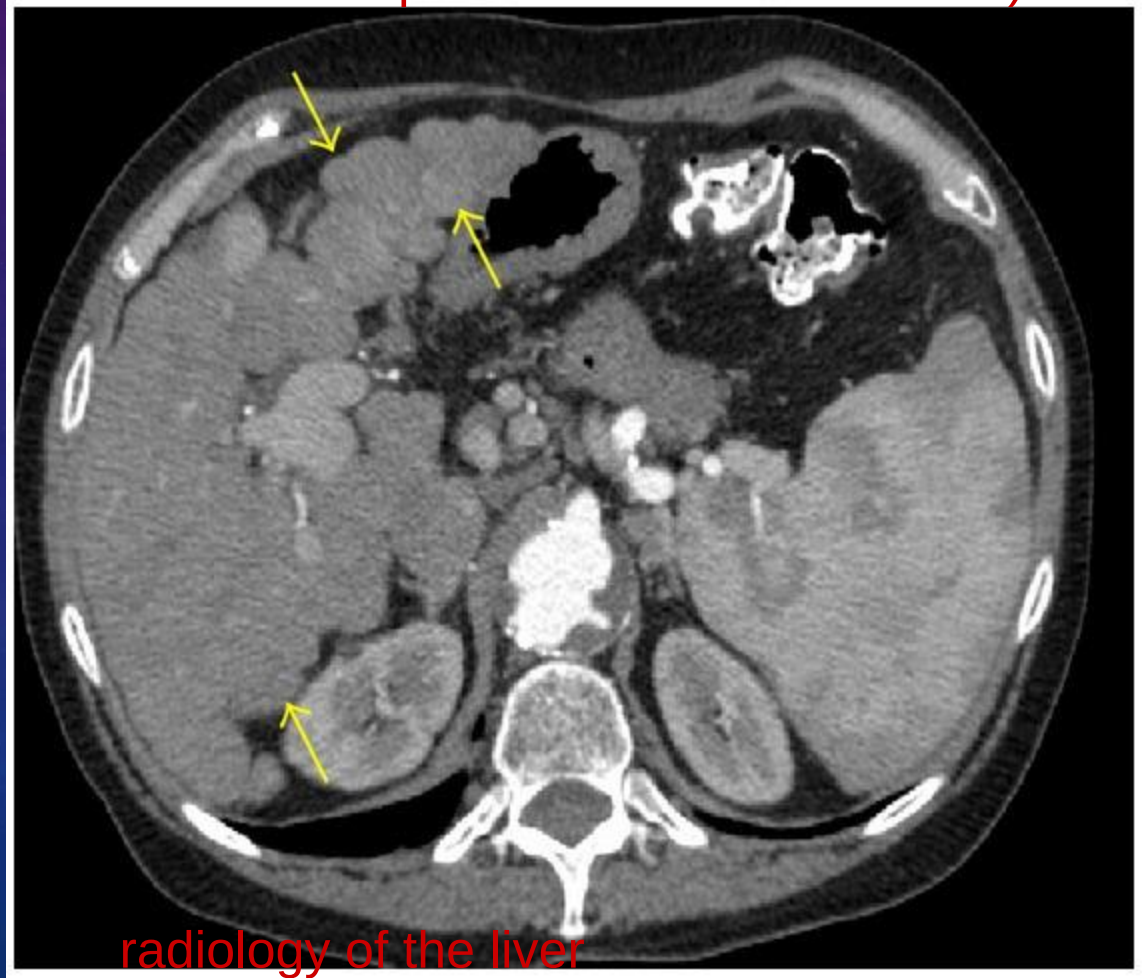
- Fibrosis: excessive production of collagen type I / III by hepatic stellate cells

- Regeneration of hepatocytes through proliferation of progenitor cells of the ductular reaction proliferation of duct (bile duct in portal triad) to compensate the injury that occured

