

Liver Function Tests

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Major Metabolic Functions of the Liver:

- **Synthetic Function**
Plasma proteins (albumin, globulins), cholesterol, triglycerides and lipoproteins
- **Detoxification and excretion**
Ammonia to urea (urea cycle), bilirubin, cholesterol, drug metabolites
- **Storage Function**
Vitamins A, D, E, K and B₁₂
- **Production of bile salts**
Helps in digestion

Some example of liver dysfunction:

- Hepatocellular disease
- Cholestasis (obstruction of bile flow)
- Cirrhosis (scarring of the liver)
- Hepatitis
- Jaundice
- Liver cancer
- Steatosis (fatty liver)
- *Genetic Disorders*
Hemochromatosis (iron storage) (excess iron in the body)

Liver Function Tests:

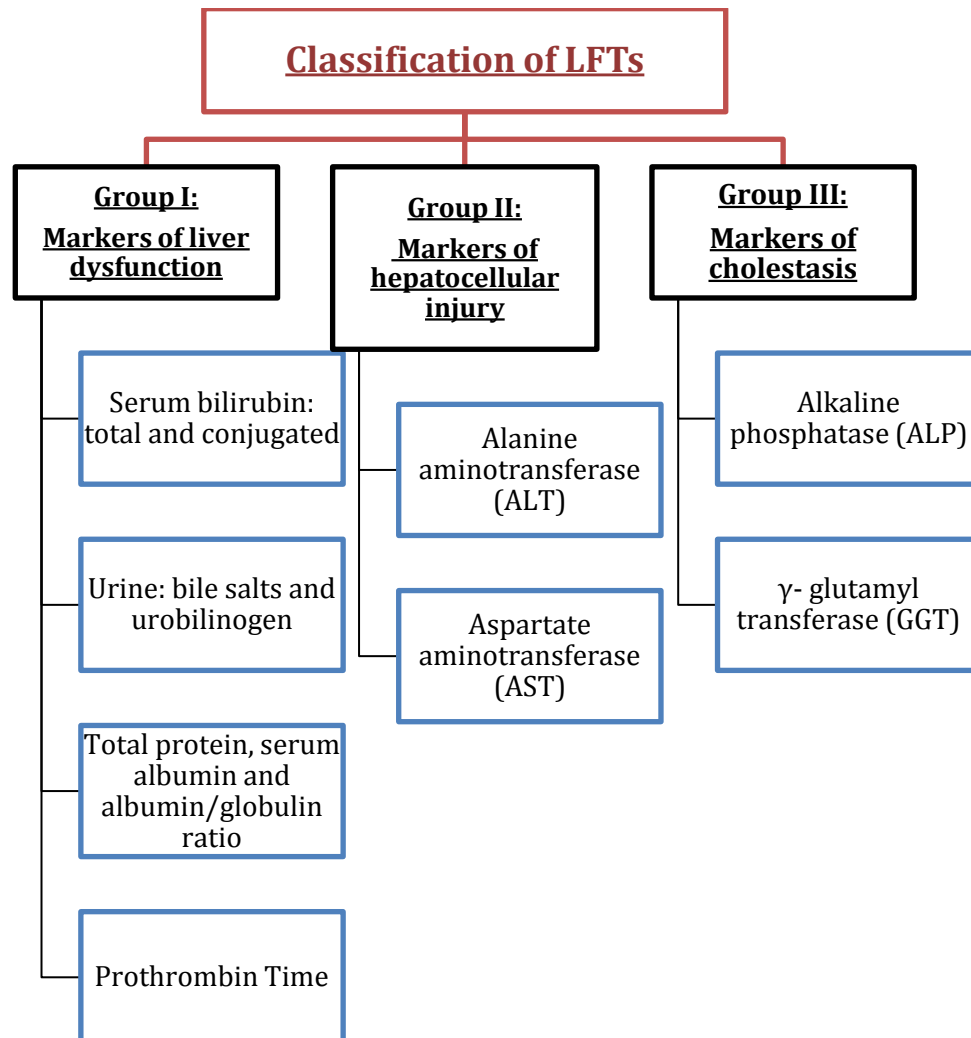
- Noninvasive methods for screening of liver dysfunction
- Help in identifying general type of disorder
- Assess severity and allow prediction of outcome
- To follow the course of the disease, evaluate response to treatment, and adjust treatment when necessary

- **Broadly classified as :**

1. **Tests to detect hepatic injury:**

- mild or severe; acute or chronic
- Nature of liver injury (hepatocellular or cholestasis) (cholestasis=obstruction)

