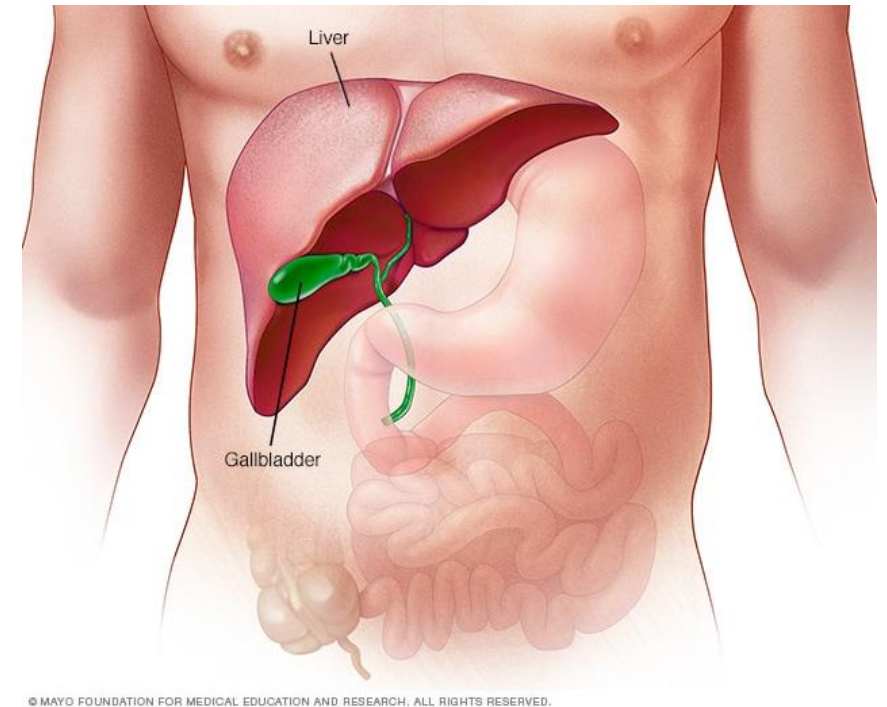


# Cirrhosis and cholestasis

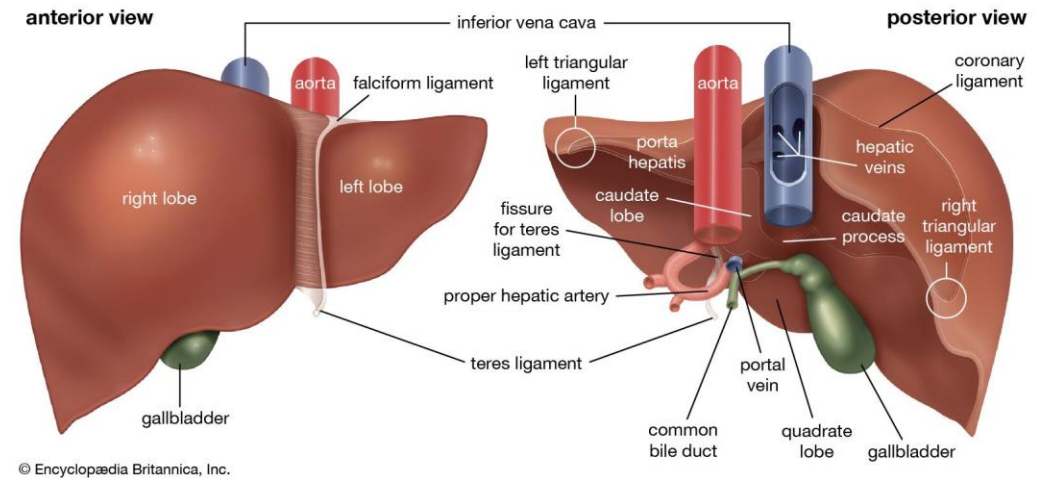


Dr. eman Krieshan, m.d.