DIAGNOSIS

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

non invasive test mostly the AST, ALT and LDH (1st group to be affected)will be affected since they represent the livers integrity (cirrohsis -> abnormal integrity -> so abnormal AST , ALT and LDH the 2nd group to be affected is the hepatocyte function test; when there is abnormal hepatocytes that means the synthetic capacity will be affected (including the albumin and decrease of clotting factors , prolonged ptt and pt will cause build up of bilirubin and ammonia)



radiology of the liver

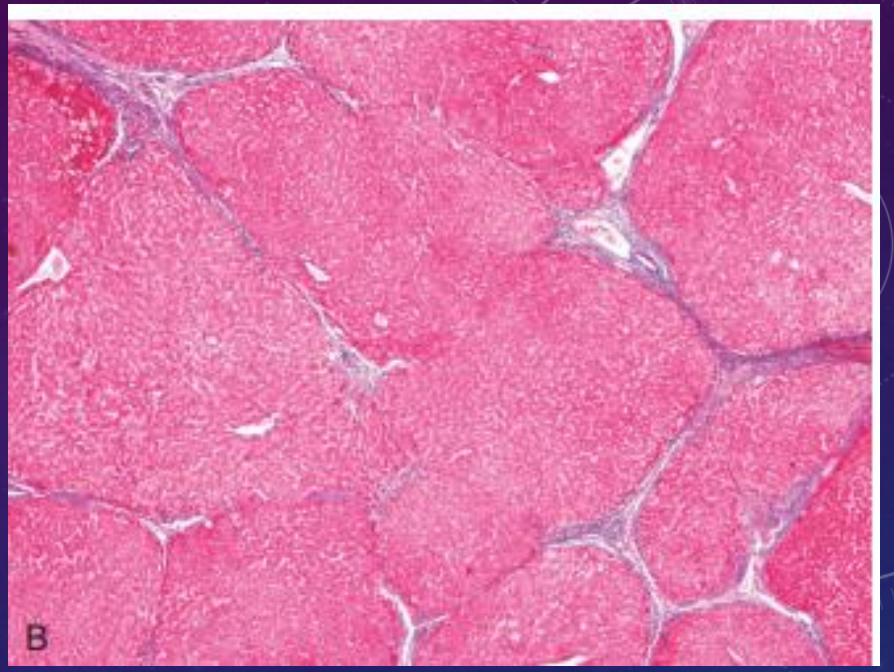
the biopsy will show cirrhosis : transformation of liver parenchyma into multiple nodules

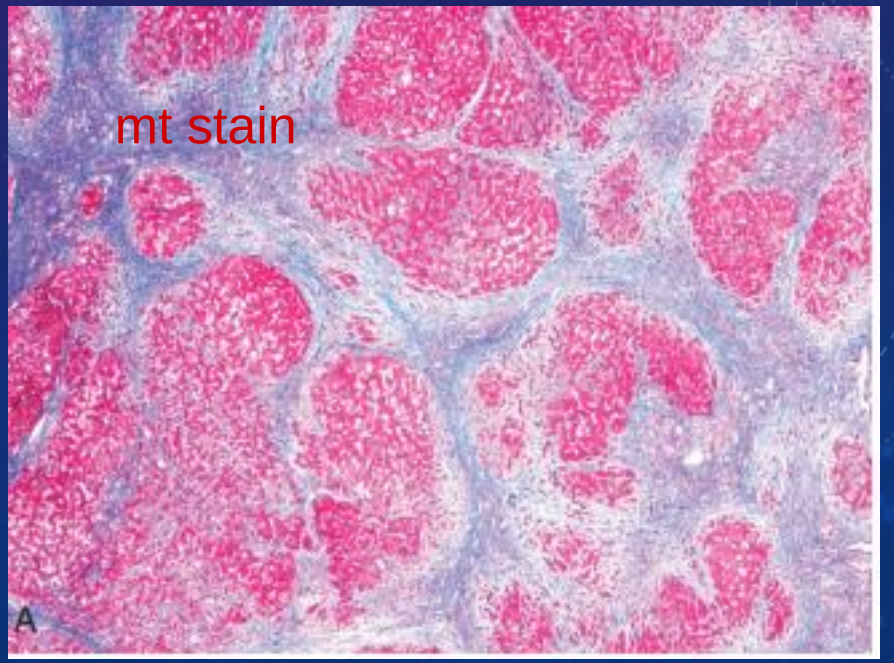
HISTOPATHOLOGY

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

* ductular reactions.

