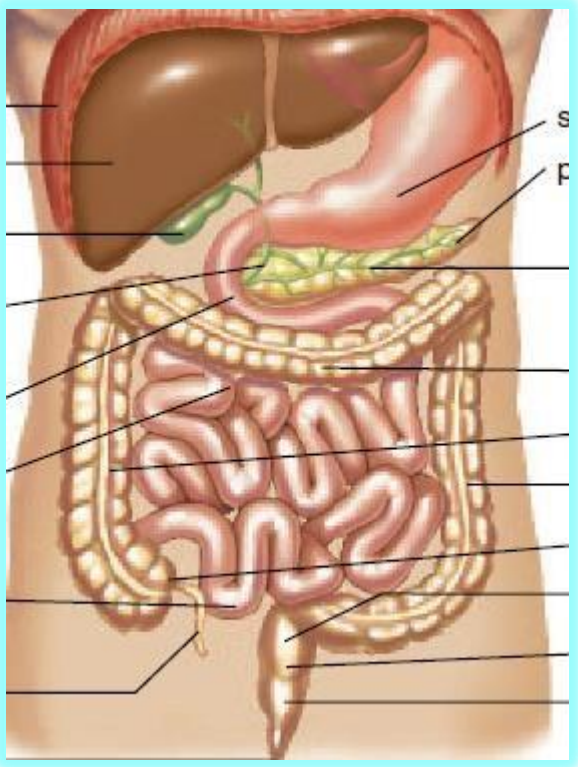
The liver Function

By Dr. Safa Ammer

Anatomy

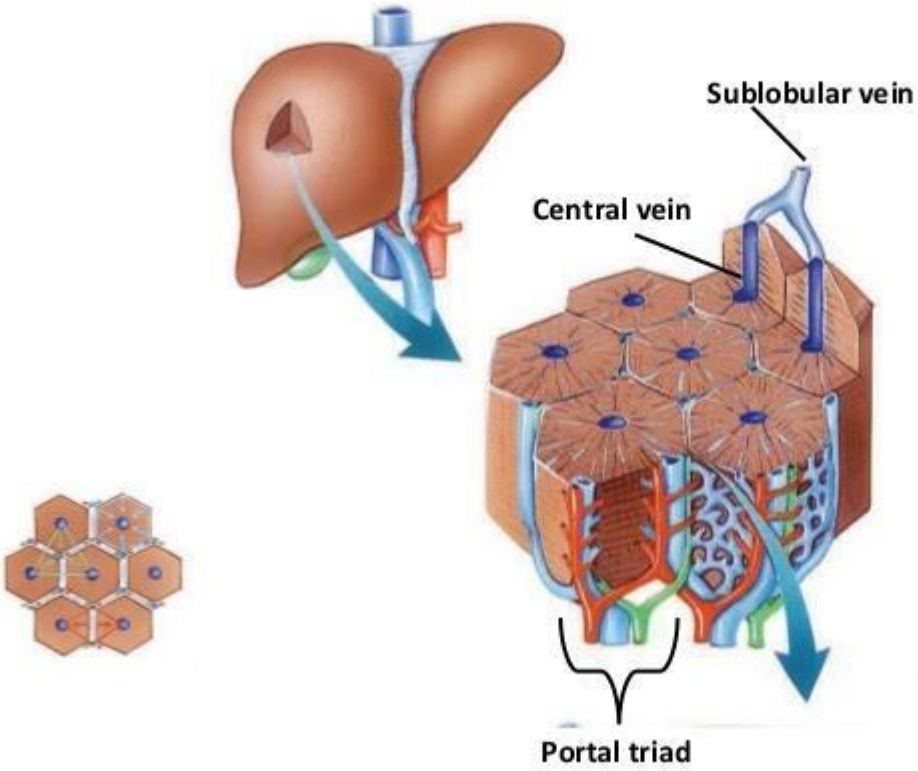
- The liver is a large, bilobed, complex organ.
- receiving a large amount of blood and nutrients from the gastrointestinal system
  - Hepatic artery: Provides it's blood supply
  - Portal vein: Transports absorbed substances from the GI tract