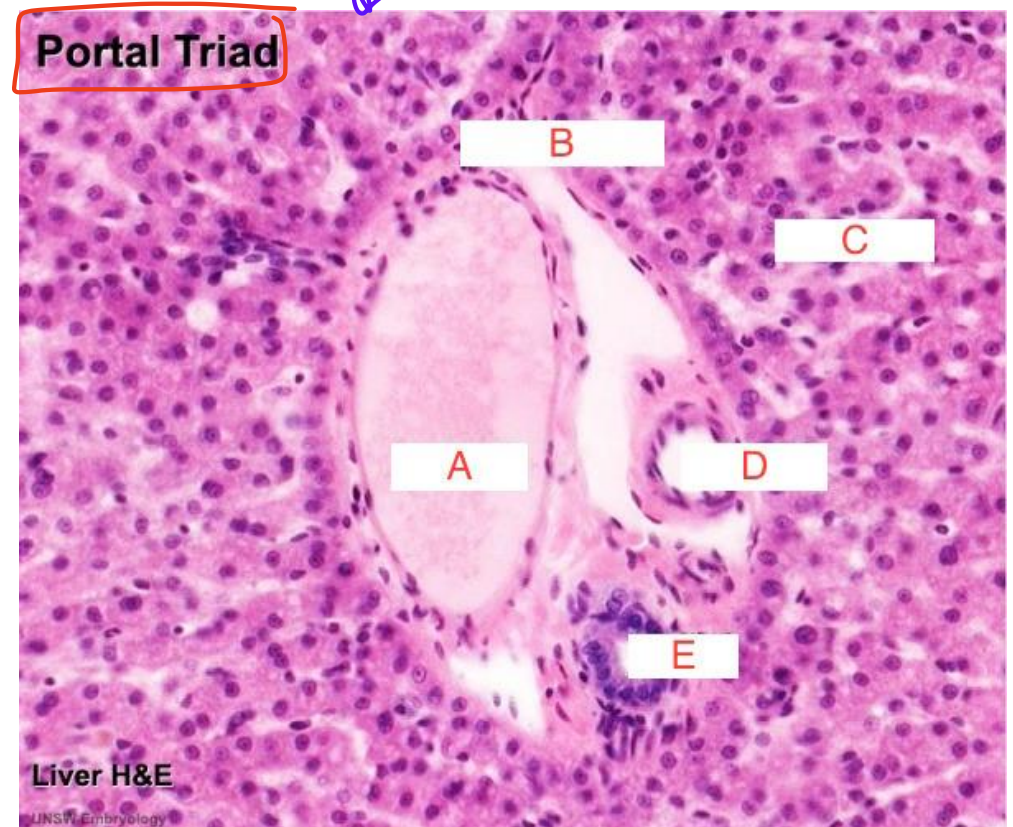
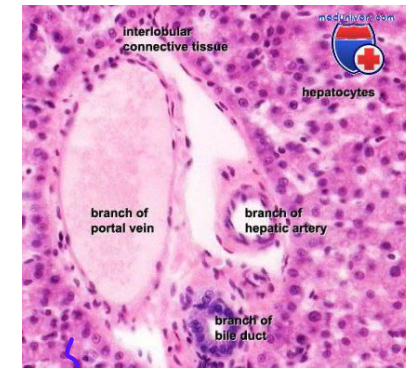
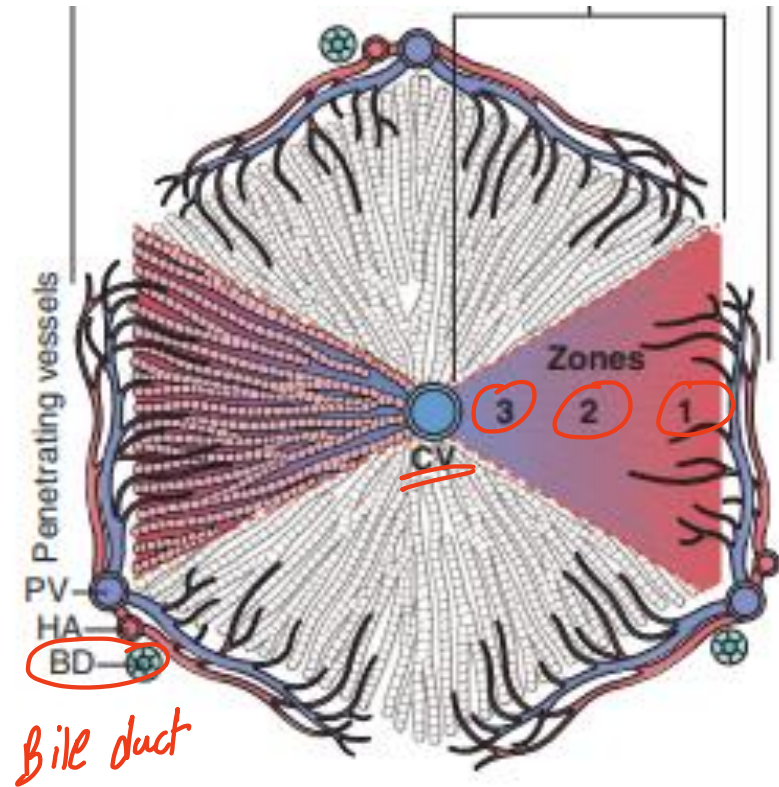
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دکتر