* (Masson trichrome stain) highlights these fibrous septa.





jaundice happens when there is no good excretion of bilirubin so it builds up in blood and deposits in the tissues causing yellowness in the sclera, skin and mucus membranes its the 1st sign of failure of liver

CLINICAL FEATURES

bruising and hemorrhage is caused by the defect of synthetic capacity which reduces the clotting factors and prolongs ptt and pt (2nd sign)

encephalopathy (hepatic coma) secondary to build up and secretion of amonnia it has a wide range of signs starting from changes in mood, personality , and levels of consciousness lastly the patient enters in hepatic coma

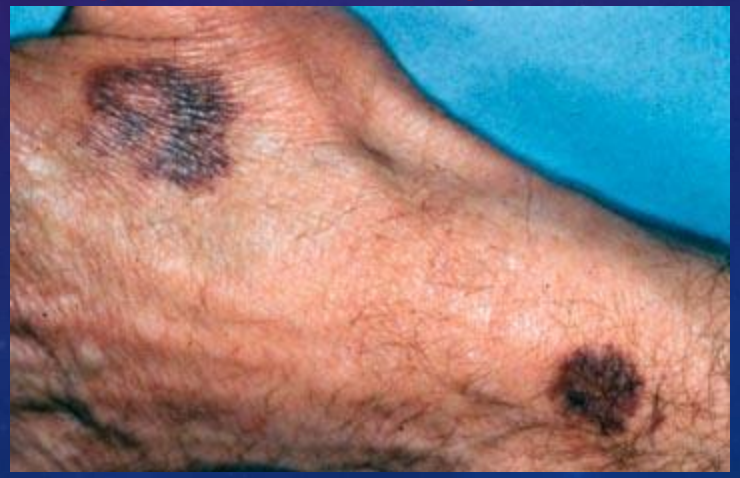
- 1. 40% of individuals with cirrhosis are asymptomatic until the most advanced stages of the disease. the most advanced stage of the disease is diffusion of the liver
- 2. Non specific symptoms such as anorexia, weight loss, weakness. seen in any chronic stage
- 3. signs and symptoms of liver failure e.g Jaundice, encephalopathy, and coagulopathy.

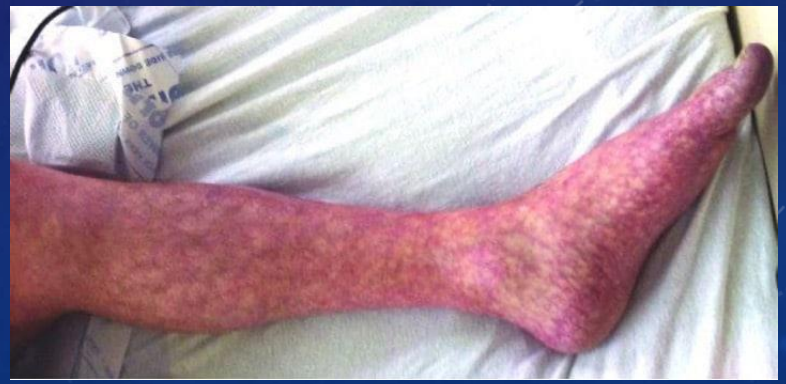
pruritus is accmulation of bile salts under the skin which causes itching

- 4. Pruritus, portal hypertention (intrahepatic vascular resistance). the changes in the structure of the liver will cause elevations in the intrahepatic vascular resistance leading to blood flow resisitance -> hypertension