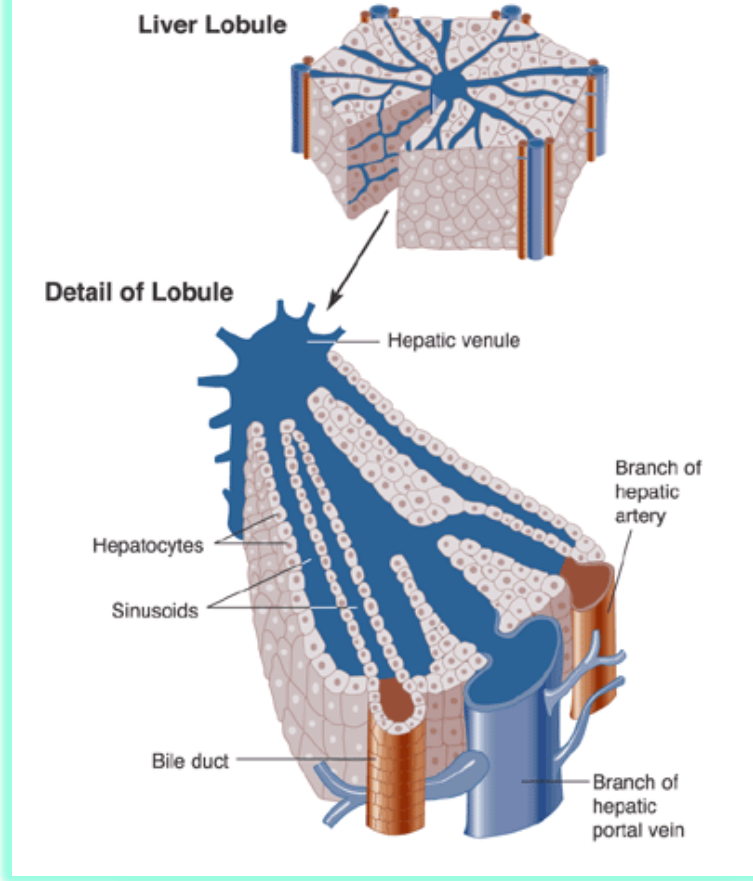


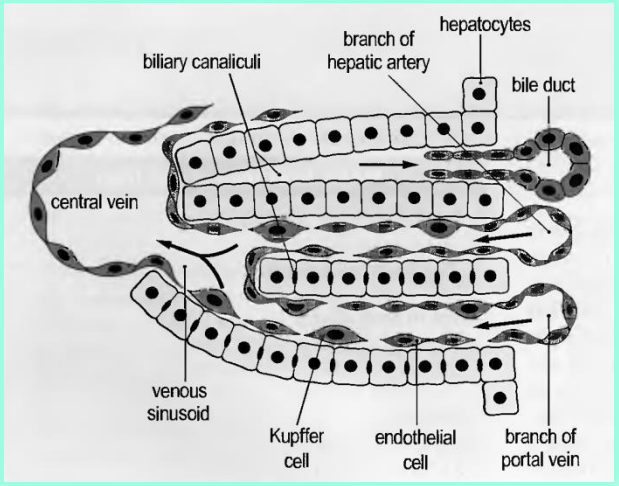
Structural Unit

- **Lobules** are the functional units,
- consisting of clusters of hepatocytes around a central vein
- Sinusoids, vascular spaces, are lined by Kupffer cells.
  - Blood from these spaces drain into the central veins.

CLASSIC HEPATIC LOBULE







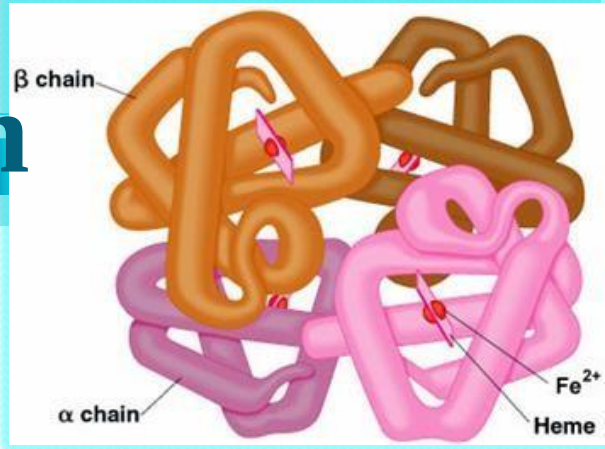
Major functions of the liver

- The liver performs four major functions:
  - excretion,
  - synthesis,
  - detoxification,
  - and storage.
- The liver is so important that if the liver becomes nonfunctional, death will occur with 24 hours due to hypoglycemia.