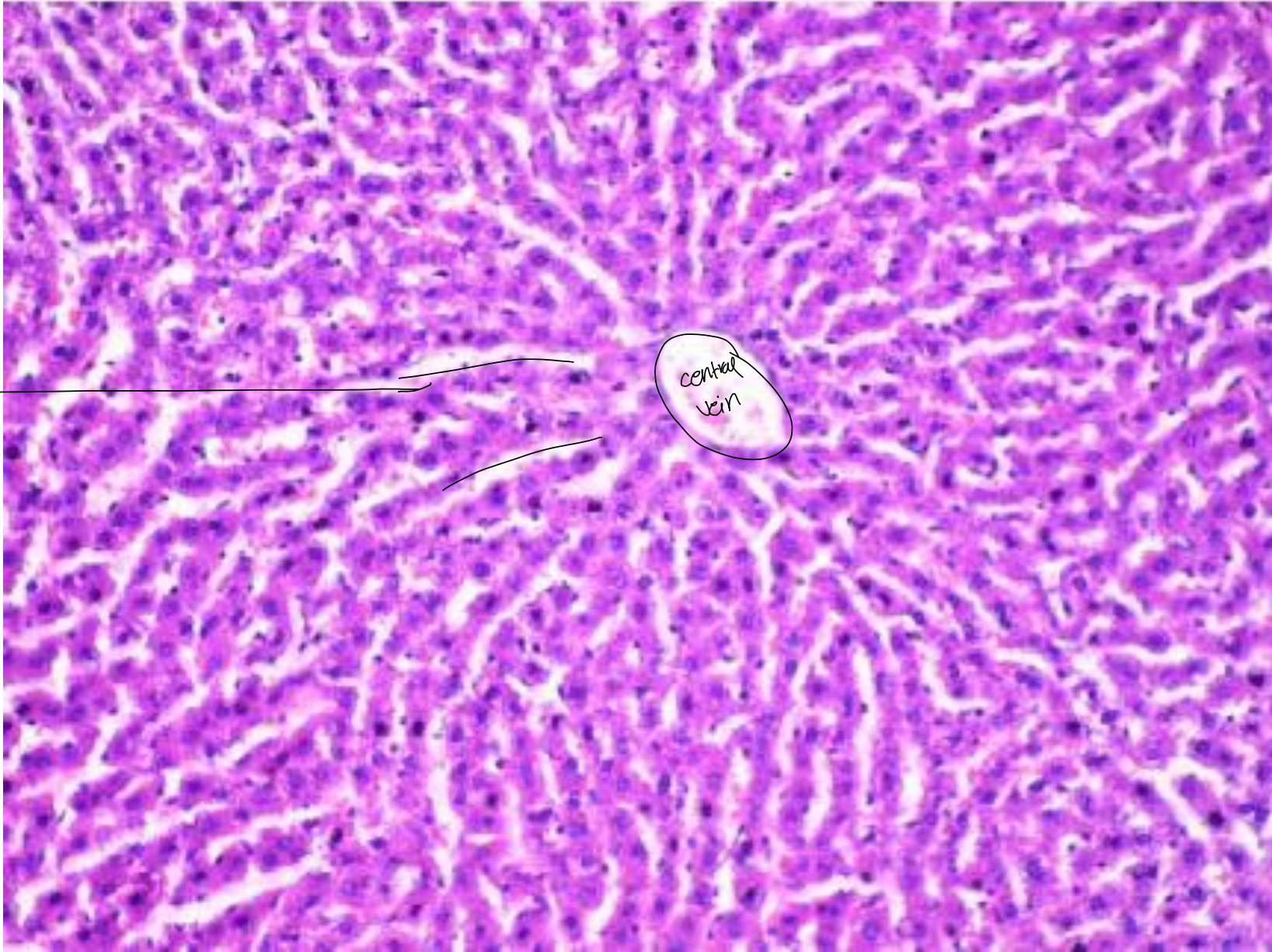
- The normal adult liver weighs 1400 to 1600 gm. It has a dual blood supply, with the portal vein providing 60% to 70% of hepatic blood flow and the hepatic artery supplying the remaining 30% to 40%.
- Portal tract? *bile duct  
hepatic A  
portal V*



# Models of liver anatomy







عبارة عن فرخانة  
سیت hepatocyt .

لومالیت های الفرخانة

هذه هي hepatocellular carcinoma ←

**Table 16.1 Laboratory Evaluation of Liver Disease**

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

GGT > = = AST >   
 Alkaline phosphatase ALT   
 S = =   
 Bile duct   
 hepatocyte