jaundice of sclera of eye

bruising and hemorrahge under skin





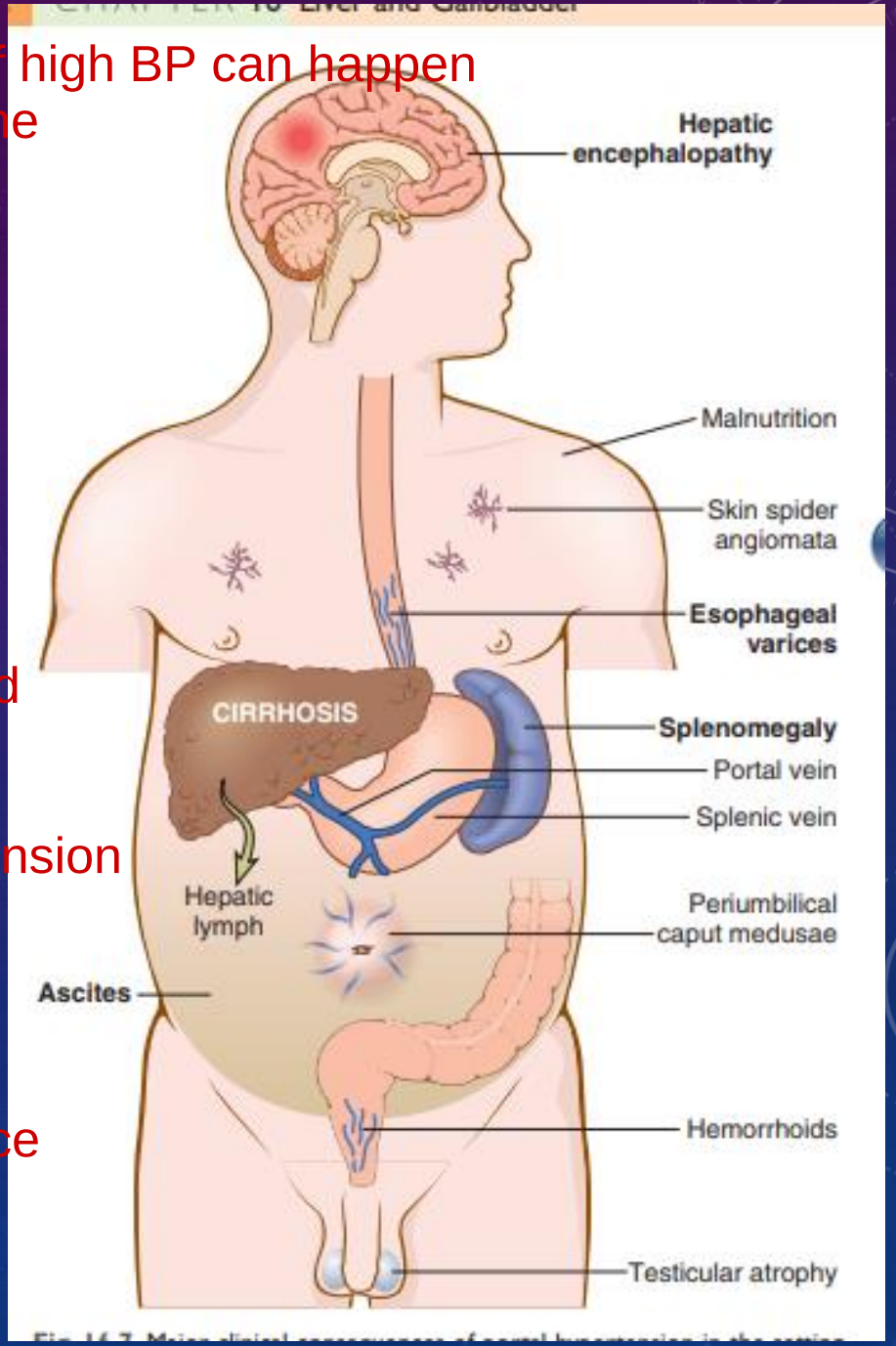
the treatment is to open some places so stress relief/relief of high BP can happen (opening of collaterals) it leads to reducing the pressure in the portal circulation

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

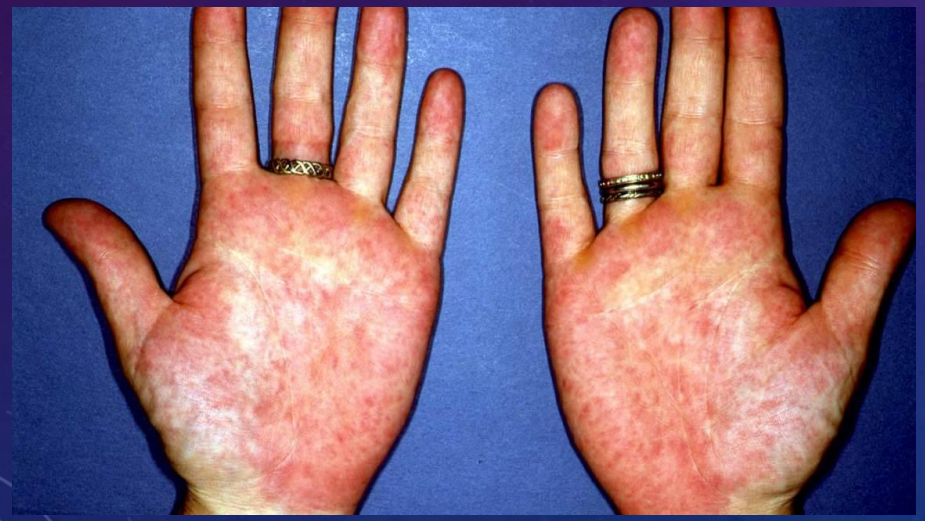
opening sites are:
1.lower esophagus: opening of veins to reduce the pressure these new blood vessels are fragile and are easiy traumatized so bleeding can happen easily
note: esophageal varices can cause hematemesis (vomiting of blood) these varices were formed due to the portal hypertension

