

# Liver Function Tests (LFTs)

GNT/Hematology Block

# Objectives

**Upon completion of this lecture, the students should be able to:**

- Understand the major metabolic functions of the liver and causes of liver dysfunction.
- Discuss markers of liver function tests such as liver enzymes, bilirubin, albumin and prothrombin time that can diagnose hepatic injury and assess hepatic function.

# 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 B<sub>12</sub>

- **Production of bile salts**

- Helps in digestion

# Some example of liver dysfunction

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

# Liver Function Tests (LFTs)

- Noninvasive methods for screening of liver dysfunction
- Help in identifying general types of disorder
- Assess severity and allow prediction of outcome
- Disease and treatment follow up

# Liver Function Tests (LFTs)

Broadly classified as:

## 1. Tests to detect hepatic injury:

- Mild or severe; acute or chronic
- Nature of liver injury (hepatocellular or cholestasis)

## 2. Tests to assess hepatic function

# Classification of LFTs

## **Group I: Markers of liver dysfunction**

- Serum bilirubin: total and conjugated
- Urine: bile salts and urobilinogen
- Total protein, serum albumin and albumin/globulin ratio
- Prothrombin Time

# Classification of LFTs

## **Group II: Markers of hepatocellular injury**

- Alanine aminotransferase (ALT)
- Aspartate aminotransferase (AST)



# Classification of LFTs

## **Group III: Markers of cholestasis**

- Alkaline phosphatase (ALP)
- $\gamma$ -glutamyltransferase (GGT)

# Limitations of LFTs

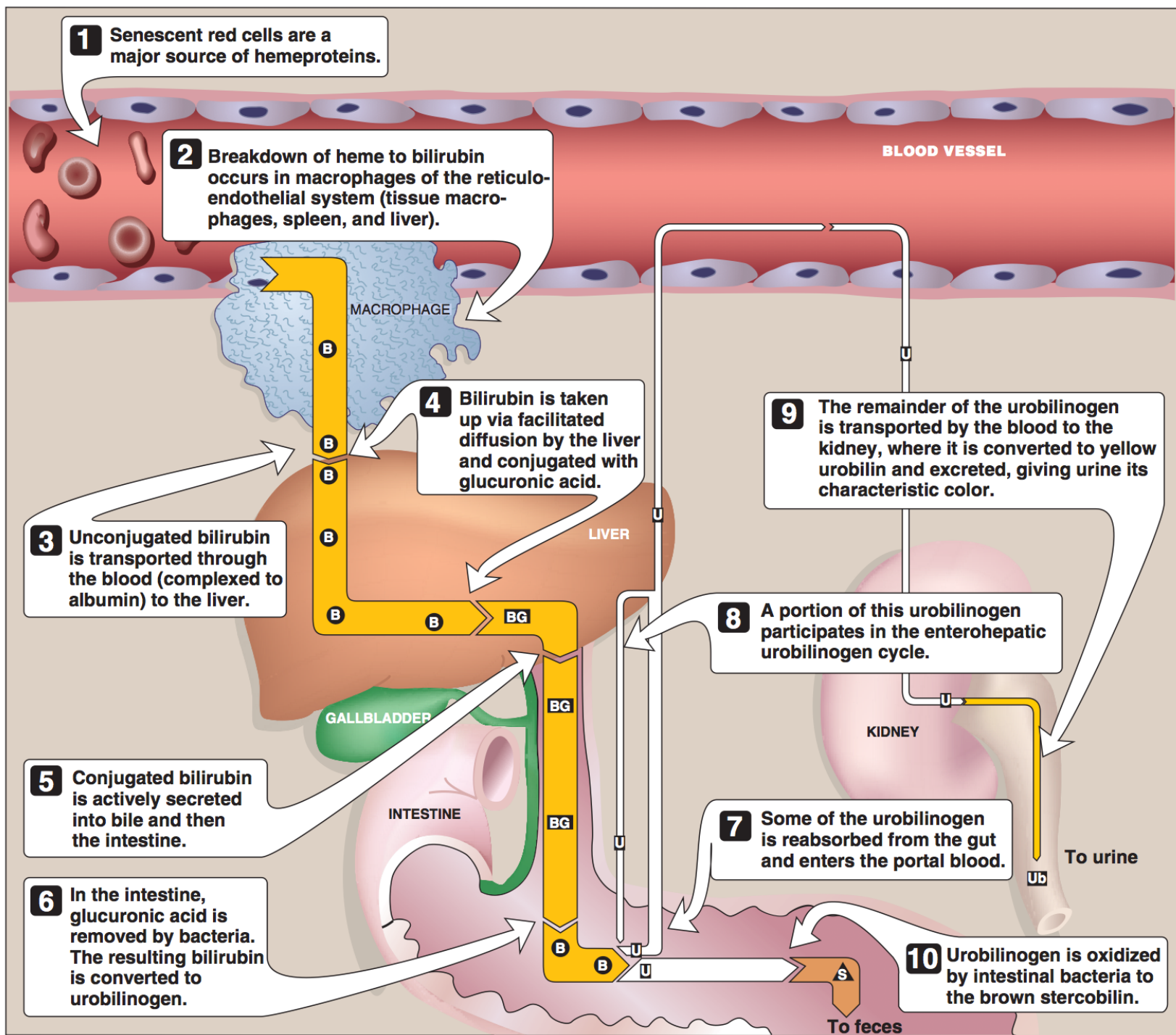
- Normal LFT values do not always indicate absence of liver disease
  - Liver has a very large reserve capacity
- Asymptomatic people may have abnormal LFT results
  - Diagnosis should be based on clinical examination

