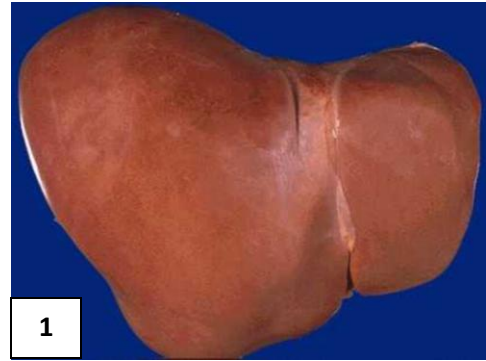




- **Introduction about the liver:**

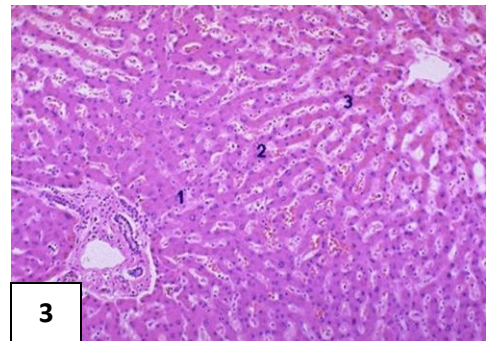
- It belongs to the reticuloendothelial system (containing macrophages known as Kupffer cells) and the digestive system.
- Before birth, liver produces red blood cells (later, this function will be taken by the bone marrow).
- It weighs 1.5 kg and it is located in the right hypochondrium.
- It is supplied by blood from two sources:
 - ✓ Hepatic artery.
 - ✓ Portal vein.
- Histologically, it is composed of hepatic lobules.
- Notice that the right lobe of the liver is larger than the left lobe.
- **Image (1):** normal liver; brown in color; smooth surface.
- **Image (2):** cut surface of normal liver; left: portal vein carrying blood to the liver accompanied by hepatic artery and bile duct; right: a branch of hepatic vein draining blood from the liver to the inferior vena cava (IVC).



- **Image (3): Histology of the liver**

- ✓ It is divided into lobules with a central vein in the center of each lobule.
- ✓ Functionally, liver can be divided into three zone (based on the oxygen supply):

- ❖ *Zone 1:* encircles portal tract where the oxygenated blood from hepatic artery enters. Notice that this zone is affected first by viral hepatitis.
- ❖ *Zone 3:* it is located around central veins, where oxygenation is poor. Notice that this zone is affected first by ischemia.
- ❖ *Zone 2:* intermediate zone (in between).



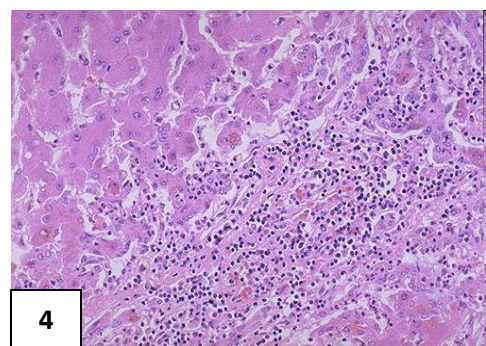
- **Functions of the liver:** please review physiology note of problem 1 (Viral Hepatitis).

- **Viral hepatitis:**

- **Types which have been identified:** A, B, C, D and E.
- **Other viruses which can cause hepatitis include the following:**
 - ✓ EBV.
 - ✓ CMV.
 - ✓ Herpes Simplex Virus (HSV).

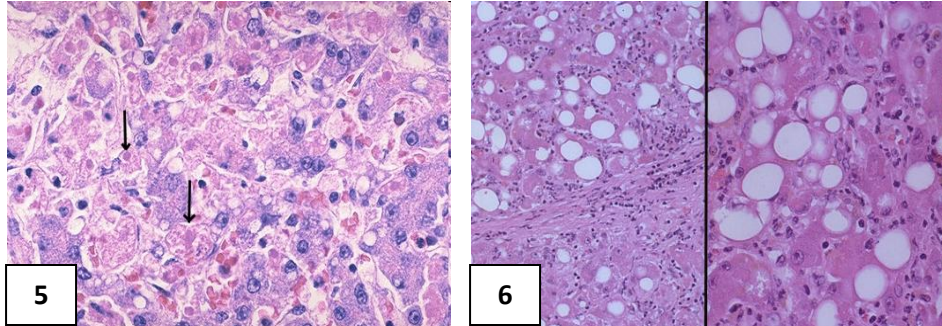
- **Histopathology:**

- ✓ Image (4): mononuclear inflammatory cell infiltrate extending from portal areas and disrupting plates of hepatocytes which are undergoing (piecemeal necrosis).