2. **Tests to assess hepatic function**

**Limitations of LFT:**

- Normal LFT values do not always indicate absence of liver disease
 - Liver has very large reserve capacity
- Asymptomatic people may have abnormal LFT results
 - Diagnosis should be based on clinical examination

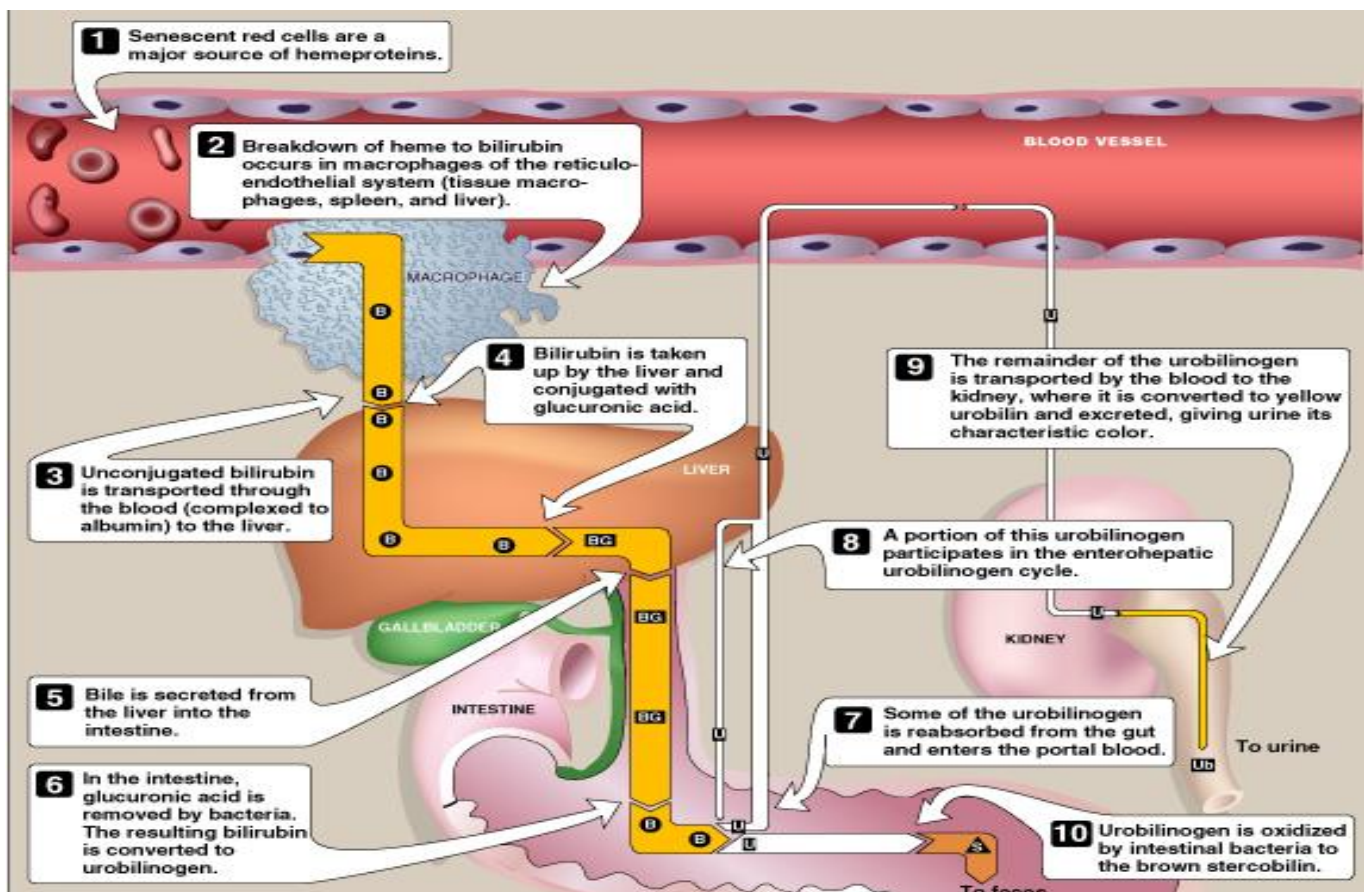
Common serum liver chemistry tests:

