Liver

Characteristics

- 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 duct — Triad
  - Portal vein
  - Bile duct
  - Hepatic artery

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)‡

Memorize:
AST
ALT
LDH

Serum alkaline phospatase
CGT

Albumin
Ammonia
Clotting factors

The major hepatic diseases can be classified as

- Primary
  - Viral hepatitis.
  - Alcoholic liver disease.
  - Aonalcoholic fatty liver disease (NAFLD).
  - Cirrhosis.
  - Hepatocellular carcinoma (HCC).
- Secondary
  - Cardiac disease
  - Disseminated cancer
  - Extrahepatic infections

Cirrhosis

- **Charateristics**
  - Cirrhosis is the morphologic change most often associated with chronic liver disease it refers to
    - 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
      - Ductular reaction (DR) is characterized by the proliferation of reactive bile ducts induced by liver injuries
- **Diagnosis**
  - Liver function test
    - AST
    - ALT
    - Albumin
    - Blood clotting factors
    - جرب الخ دول
  - Radiology.
  - 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**
  - 40% of individuals with cirrhosis are asymptomatic until the most advanced stages of the disease.
  - Non specific symptoms such as anorexia, weight loss, weakness.
  - Signs and symptoms of liver failure e.g Jaundice, encephalopathy, and coagulopathy.
  - Pruritus, portal hypertention
  - Hyperestrogenemia
    - Due to impaired estrogen metabolism in male patients with chronic liver failure can give rise to
      - Palmar erythema (a reflection of local vasodilatation)
      - Spider angiomas of the skin
    - Such male hyperestrogenemia also leads to hypogonadism and gynecomastia
  - Hepatocellular carcinoma (HCC).

Cholestasis

- **Definition**
  - 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 diagnosis**
  - Elevated
    - Serum alkaline phosphatase and
    - γ-glutamyl transpeptidase (GGT)
- **Factors/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**
  - 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
  - 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
  - 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
  - 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