# Common serum liver chemistry tests

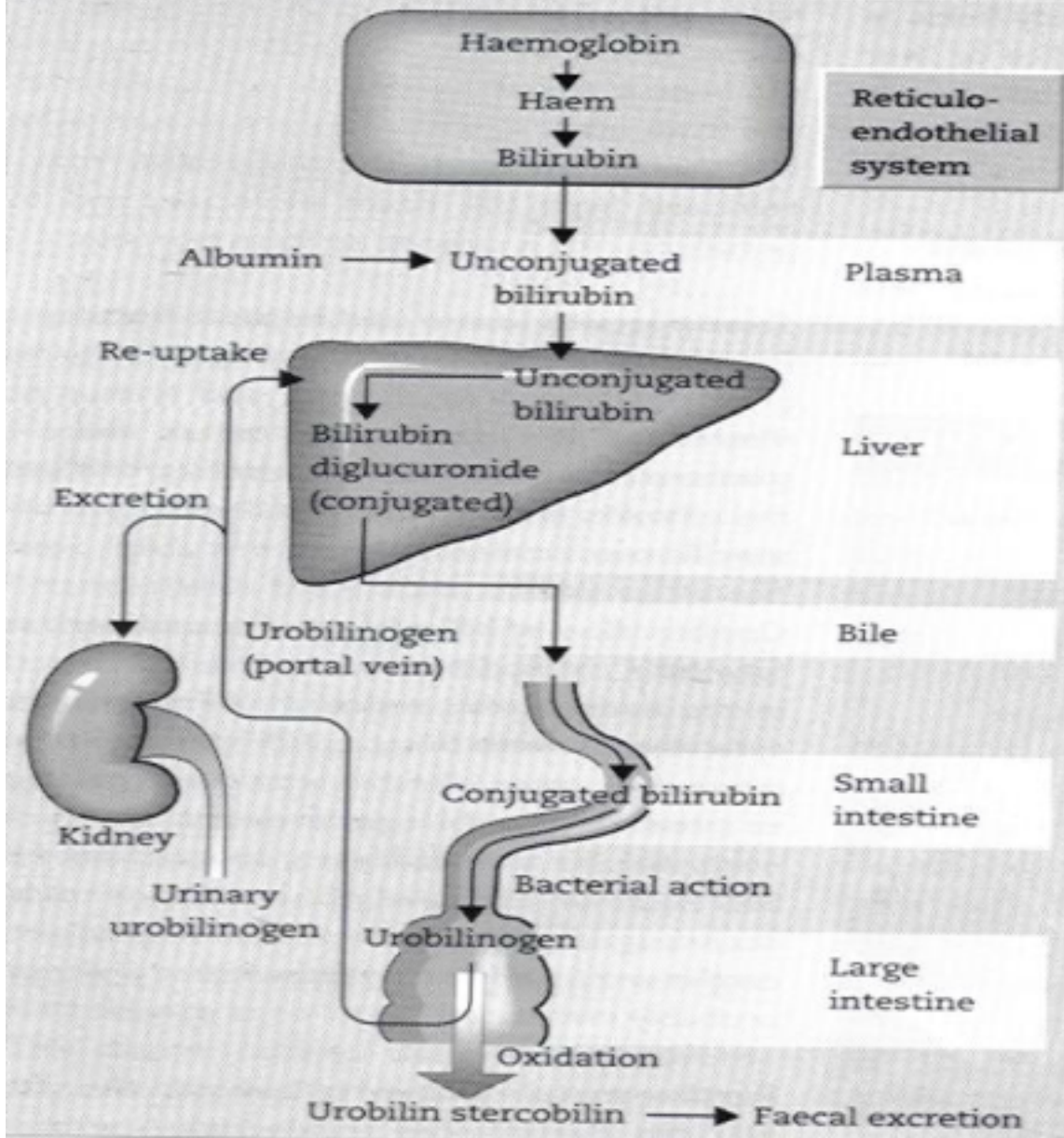
Liver chemistry test	Clinical implication of abnormality
Alanine aminotransferase	Hepatocellular damage
Aspartate aminotransferase	Hepatocellular damage
Bilirubin	Cholestasis, impaired conjugation, or biliary obstruction
Alkaline phosphatase	Cholestasis, infiltrative disease, or biliary obstruction
Prothrombin time	Synthetic function
Albumin	Synthetic function
$\gamma$ -glutamyltransferase	Cholestasis or biliary obstruction
Bile acids	Cholestasis or biliary obstruction