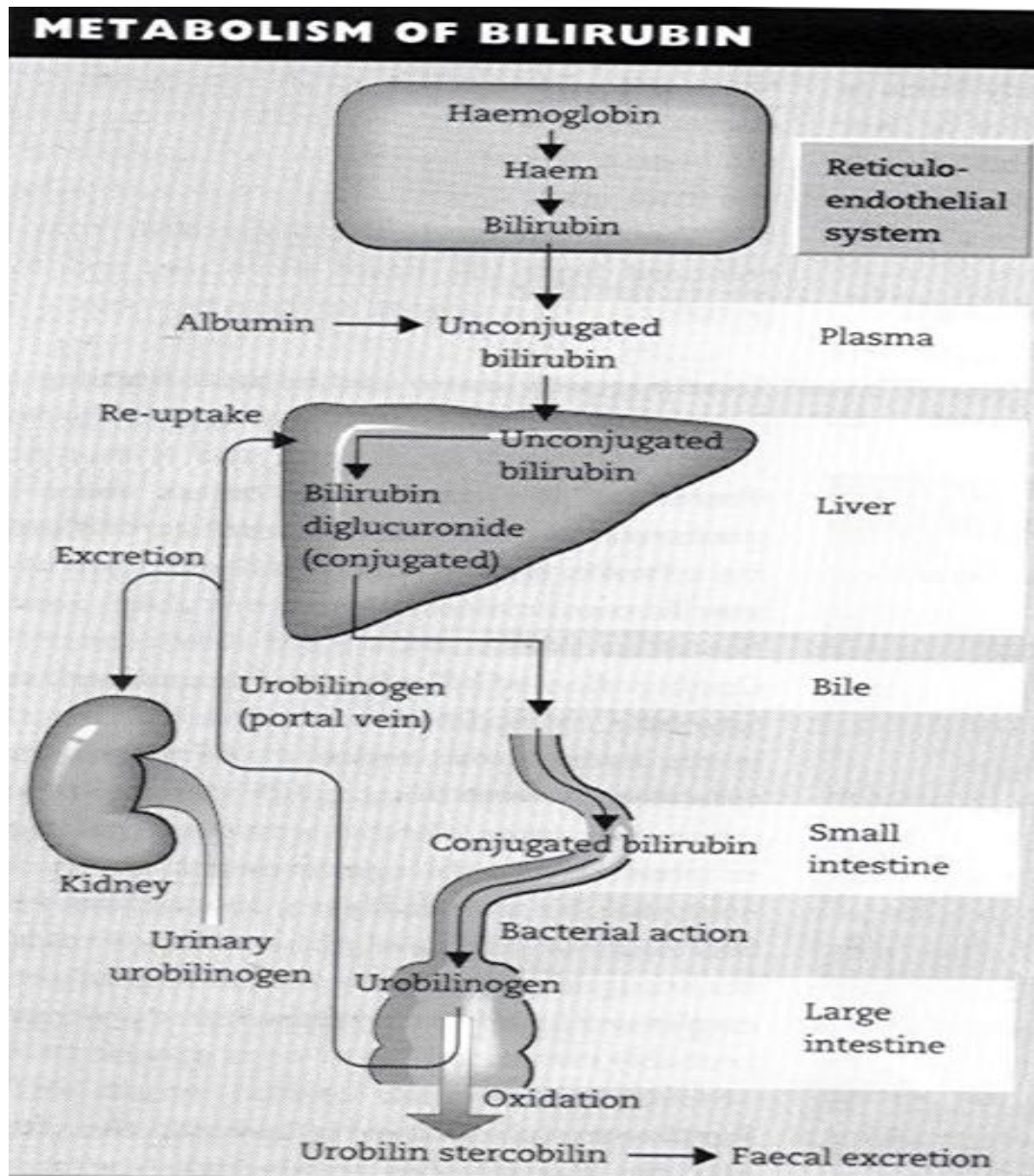
Liver chemistry test	Clinical implication of abnormality
Alanine aminotransferase	Hepatocellular damage
Aspartate aminotransferase	Hepatocellular damage
Bilirubin	Cholestasis, impaired conjugation, or biliary obstruction
Alkaline phosphatase	Cholestasis, infiltrative disease, or biliary obstruction
Prothrombin time	Synthetic function
Albumin	Synthetic function
γ -glutamyltransferase	Cholestasis or biliary obstruction
Bile acids	Cholestasis or biliary obstruction
5'-Nucleotidase	Cholestasis or biliary obstruction
Lactate dehydrogenase LDH	Hepatocellular damage, not specific for hepatic disease

LD5 → specific for the liver

Bilirubin (insoluble molecule):