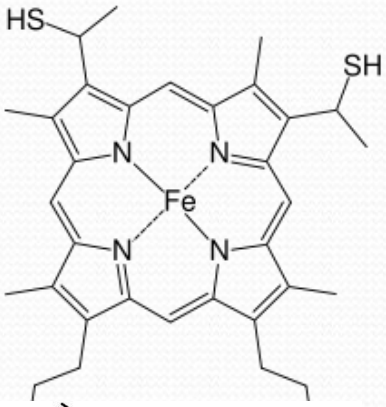
1- Excretory Function

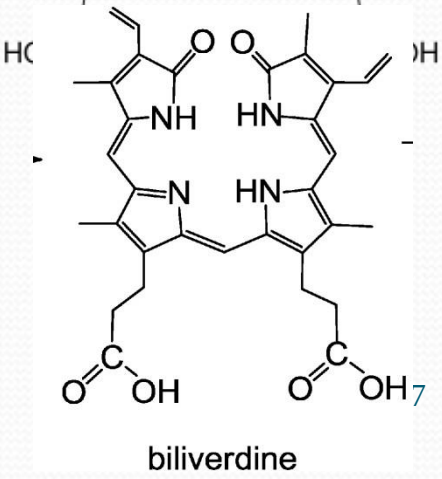
- One of the most important liver functions, and one that is disturbed in a large number of diseases is the excretion of bile
- Bile comprises:
  - bile acids or salts,
  - bile pigments & others
- Total bile production averages 3 liters/ day
- Bilirubin is the principal pigment in bile
  - Derived mainly from breakdown of hemoglobin

Formation of Bilirubin



1. Aged RBCs are phagocytized by reticuloendothelial system (RE) in the spleen, liver and bone marrow.
   - Hemoglobin is catabolized into amino acids, and heme.
2. Heme ring is broken open and porphyrin converted to Biliverdin, and then to **unconjugated** (indirect) **bilirubin**.