- ✓ Image (5): two arrows pointing ballooning degeneration that occurs in acute viral hepatitis.
- ✓ Image (6): steato-hepatitis which is characterized by:
 - ❖ Mallory hyaline: they are intermediate filaments.
 - ❖ Neutrophils infiltration.
 - ❖ Necrosis of hepatocytes.
 - ❖ Ballooning degeneration.
 - ❖ Fatty change.



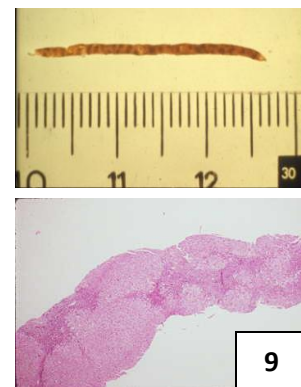
- **Cirrhosis:**

- **Definition:** it is characterized by the following:
 - ✓ Diffuse involvement of the liver.
 - ✓ Destruction of normal hepatic architecture resulting from liver necrosis.
 - ✓ Replacement by extensive fibrosis.
 - ✓ Regenerating nodule of hepatocytes (lacking a central vein!).
- **What are the causes of cirrhosis?**
 - ✓ Alcoholic liver disease (70% of cases!).
 - ✓ Viral infections such as hepatitis (10% of cases).
 - ✓ Biliary diseases such as primary and secondary biliary cirrhosis (5% of cases).
 - ✓ Metabolic such as hemochromatosis (5% of cases).
 - ✓ Cryptogenic cirrhosis = due to unknown reason (10% of cases).
- **Morphology of cirrhosis:**
 - ✓ Micronodular (early) = image (7): < 3mm uniform nodules separated by thin fibrous septa (examples: alcoholic cirrhosis is the most common cause; primary and secondary biliary cirrhosis; hemochromatosis; wilson’s disease).
 - ✓ Macronodular (late) = image (8): > 3mm variable irregular nodules separated by broad thick fibrous septa (example: chronic viral hepatitis).



- **What is the benefit behind doing needle liver biopsy?**

- ✓ To look for the following things:
 - ❖ Etiology.
 - ❖ Activity.
 - ❖ Cirrhosis (types).
 - ❖ Neoplasia (if present).
- ✓ Image (9): biopsy of a cirrhotic liver with multiple small nodules surrounded by fibrous tissue.





- ✓ Features to document in the report of a cirrhotic biopsy:

Step	Documentation
Establishing diagnosis	Certain, probable or possible
Anatomic type	Micro, Macro or mixed nodular
Grade activity	Mild, moderate or severe
Stage of evolution	Developing or fully established
Etiology	Based on histological findings
Complications	Hepatocellular carcinoma; loss of hepatic ductules

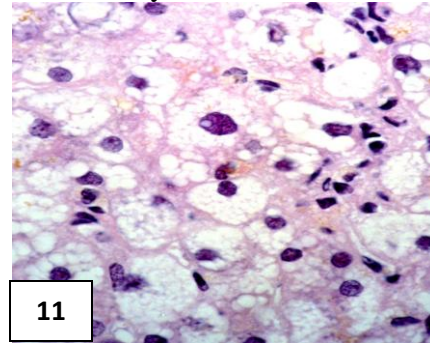
- Pathogenesis of alcoholic liver injury:

- **Acetaldehyde (a metabolite of ethyl alcohol) is hepatotoxic resulting in:**

- ✓ Increased peripheral release of fatty acids.
- ✓ Stimulation of collagen synthesis.
- ✓ Inflammation with portal bridging fibrosis.
- ✓ Micronodular cirrhosis.

- **Morphology of fatty liver:**

- ✓ Image (10): slightly enlarged liver with a pale-yellow appearance.
- ✓ Image (11): this is the histologic appearance of hepatic fatty change; lipid accumulates in hepatocytes as vacuoles; the most common cause of fatty liver change in developed countries is alcoholism; the most common cause of fatty liver change in developing countries is kwashiorkor in children; other causes of fatty liver change are diabetes mellitus and obesity.



- Primary biliary cirrhosis:

- **Definition:** a rare autoimmune disease affecting middle-aged women that is characterized by destruction of bile ductules within the triads of the liver. Notice that antimitochondrial antibody can be detected in the serum.

- **There are four stages in pathogenesis:**

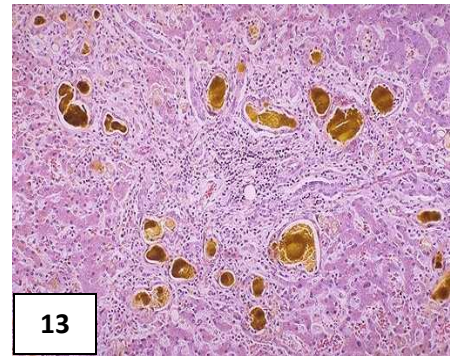
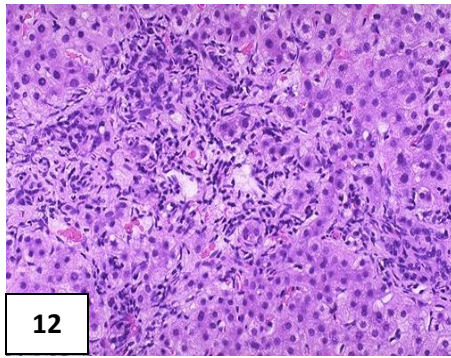
- ✓ Florid ductal lesion: lympho-plasmacytic infiltration around bile ducts; ductal epithelium necrosis and granuloma close to bile ducts.
- ✓ Ductular proliferation.
- ✓ Scarring.
- ✓ Cirrhosis.