- A byproduct of red blood cell breakdown
- It is the yellowish pigment observed in jaundice
- High bilirubin levels are observed in gallstones, acute and chronic hepatitis





- Serum bilirubin levels**

Normal	0.2 to 0.8 mg/dL
Unconjugated/free/indirect (bilirubin-albumin complex)	0.2 to 0.7 mg/dL
Conjugated/direct	0.1 to 0.4 mg/dL
Latent jaundice(asymptomatic) :	Above 1 mg/dL
Jaundice(symptomatic=albumin is deposited in the tissue)	Above 2 mg/dL

Bilirubin levels and jaundice:

<u>Class of Jaundice</u>	<u>Type of Bilirubin raised</u>	<u>Causes</u>
Pre-hepatic or hemolytic	Unconjugated	Abnormal red cells; antibodies; drugs and toxins; thalassemia Hemoglobinopathies (Gilbert's, Crigler-Naajjar syndrome)
Hepatic or Hepatocellular	Unconjugated and conjugated	Viral hepatitis, toxic hepatitis, intrahepatic cholestasis
Post-hepatic	Conjugated	Extrahepatic cholestasis; gallstones; tumors of the bile duct, carcinoma of pancreas

Urinary urobilinogen(UBG) and urine bile salts:

- Most UBG is metabolized in the large intestine, a fraction is excreted in urine (less than 4 mg/day)
- Normally bile salts are NOT present in urine
- Obstruction in the biliary passages causes leakage of bile salts into circulation leading to its excretion in urine

Serum Albumin:

- The most abundant protein synthesized by the liver (we can see increased albumin level in case of massive & prolonged injury)
- Normal serum levels: 3.5 to 5g/dL
- Its synthesis depends on the extent of functioning liver cell mass
- Longer half-life of 20 days
- Its levels decrease in all chronic liver diseases

Serum Globulin:

- Normal serum levels: 2.5 to 3.5g/dL
- a and b-globulins mainly synthesized by the liver
- They constitute immunoglobulins (antibodies)
- High serum g-globulins are observed in chronic hepatitis and cirrhosis:
 - IgG in autoimmune hepatitis
 - IgA in alcoholic liver disease

Albumin to globulin (A/G) ratio: (compensatory mechanism when one is decreased the other is increased)

- Normal A/G ratio: 1.2/1 – 1.5/1
- Globulin levels increase in hypoalbuminemia as a compensation
- **Prothrombin Time (PT)** (The needed for coagulation) :
 - Prothrombin: synthesized by the liver, a marker of liver function
 - Its half-life is 6 hrs. (because its half life is short it will indicate the present function of the liver)
 - PT is prolonged only when liver loses more than 80% of its reserve capacity
 - Vitamin K deficiency also causes prolonged PT
 - Dosage of vitamin K does not affect PT in liver disease

Aspartate aminotransferase (AST):

- Normal range: 8 – 20 U/L
- A marker of hepatocellular damage
- High serum levels are observed in chronic hepatitis, cirrhosis and liver cancer

Alanine aminotransferase (ALT):

- More liver-specific than AST
- Normal range (U/L): (you don't have to memorize the normal ranges ,just the abnormal e.g. acute hepatitis (300-1000U/L))
 - Male: 13-35
 - Female: 10-30
- High serum levels are observed in acute hepatitis (300-1000U/L)
- Moderate elevation is observed in alcoholic hepatitis (100-300U/L)
- Minor elevation is observed in cirrhosis, hepatitis C and non-alcoholic steatohepatitis (NASH) (50-100U/L)
- Appears in plasma many days before clinical signs appear
- A normal value does not always indicate absence of liver damage
- Obese but otherwise normal individuals may have elevated ALT levels

Alkaline phosphatase (ALP):

- A non-specific marker of liver disease
- Produced by bone osteoblasts (for bone calcification)
- Normal range: 40 – 125 U/L
- Moderate elevation observed in:
 - Infective hepatitis, alcoholic hepatitis and hepatocellular carcinoma
- High levels are observed in:
 - Extrahepatic obstruction (obstructive jaundice) and intrahepatic cholestasis
- Very high levels are observed in:
 - Bone diseases

γ -glutamyltransferase (GGT):

- Used for glutathione synthesis
- Normal range: 10 – 30U/L
- Moderate elevation observed in:
 - Infective hepatitis and prostate cancers
- GGT is increased in alcoholics despite normal liver function tests
 - Highly sensitive in detecting alcohol abuse