biliverdine

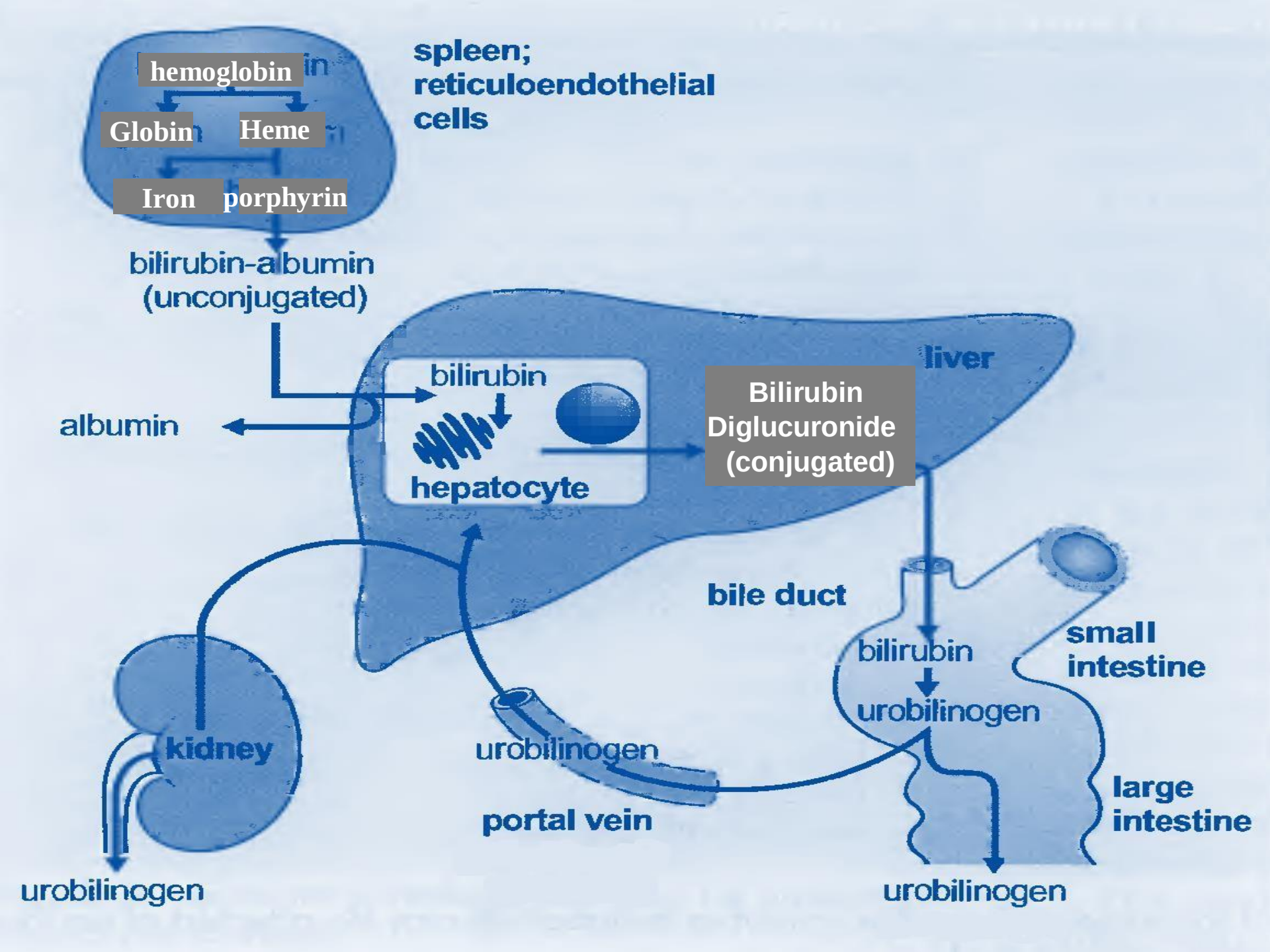
Formation of Bilirubin

3. RE cells secrete unconjugated bilirubin intothe plasma, where bilirubin is bound by albumin.
4. Albumin – bilirubin complex travels to the liver.
5. Hepatocytes conjugates bilirubin with gluconic acid by uridyl diphosphate glucuronyl transferase (UDPGT) enzyme to form **Conjugated bilirubin**
6. Conjugated bilirubin (water soluble) secretedinto the bile ducts (GI tract)

Formation of Bilirubin

7. GI bacterial normal flora convert conjugated bilirubin into urobilinogen (colorless).
   - Oxidation of urobilinogen → urobilin (red-brown pigment)
8. Urobilinogen may be excreted into the stool, small portion reabsorbed into the plasma and excreted in the urine

- 80% of bilirubin comes from Hb and 20% from heme containing protein (myoglobin)


hemoglobin
Globin
Heme
Iron
porphyrin
spleen;
reticuloendothelial
cells
bilirubin-albumin
(unconjugated)
albumin
bilirubin
hepatocyte
liver
Bilirubin
Diglucuronide
(conjugated)
bile duct
bilirubin
urobilinogen
small
intestine
large
intestine
kidney
urobilinogen
portal vein
urobilinogen
urobilinogen

Major functions of the liver

2. Synthetic

- **Carbohydrate metabolism**
  - gluconeogenesis,
  - glycogen synthesis and breakdown
- **Fat metabolism**
  - fatty acid synthesis,
  - cholesterol synthesis and excretion,
  - lipoprotein synthesis…..
- **Protein metabolism**
  - synthesis of plasma proteins (including some coagulation factors but not immunoglobulins)

Major functions of the liver

3. Detoxification and Drug Metabolism

- Every substance that is absorbed in the GIT must firstpass through the liver (**first pass**).
- This allows important substances to reach the circulation and prevent toxic or harmful substances from reaching the circulation
- The body has two mechanisms for detoxification of foreign materials and metabolic products:
  - It may either bind the material reversibly so as to inactivate the compound,
  - or it may chemically modify the compound so it can be excreted

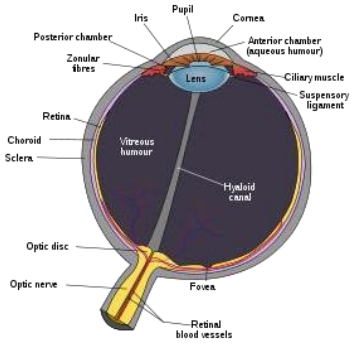
4. Storage

- Glycogen, vitamin A , vitamin B12

Disorders of Liver

- Jaundice
- Cirrhosis
- Tumors
- Hepatitis
- Drug & Alcohol related disorders

Jaundice



- **Jaundice or Icterus**
  - Yellowish discoloration of the skin and sclera from increased plasma bilirubin
  - Usually the concentration of bilirubin in the blood must exceed 2–3 mg/dl for the coloration to be easily visible

- **Icteric:** Plasma /serum with yellowish color from ↑ bilirubin

- **Reference ranges**
  - Total Bilirubin (conjugated + unconjugated) 0.2 - 1.0 mg / dl
  - Conjugated bilirubin 0.0 - 0.2 mg / dl
  - Fullterm newborns 2.0 – 6.0 mg / dl

Jaundice

- **General classifications of jaundice**

1. **Prehepatic**
   - Excess RBC destruction,
   - Excessive amounts of bilirubin is presented tothe liver (**Not** impaired liver function)
   - Increased unconjugated bilirubin
   - Unconjugated bilirubin is water insoluble and is bound to albumin
   - It is not filtered by the kidney and will not appear in urine.