- 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



# تشمع الكبد cirrhosis → last stage of chronic cases.

Fibrosis  
nodules

- 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 → غير معروف



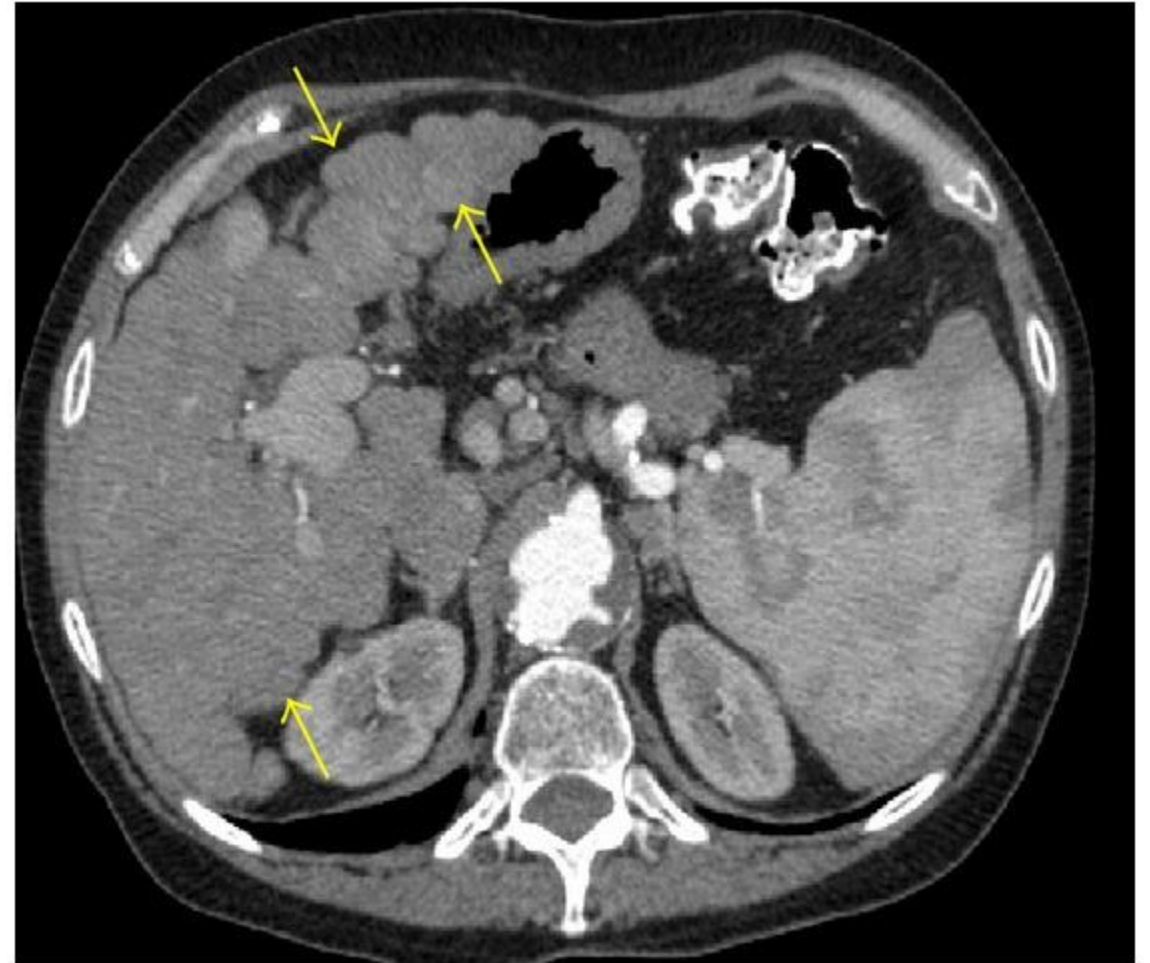
# Pathophysiology

- 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 of cirrhosis

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



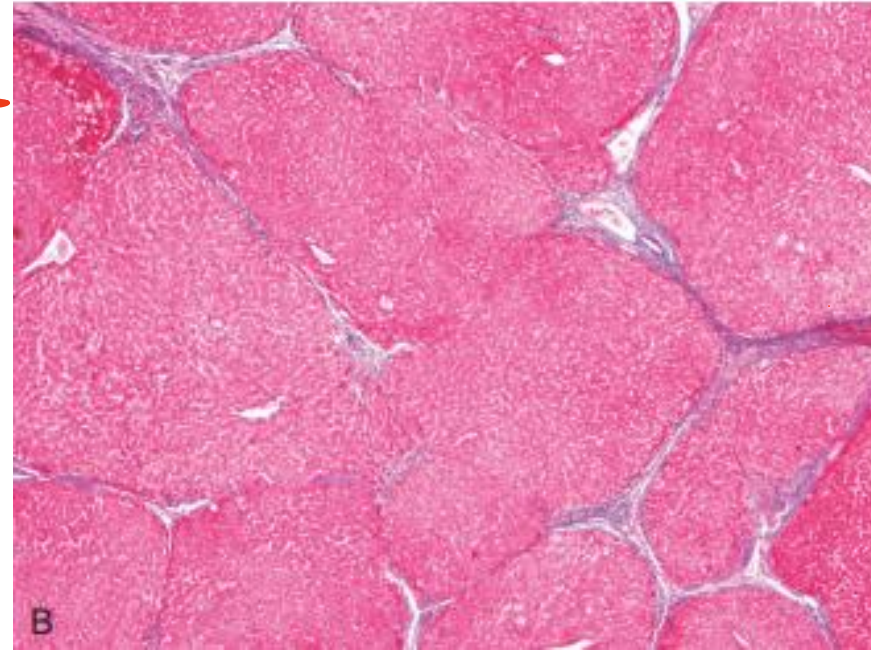
# histopathology

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

\* ductular reactions.

\* (Masson trichrome stain) highlights these fibrous septa.