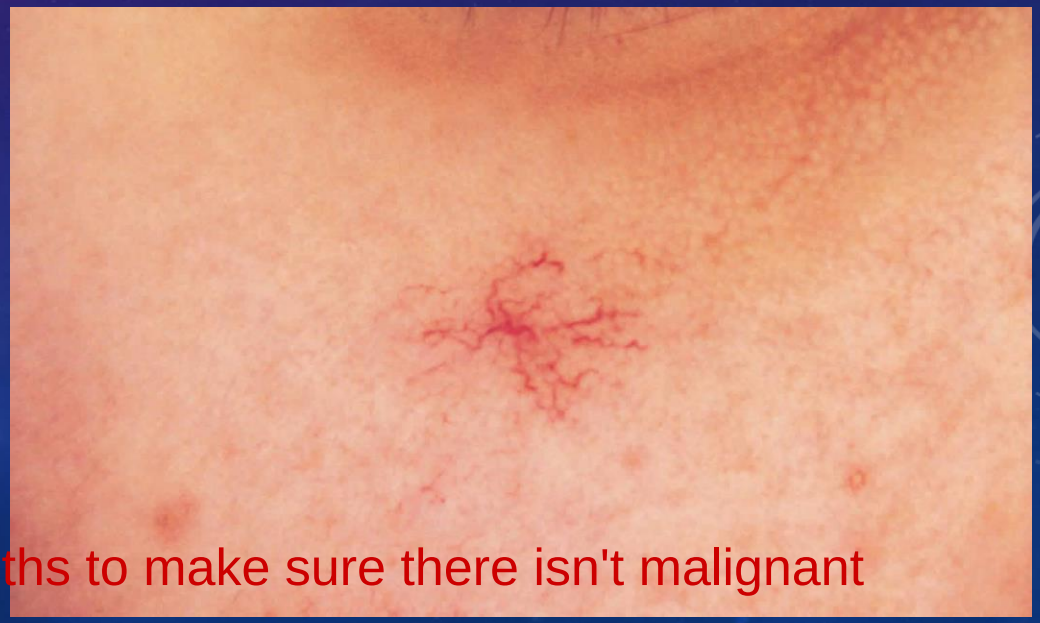
2.periumbilical veins (caput medusa): collateral veins they're openings due to hypertension

3.rectum: varices and the clinical manifestation is the presence of hemorrhoids



- 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).