Notes:

- ❖ *Granulomas*: favorable prognosis.
- ❖ *Central cholestasis and cirrhosis*: poor prognosis.

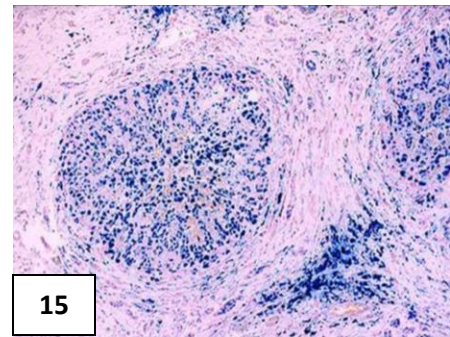
- **Morphology:**

- ✓ Image (12): portal tract with intense chronic inflammatory infiltrate and loss of bile ductules.
- ✓ Image (13): yellowish-greenish accumulations of bile due to extrahepatic biliary tract obstruction.



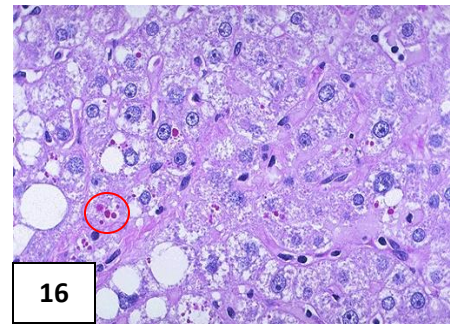
- **Hemochromatosis:**

- **Image (14):** dark brown color of the liver, pancreas and lymph node is due to extensive iron deposition.
- **Cause of this disease:** mutation of hemochromatosis gene (HFE: C282Y) which leads to increased iron absorption from the gut.
- **Image (15):** prussian blue iron stain (Perl's stain) demonstrates the blue granules of hemosiderin in hepatocytes and Kupffer cells.
- **Hemochromatosis can be:**
 - ✓ Primary: due to autosomal recessive genetic disease.
 - ✓ Secondary: due to:
 - ❖ Excess iron intake or absorption.
 - ❖ Liver disease,
 - ❖ Numerous blood transfusions.
- **Complications of hemochromatosis:**
 - ✓ Bronze pigmentation of the skin.
 - ✓ Diabetes mellitus (due to involvement of pancreas).
 - ✓ Cardiac arrhythmias (due to myocardial involvement).



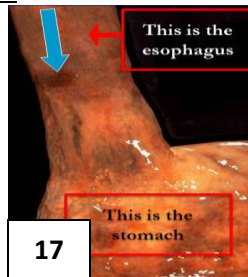
- **α_1 -antitrypsin deficiency:**

- **Complications:**
 - ✓ Panlobular emphysema: more likely to occur in adults.
 - ✓ Chronic hepatitis and cirrhosis: more likely to occur in children.
- **Morphology- image (16):**
 - ✓ Periportal red hyaline globules which represent collections of α_1 -antitrypsin not being excreted from hepatocytes.



- **Portal hypertension:**

- **Complications:**
 - ✓ Esophageal varices: dilation of submucosal veins which is considered as the most common cause of death in patient with cirrhosis. See image (17).
 - ✓ Caput medusae: dilated veins of anterior abdominal wall. See image (18).





- **Hepatocellular carcinoma:**

- **Most common primary malignant tumor of the liver in adults which spreads hematogenously.**
- **Associated with:**
 - ✓ Hepatitis B and C.
 - ✓ Wilson's disease.
 - ✓ Hemochromatosis.
 - ✓ α_1 -antitrypsin deficiency.
 - ✓ Alcoholic cirrhosis.
- **Findings:**
 - ✓ Jaundice.
 - ✓ Tender hepatomegaly.
 - ✓ Ascites.
 - ✓ Anorexia.
- **Diagnosis:**
 - ✓ \uparrow α -fetoprotein.
 - ✓ Ultrasound or contrast CT.
- **Morphology:**
 - ✓ Gross- image (19): the tumor is large, bulky and has greenish cast because it contains bile.
 - ✓ Histology- image (20): malignant cells of hepatocellular carcinoma (seen mostly on the right) are well differentiated and interdigitate with normal larger hepatocytes (seen mostly on the left).