مس



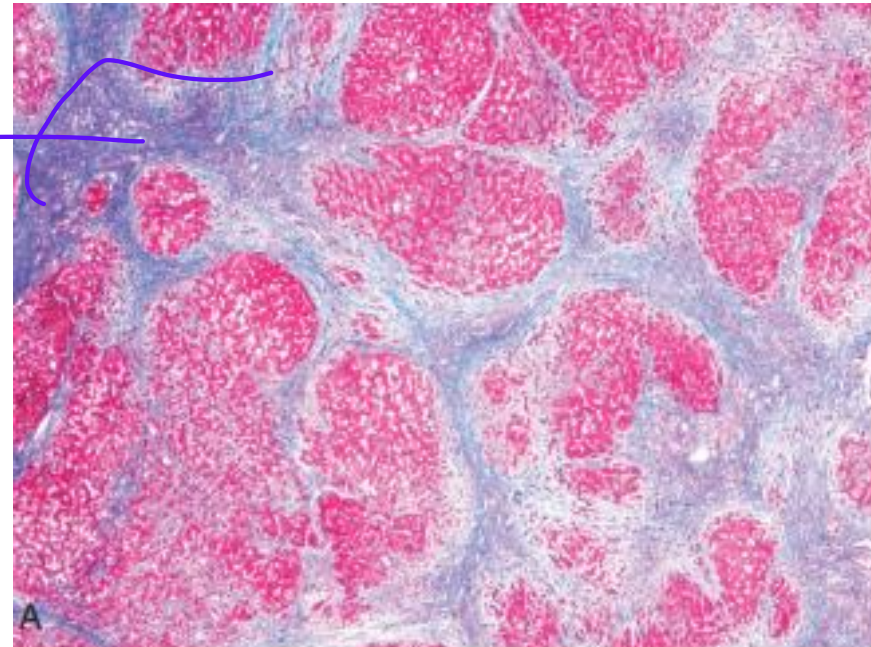
[Masson...] استخدام صبغة

Blue في لون

إذا عني

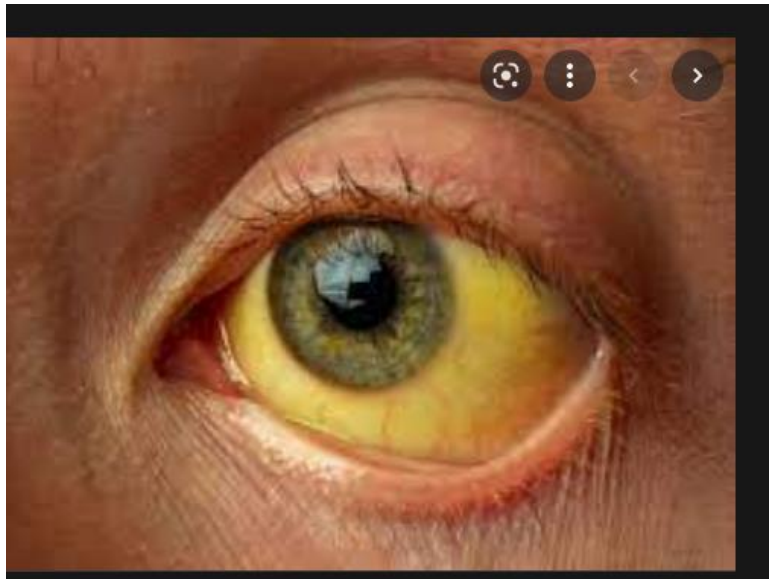
Fibrosis

↓  
Cirrhosis



# 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 hypertension (intrahepatic vascular resistance).





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

المرافق بغير زنتية  
portal ↑ tension  
fibrosis  
السبب

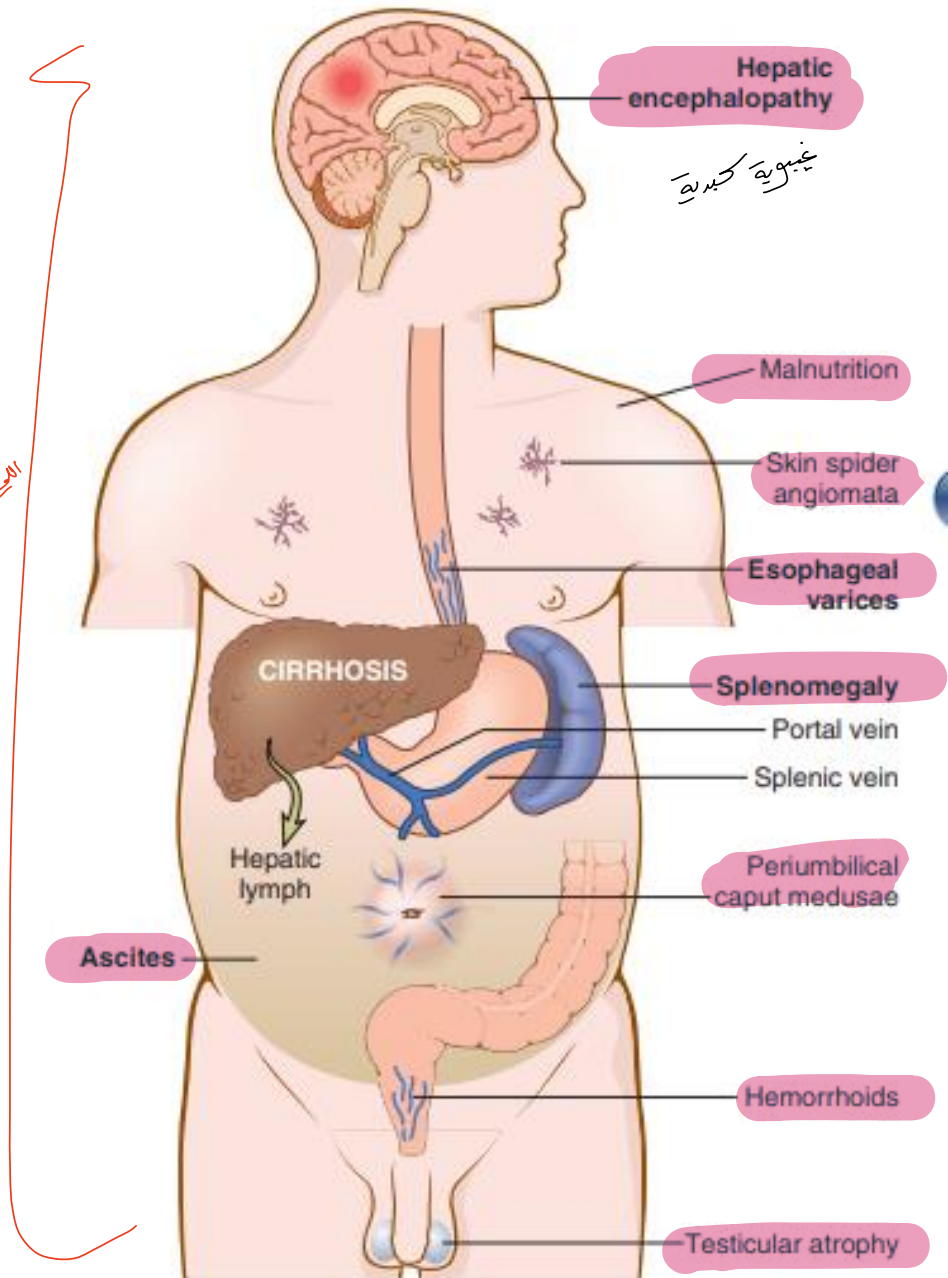


FIG. 14-7 Major clinical consequences of portal hypertension in the setting of cirrhosis.

- 5. **Hyperestrogenemia**: *in male*