# Bilirubin

- 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



# METABOLISM OF BILIRUBIN



# Serum bilirubin levels

- Normal
  - 0.2 – 0.8 mg/dL
- Unconjugated (indirect):
  - 0.2 – 0.7 mg/dL
- Conjugated (direct):
  - 0.1 – 0.4 mg/dL
- Latent jaundice:
  - Above 1 mg/dL
- Jaundice:
  - Above 2 mg/dL

# Bilirubin levels and jaundice

Class of Jaundice	Causes
Pre-hepatic or hemolytic	Abnormal red cells; antibodies; drugs and toxins; thalassemia Hemoglobinopathies, Gilbert's, Crigler-Najjar syndrome
Hepatic or Hepatocellular	Viral hepatitis, toxic hepatitis, intrahepatic cholestasis
Post-hepatic	Extrahepatic cholestasis; gallstones; tumors of the bile duct, carcinoma of pancreas



# Urobilinogen (UBG) and bile salts

- Most UBG is metabolized in the large intestine but 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
  - Excretion in urine

# Serum Albumin

- The most abundant protein synthesized by the liver
- Normal serum levels: 3.5 – 5 g/dL
- Synthesis depends on the extent of functioning liver cell mass
- Longer half-life: 20 days
- Its levels decrease in all chronic liver diseases

# Serum Globulin

- Normal serum levels: 2.5 – 3.5g/dL
- $\alpha$  and  $\beta$ -globulins mainly synthesized by the liver
- They constitute immunoglobulins (antibodies)
- High serum  $\gamma$ -globulins are observed in chronic hepatitis and cirrhosis:
  - IgG in autoimmune hepatitis
  - IgA in alcoholic liver disease

# Albumin to globulin (A/G) ratio

- Normal A/G ratio: 1.2/1 – 1.5/1
- Globulin levels increase in hypoalbuminemia as a compensation

# Prothrombin Time (PT)

- Prothrombin: synthesized by the liver, a marker of liver function
- Half-life: 6 hrs. (indicates 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
- Intake 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):
  - Male: 13-35
  - Female: 10-30
- High serum levels in acute hepatitis (300-1000U/L)
- Moderate elevation in alcoholic hepatitis (100-300U/L)
- Minor elevation in cirrhosis, hepatitis C and non-alcoholic steatohepatitis (NASH) (50-100U/L)

# Alanine aminotransferase (ALT)

- 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)
- Present on hepatocyte membrane
- Normal range: 40 – 125 U/L
- Moderate elevation observed in:
  - Infective hepatitis, alcoholic hepatitis and hepatocellular carcinoma

# Alkaline phosphatase (ALP)

- High levels are observed in:
  - Extrahepatic obstruction (obstructive jaundice) and intrahepatic cholestasis
- Very high levels are observed in:
  - Bone diseases

# $\gamma$ -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 to detecting alcohol abuse

# Take Home Messages

- LFTs help detect liver injury and function.
- LFTs do have some limitations.

# References

- Lippincott's Illustrated Reviews Biochemistry: 6<sup>th</sup> edition, Unit IV, Chapter 21, Pages 282 - 285.
- Lecture notes: Clinical Biochemistry: 9<sup>th</sup> edition, Chapter 13, Pages 174 - 187.
- Clinical Chemistry - Techniques, Principales and Correlations: 6<sup>th</sup> edition, Chapter 24, Pages 520 -521.