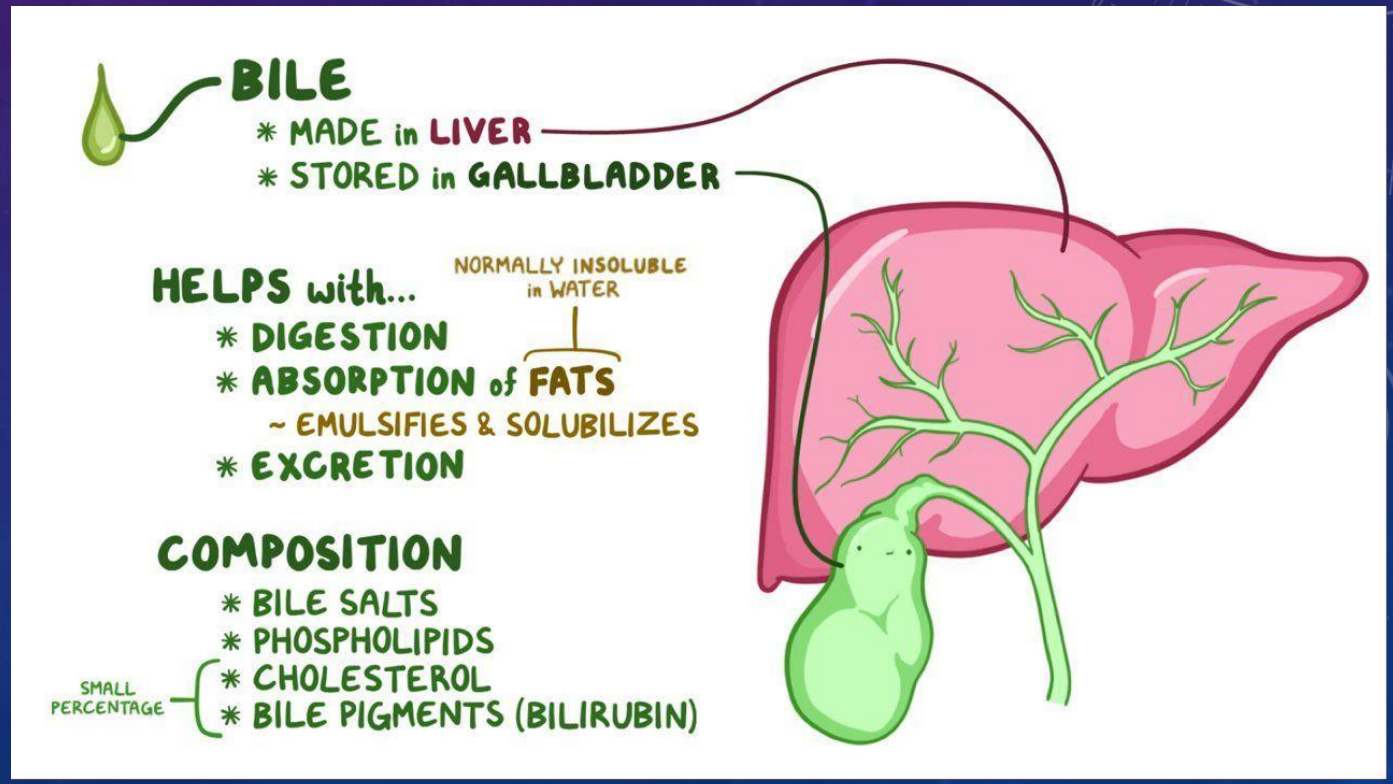




liver cirrhosis patients should do imagings every 6 months to make sure there isn't malignant transformations

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).

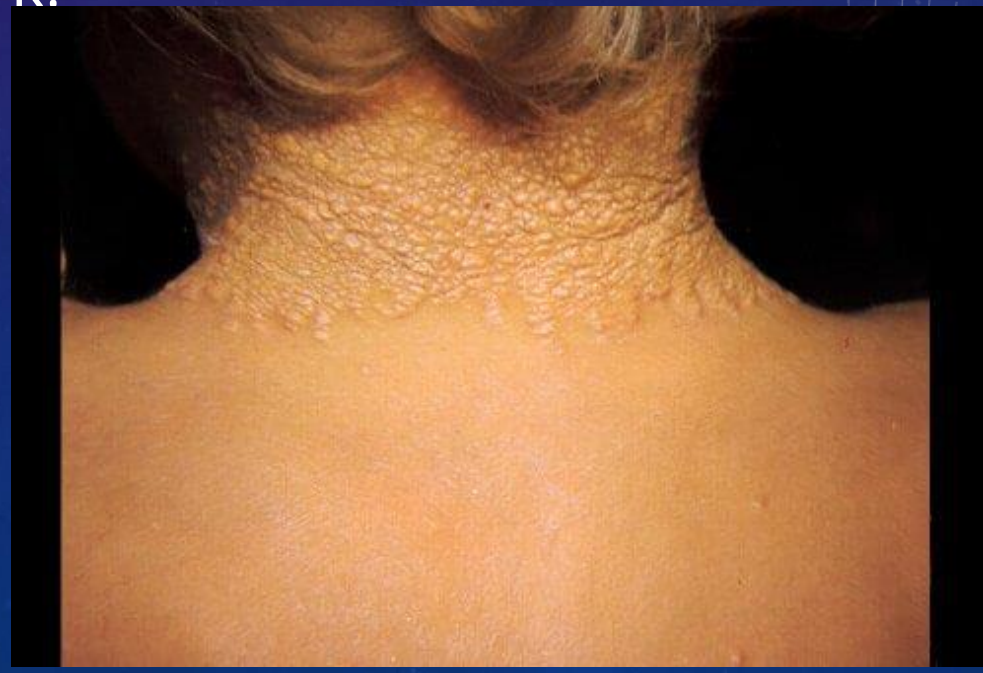
➢ symptoms related to intestinal malabsorption, including nutritional deficiencies of the fat-soluble vitamins A, D, or K.