- 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**).

↓  
تدریجاً در مردان

→ end stage  
of cirrhosis

تدریجاً در مردان

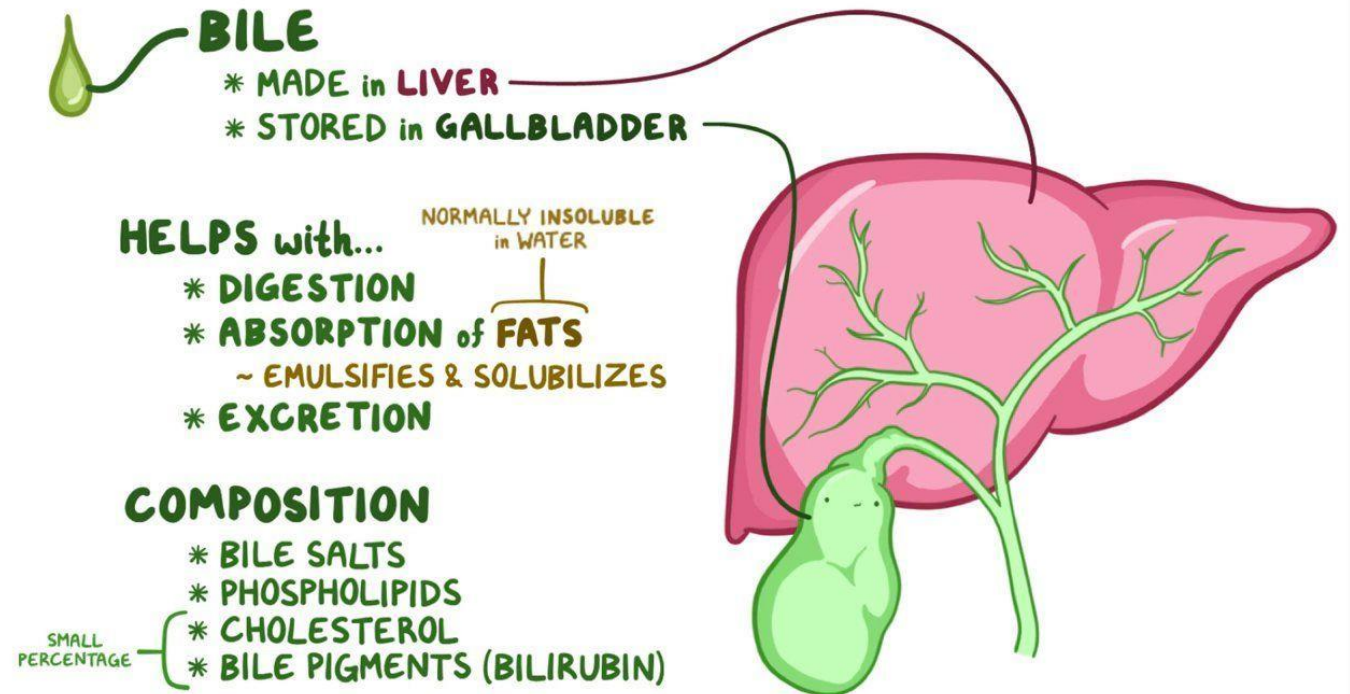


# cholestasis

توقف بيلي في التدفق

most common cause of cholestasis? cholelithiasis  
حصى المرارة

- 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. *حكة*

- skin xanthomas (focal accumulation of <sup>fat</sup> cholesterol).

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

Lab:

elevated serum alkaline phosphatase and  $\gamma$ -glutamyl transpeptidase (GGT),

*انزيمات الكبد*  
Bile Duct injury  
not hepatocyte injury.



