[lecture 1]

Liver Function Tests (LFTs)

Biochemistry Team

Teams

The Objectives

Not given ☹

Red = Import-ant

Blue = explain

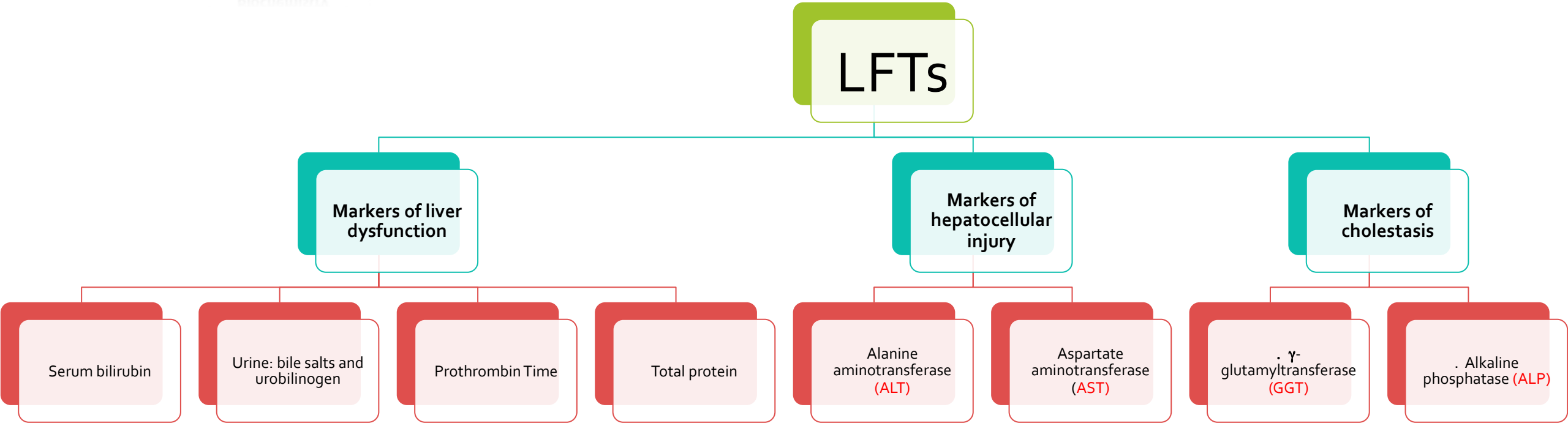
Green = addition notes

Done By : **Wael Al Saleh**

Reviewed By: **Manar ALEid**

Biochemistry Team

Mind Map



Dr.Sumbul said that ,we don't have to memorize the numbers"they will give us the levels ". We should know the ranges

Major Metabolic Functions of the Liver

1. Synthetic Function:

Liver synthesize Plasma proteins (albumin, globulins), cholesterol, triglycerides and lipoproteins

2. Detoxification and excretion:

Ammonia to urea (urea cycle), bilirubin, cholesterol, drug metabolites

Body is producing a lot of toxins which have to be neutralized.. AMMONIA can lead to death so it's converted in the liver to a non-toxic substance called "urea".

3. Storage Function:

Vitamins A, D, E, K and B_{12} Also it stores iron, copper, glycogen and other minerals.

4. Production of bile salts:

Helps in digestion

Causes of liver dysfunction: some diseases or drugs or toxins or infections or trauma can Cause liver dysfunction. As a result, certain markers will be high.

1. Hepatocellular disease
2. Cholestasis (obstruction of bile flow)
3. Cirrhosis
4. Hepatitis
5. Jaundice
6. Liver cancer
7. Steatosis (fatty liver) A lot of fat accumulated in the liver abnormally
8. *Genetic Disorders :* Such as Hemochromatosis (high iron storage)

Liver Function Tests (LFTs)

- Noninvasive methods for screening of liver dysfunction. You don't need to take a biopsy or cut out of liver just to do serum markers via blood sample
- Help in identifying general types of disorder.
- Assess severity and allow prediction of outcome
- Disease and treatment follow up

Broadly classified as:

A. Tests to detect hepatic injury:
   A. Could be: mild or severe, acute or chronic
   B. Nature of liver injury (hepatocellular or cholestasis)

B. Tests to assess hepatic function.

Limitations of LFTs:

1. Normal LFT values do not always indicate absence of liver disease because the Liver has very large reserve capacity. It compensates other areas. So, only a large amount of damage will alter results of LFTs
2. Asymptomatic people may have abnormal LFT results. So, Diagnosis should be based on clinical examination

Classification of LFTs:

Group I: Markers of liver dysfunction

- Serum bilirubin: total and conjugated
- Urine: bile salts and urobilinogen. Normally bile salts are not present in the urine. (found in cholestasis)
- Total protein, serum albumin and albumin/ globulin ratio >decrease in the liver dysfunction and It may cause edema
- Prothrombin Time >delayed in the liver dysfunction