not water soluble

Lab:

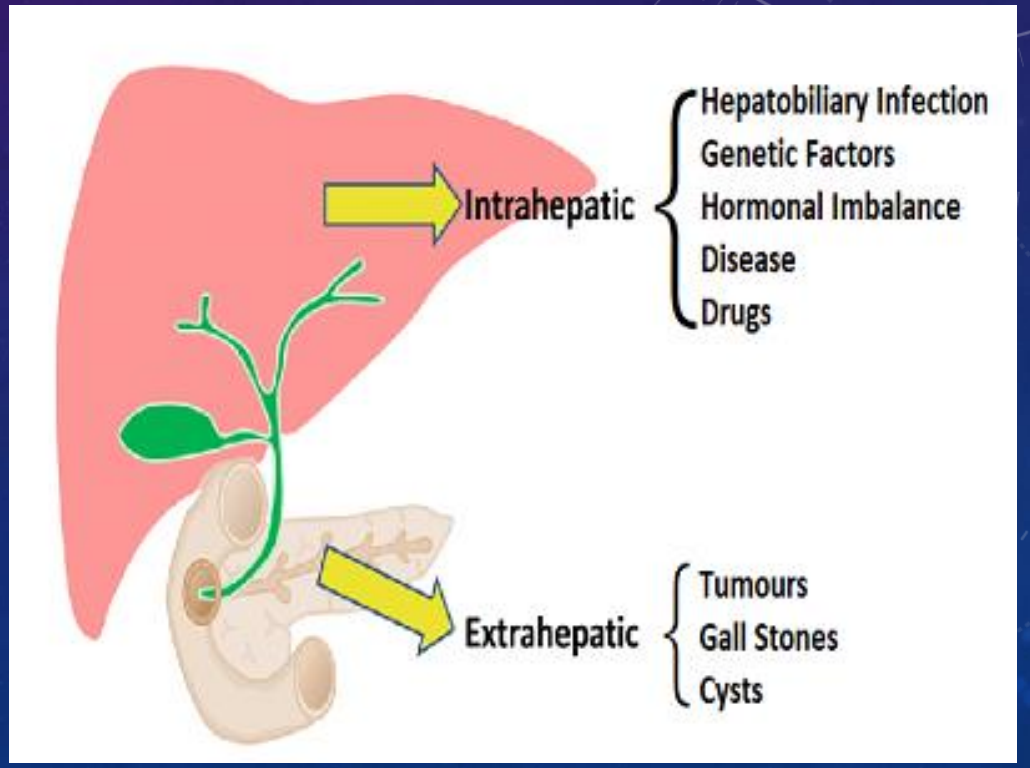
elevated serum alkaline phosphatase and

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 not commonly seen



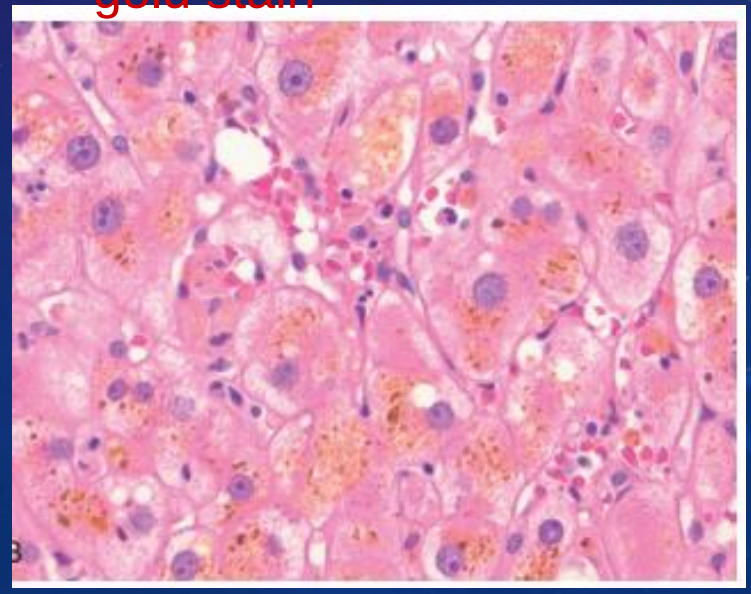
PATHOPHYSIOLOGY

- Bile is produced in hepatocytes and flows as follows:
- hepatocyte canaliculi → canals of Hering → bile ductules → interlobular bile ducts → larger bile ducts → duodenum to help for metabolism
- 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. (macrophage)
- feathery degeneration:
- Droplets of bile pigment accumulate within hepatocytes, give them foamy appearance