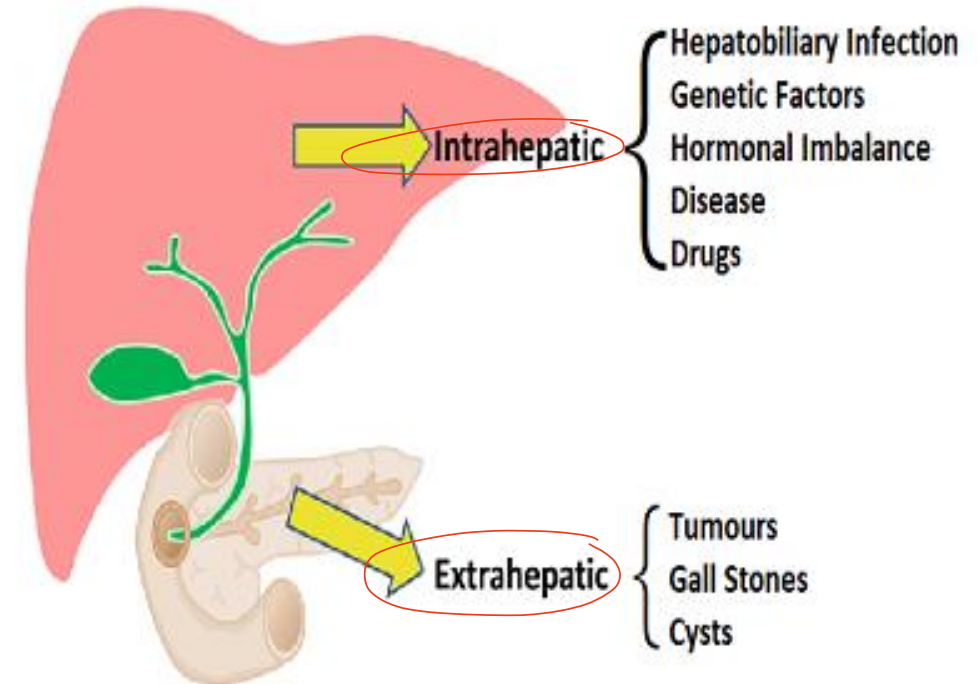
Q. Most common cause of cholestasis is?  
# extrahepatic.

# causes

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

بیلیاری  
مرضات  
بیلیاری  
مرضات  
بیلیاری  
مرضات

Chronic  
Cancer  
in  
Bile Duct.



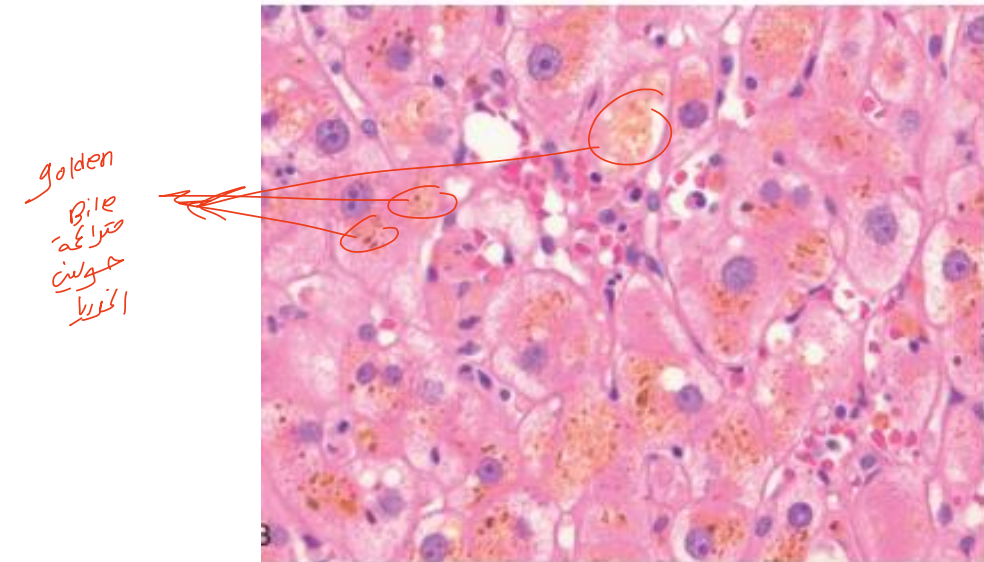
# Pathophysiology

- Bile is produced in hepatocytes and flows as follows:
- hepatocyte canaliculi → canals of Hering → bile ductules → interlobular bile ducts → larger bile ducts → <sup>gall bladder</sup> duodenum <sub>pancreas</sub>
  - Injury or obstruction at any point along biliary flow can lead to cholestasis
- Handwritten notes:*  
• اے خلیے میں پیدا ہوتا ہے  
• اے خلیے میں پیدا ہوتا ہے  
• Bile  
• hepatocyte