Group II: Markers of hepatocellular injury

If high= indicates damage in the liver

1) Alanine aminotransferase (ALT) is more specific for liver than AST To remember: ALT = LIVER

2) Aspartate aminotransferase (AST) is less specific for liver and it present in muscles heart and kidney

Group III: Markers of cholestasis

1. Alkaline phosphatase (ALP)
2. γ-glutamyltransferase (GGT)

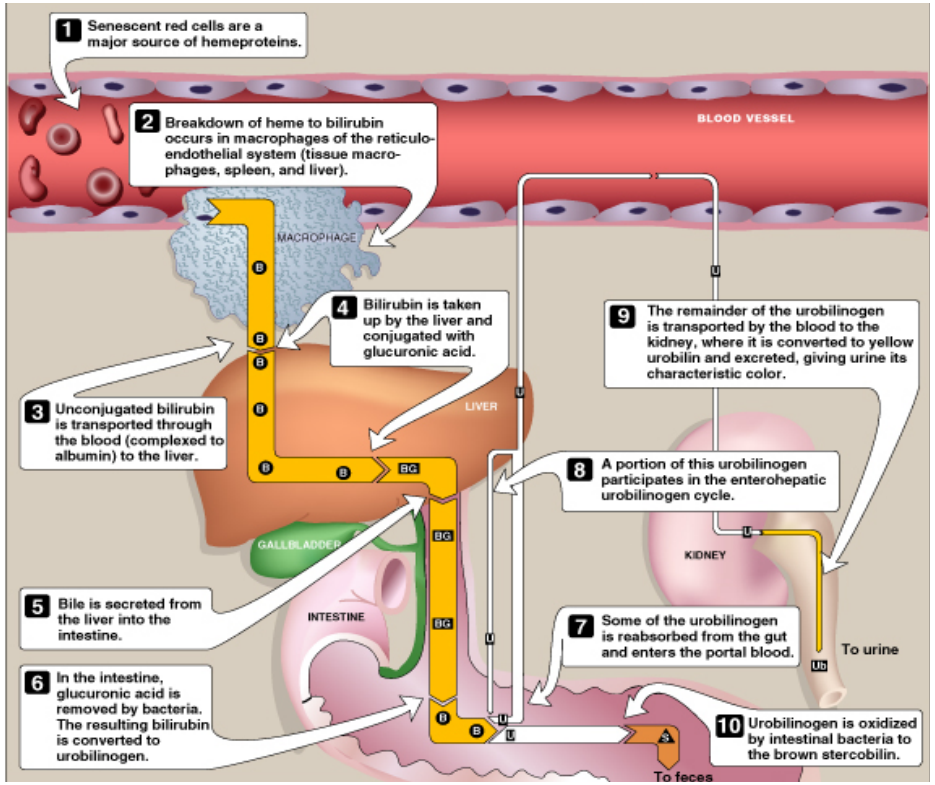
GGT is more specific for cholestasis than ALP

Common serum liver chemistry tests	
ALT & AST	**For hepatocellular Damage**
Bilirubin & ALP	**For cholestasis, impaired conjugation and biliary obstruction**
Prothrombin time& Albumin	**For Synthetic Function**
GGT & Bile acids	**For cholestasis or billary obstruction**

Metabolism of Bilirubin

- **Bilirubin is a byproduct of red blood cell breakdown** "Byproduct means the end product of RBC breakdown **(RBCs lifespan: 120 days)**. Hemoglobin from the RBCs break down into: heme and globulin. The heme group metabolized into Bilirubin".
- **It is the yellowish pigment observed in jaundice**
- **High bilirubin levels are observed in: Gallstones, acute and chronic hepatitis and jaundice.**

1. Hemoglobin from the RBCs break down into a heme and a globulin
2. The heme group is taken up by macrophages of the reticuloendothelial system (including tissue macrophages and that of the liver and spleen) into bilirubin
3. Birubin is insoluble in the blood so it attaches and is carried to the liver by albumin
4. Bilrubin is derived from the albumin, enters the hepatocytes and conjugates with glucoronic acid by the enzyme UDP-glucourinile transferase
5. This soluble conjugated form is excreted via the bile duct into the intestine where the bacteria removes the glucoronic acid and converts bilrubin into urobilinogen
6. some of the urobilinogen is reabsorbed from the gut and enters the portal circulation
7. some is recycled in the enterohepatic cells
8. the remainder is transported along with the blood to the kidneys where it is converted into UROBILIN that is excreted in the urine, giving it it's characteristic YELLOW color
9. mainly urobilinogen in the gut is oxidized by the bacteria into strecobilin which is excreted in the feces giving it its BROWN appearance



Bilirubin levels and jaundice

(Serum bilirubin levels)