General classifications of jaundice

2. Hepatic

- Defective liver function
- May result from:
  - **Gilbert syndrome**
    - Less in UDPGT enzyme activity (20%-30%)
  - **Crigler-Najjar Syndrome**
    - type 1, complete absence of enzyme
    - type II, severe deficiency of the enzyme
  - **Dubin-Johnson syndrome**
    - removal of conjugated bilirubin from the liver cell and the excretion into the bile is defective

General classifications of jaundice

3. Posthepatic

- Impaired ability of liver to excrete bile into theGI tract due to obstruction
  - gallstones, tumors
- Rise in serum level of conjugated bilirubin but normal to elevated unconjugated bilirubin.
- Conjugated bilirubin appears in urine
- Serum enzymes that indicate biliary obstruction, including alkaline phosphataseand GGT, are also often elevated.

Physiological Jaundice of the newborn

- Immature liver at birth
- Temporary deficiency of UDPGT
- Small / moderate elevated unconjugated bilirubin lasting a few days.
- If not processed it is deposited in the brain and nerve cells, causing cell damageand death in the newborn

Type Of Jaundice	SERUM		
	Total Bilirubin	Conjugated Bilirubin	**Unconjugated Bilirubin**
	↑	↔	↑
Hepatic			
• Gilbert disease	↑	↔	↑
• Crigler-Najjar syndrome	↑	↓	↑
• Dubin-Johnson	↑	↑	↔
• Jaundice of newborn	↑	↔	↑
	↑	↑	↑

Other Disorders of Liver

- **Cirrhosis**
  - A consequence of chronic liver disease characterized by replacement of liver tissue by fibrous scar tissue leading to progressive loss of liver function.
  - Cirrhosis is most commonly caused by alcoholism, hepatitis B and C and fatty liver disease but has many other possible causes.

Other Disorders of Liver

- **Tumors**
  - Cancers of the liver are classified as:
    - Primary (cancer that begins in the liver cells)
    - metastatic when tumors from other parts of the body spread (metastasize) to the liver.
  - Cancers of the liver may also be classified as:
    - benign
    - or malignant
  - Whether primary or metastasic, any malignant tumorin the liver is:
    - a serious finding
    - and carries a poor prognosis, with survival times measured in months.

Other Disorders of Liver

- **Drug- and Alcohol-Related Disorders**
  - most common mechanism of toxicity is via an immune-mediated injury to the hepatocytes
- **Hepatitis**
  - Inflammation of the liver
  - Caused by viruses, bacteria, chemicals and others
  - Among viruses causing hepatitis are hepatitis types A, B, C, D & E

Liver function tests

Liver function tests check the levels of certain enzymes and proteins in your blood. Levels that are higher or lower than usual can mean liver problems. The pattern and degree of elevation of these tests along with the overall clinical picture can provide hints to the underlying cause of these problems.

Some common liver function tests include:

- Alanine transaminase (ALT). ALT is an enzyme found in the liver that helps convert proteins into energy for the liver cells. When the liver is damaged, ALT is released into the bloodstream and levels increase. This test is sometimes referred to as SGPT.
- Aspartate transaminase (AST). AST is an enzyme that helps the body break down amino acids. Like ALT, AST is usually present in blood at low levels. An increase in AST levels may mean liver damage, liver disease or muscle damage. This test is sometimes referred to as SGOT.

- Alkaline phosphatase (ALP). ALP is an enzyme found in the liver and bone and is important for breaking down proteins. Higher-than-usual levels of ALP may mean liver damage or disease, such as a blocked bile duct, or certain bone diseases, as this enzyme is also present in bones.
- Albumin and total protein. Albumin is one of several proteins made in the liver. Your body needs these proteins to fight infections and to perform other functions. Lower-than-usual levels of albumin and total protein may mean liver damage or disease. These low levels also can be seen in other gastrointestinal and kidney-related conditions.
- Bilirubin. Bilirubin is a substance produced during the breakdown of red blood cells. Bilirubin passes through the liver and is excreted in stool. Higher levels of bilirubin might mean liver damage or disease. At times, conditions such as a blockage of the liver ducts or certain types of anemia also can lead to elevated bilirubin.