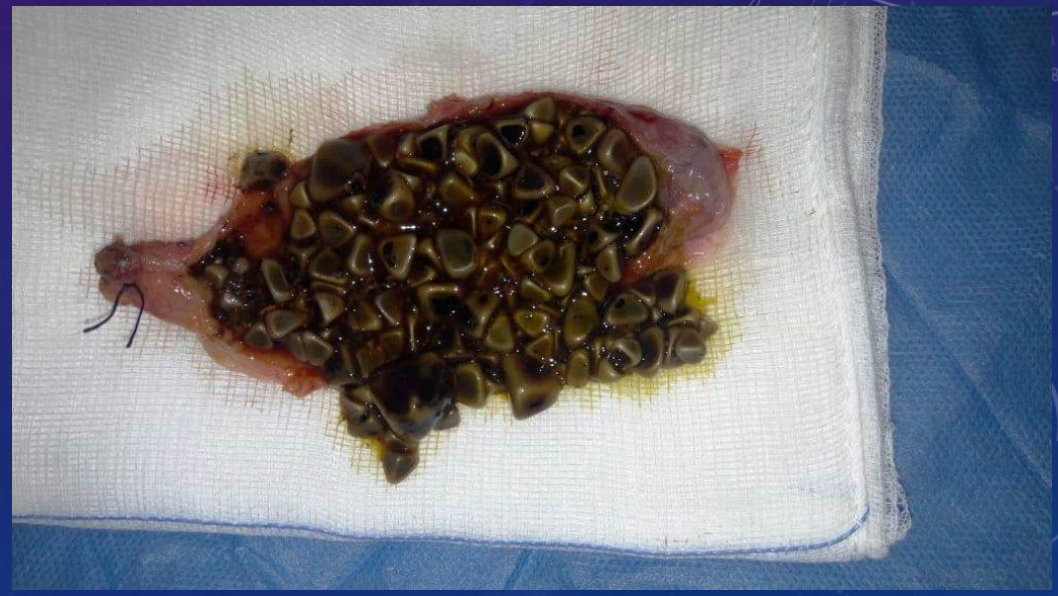
gold stain



normally the cytoplasm should have a pink color but in this picture there is abnormal dark brown material found in the cytoplasm

CAUSES: A. BILE DUCT OBSTRUCTION.

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



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

important

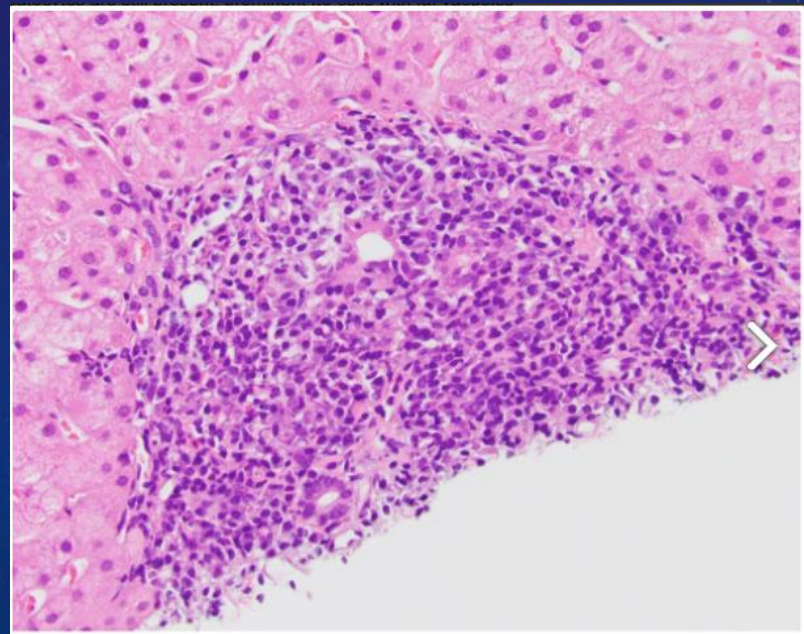
B. NEONATAL CHOLESTASIS

- 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



fibrosis

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