A. **Normal:**
   A. 0.2 – 0.8 mg/dL

B. **Unconjugated (indirect):**
   A. 0.2 – 0.7 mg/dL

C. **Conjugated (direct):**
   A. 0.1 – 0.4 mg/dL

D. **Latent jaundice:**
   A. *Above 1 mg/dL
   Latent = Subclinical

E. **Jaundice:**
   A. *Above 2 mg/dL

Classification of Jaundice

Class of Jaundice	Type of Bilirubin raised	Causes
Pre-hepatic or hemolytic "Increase the hemolysis will elevate High free bilirubin in the blood"	Unconjugated Always Genetic syndromes result from deficiency in UDP- glucourinile transferase enzyme > inability of liver to conjugate bile > high level of Unconjugated bilirubin.	1. Abnormal red cells (Sickle cell anemia) 2. Antibodies :against RBC's (Autoimmunity) 3. drugs and toxins 4. Thalessemia 5. Hemoglobinopathies 6. Gilbert's and Crigler-Najjar** syndrome
Hepatic or Hepatocellular	Unconjugated and conjugated	1. Viral hepatitis 2. toxic hepatitis 3. Intrahepatic cholestasis
Post-hepatic	Conjugated Always	1. Extrahepatic cholestasis 2. gallstones 3. tumors of the bile duct 4. carcinoma of pancreas

Urobilinogen (UBG) and bile salts

- Most UBG is metabolized in the large intestine "into strecobilin and excreted via feces" but a fraction is excreted in urine (less than 4 mg/day)
- Normally bile salts are NOT present in urine

- Obstruction "due to any tumor or gallstones" in the biliary passages causes:
  - ❑ Leakage of bile salts into circulation
  - ❑ Excretion in urine

(Obstruction can occur in obstructive jaundice and also in hepatic jaundice due to obstruction of microbiliary channels caused by inflammation)

*We mean the conjugated

**in Crigler-najjar, the enzyme is absent

Albumin and globulin

Serum Albumin

Very good marker for synthetic function

- 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

- α and β-globulins mainly synthesized by the liver
- They constitute immunoglobulins (antibodies)
- High serum γ-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

If the liver has low albumin synthesis, globulin will increase as a compensatory mechanism to maintain serum protein, results in decreased ratio.

Alanine aminotransferase (ALT) & Aspartate aminotransferase (AST) & γ-glutamyltransferase (GGT)

Alanine aminotransferase (ALT)

- More liver-specific than AST > To remember: ALT = LIVER
- 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)
- Appears in plasma many days before clinical signs appear > Good marker in asymptomatic patients
- A normal value does not always indicate absence of liver damage
- Obese but otherwise normal individuals may have elevated ALT levels

- In chronic liver diseases sometimes AST & ALT are not found because they have short half life..=)
- ALT usually elevates in obese people.

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

γ-glutamyltransferase (GGT)

- Used for glutathione synthesis which is an antioxidant presents inside the cells
- 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

Alkaline phosphatase (ALP) & Prothrombin Time (PT)

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
- Modearte 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
- Not more done nowadays

Not specific because it increases in children and during pregnancy

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
- Dosage of vitamin K does not affect PT in liver disease

Prothrombin Time means The time it takes to clot the blood

PT prolonged because the liver not producing enough Prothrombin (loss in synthetic function)

ABCs for abnormal LFTs mnemonic

Causes of Elevated ALT or AST Values in Asymptomatic Patients*

A

Autoimmune hepatitis

B

Hepatitis B

C

Hepatitis C

D

Drugs or toxins

E

Ethanol

F

Fatty liver

G

Growths (i.e., tumors)

H

Hemodynamic disorder (congestive heart failure)

I

Iron (hemochromatosis), copper (Wilson's disease) or alpha1-antitrypsin deficiency

M

Muscle injury

For your Knowledge

Test your knowledge ..!

1) A 26 year old male comes to the clinic with a yellowish tinge to the eyes and skin and complains of abdominal pain, fatigue and weakness, liver function tests only shows mildly elevated bilirubin (mostly unconjugated) and the rest of the parameters were all normal. Which ONE of the following is the most likely diagnosis:

A. Blau syndrome
B. Gilbert's syndrome
C. Rotor syndrome
D. Dubin-Johnson syndrome

2) Increased conjugated biliribun is due to?

A. Post-hepatic
B. Pre-hepatic
C. Hepatic
D. (A&C)
E. (B&C)

3. **Which one of the following has a (very high absorbed) level in bone diseases** ?

A. Aspartate aminotransferase (AST)
B. Gamma-glutamyltransferase (GGT)
C. Urinary urobilinogen(UBG)
D. Alkaline phosphatase (ALP)

1) B
2) D
3) D
4) A

Biochemistry
Team

If you find any mistake, please contact us:)
Biochemistryteam@gmail.com

Biochemistry team leaders:
Basil AlSuwaine And Manar AlEid

Thank you