# 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.**

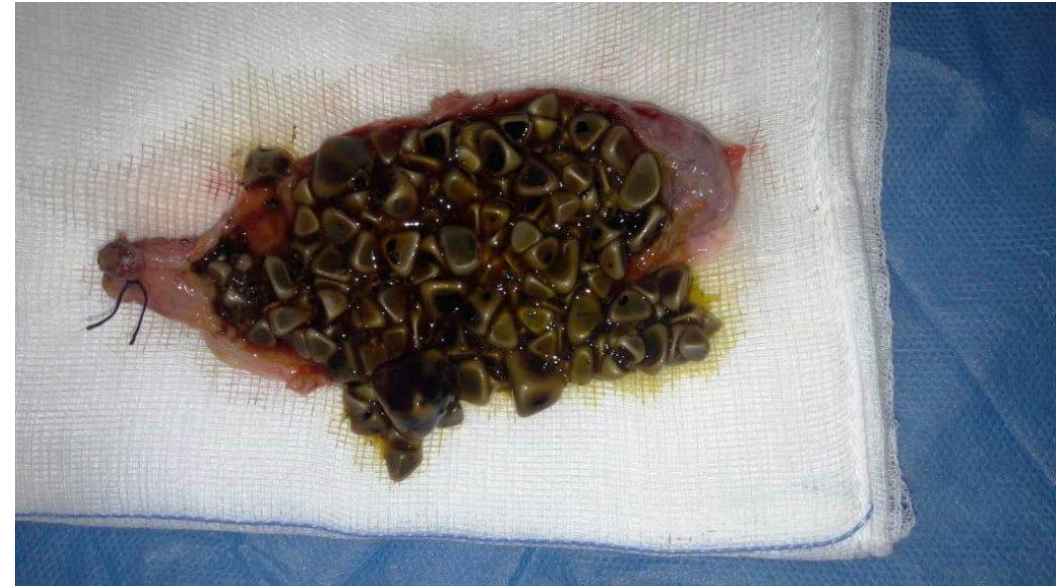
*most common cause of* → *cholelithiasis*  
*حصاة المرارة*

- The most common **cause** of bile duct obstruction in **adults** is:

- **extrahepatic cholelithiasis.** → gall bladder stone  
*حصاة المرارة*
- **malignant obstructions.**
- **postsurgical strictures.**

- Obstructive conditions in **children** include :

- **biliary atresia.** → *bile duct*  
*انسداد القناة الصفراوية*
- **cystic fibrosis.**
- **choledochal cysts**  
*خلفي*



## بيلي b. Neonatal Cholestasis

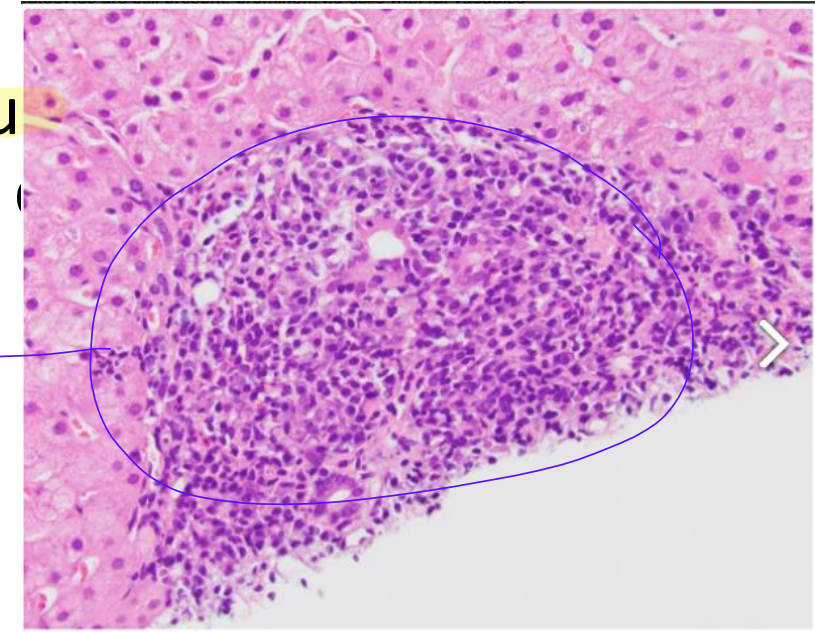
age :- less than 1 year.

- Prolonged conjugated hyperbilirubinemia in the neonate, termed neonatal cholestasis.
- The major conditions causing it are:
  - (1) cholangiopathies, primarily biliary atresia <sup>بيلي</sup> .(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 granuloma destruction and loss of medium sized interlobular bile ducts and variable within the liver



Bile Duct  
injury  
lymphocyte + plasma cell  
Bile Duct injury  
= loss

anti nuclear Ab  
anti smooth muscle Ab  
Biliary tract  
cholestasis

في نوعين Ab  
AUA  
ASMA  
مرض صناعي زائفة

تشخيصه  
Biopsy  
أكثر بعد

# d. Primary Sclerosing Cholangitis

Radiology  
تشخيص  
Biology

Fibrosis

IBD: inflammatory bowel dis  
UC: ulcerative colitis

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

تضيق القنوات الصفراوية

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

2 type Ab ↑

	primary Biliary cholangitis	primary sclerosing cholangitis
السرطان	Chronic → cancer	Chronic → cancer sat
Antibodies	Ab: AMA ASMA	Ab: AS
الخلايا	Inflammatory / lymphocyte plasma cell	Fibrosis, onion skin tissue & macrophages
التشخيص	Biology (Hb-s) CA1	Radiology

Adeno carcinoma  
or  
Cholangiocarcinoma

Bile Duct  
تضيق  
Fibrosis

