

Liver Function Tests

Classifications of LFTs

Markers of Liver Dysfunctions

Serum Bilirubin

Urine Bile Salt & UBG

Total Protein, Serum Albumin, A/G Ratio

PT

Markers of Hepatocellular Damage

ALT

AST

Markers of Cholestasis

Gamma glutamyltransferase (GTT)

Alkaline phosphatase (ALP)



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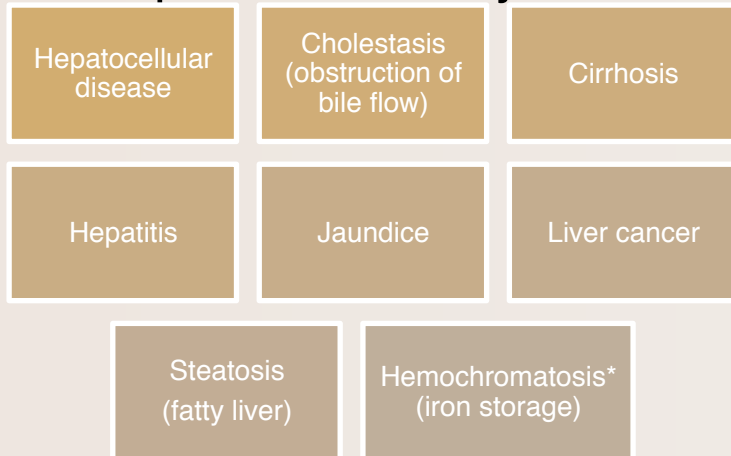
Liver Function Tests

- Noninvasive methods for screening of liver dysfunction
- Help in identifying general type of disorder
- Assess severity and allow prediction of outcome
- Disease and treatment follow up
- Broadly classified into
 - ❑ Tests to detect Hepatic Injury.
 - ❑ Tests to asses Hepatic Function.

Limitations:

- Normal LFT values don't always indicate absence of liver disease because the **Liver has very large reserve capacity**
- Asymptomatic people may have abnormal LFT results therefore, **diagnosis is based on clinical examination**

Examples of Liver Dysfunction



Major Metabolic Functions of the Liver

Synthetic Function

- Plasma Proteins (Albumin, Globulin), Cholesterol, TAGs and Lipoproteins

Detoxification & Excretion

- Urea Cycle, Bilirubin, Cholesterol, Drug Metabolites

Storage Function

- Vitamin A, D, E, K and B12

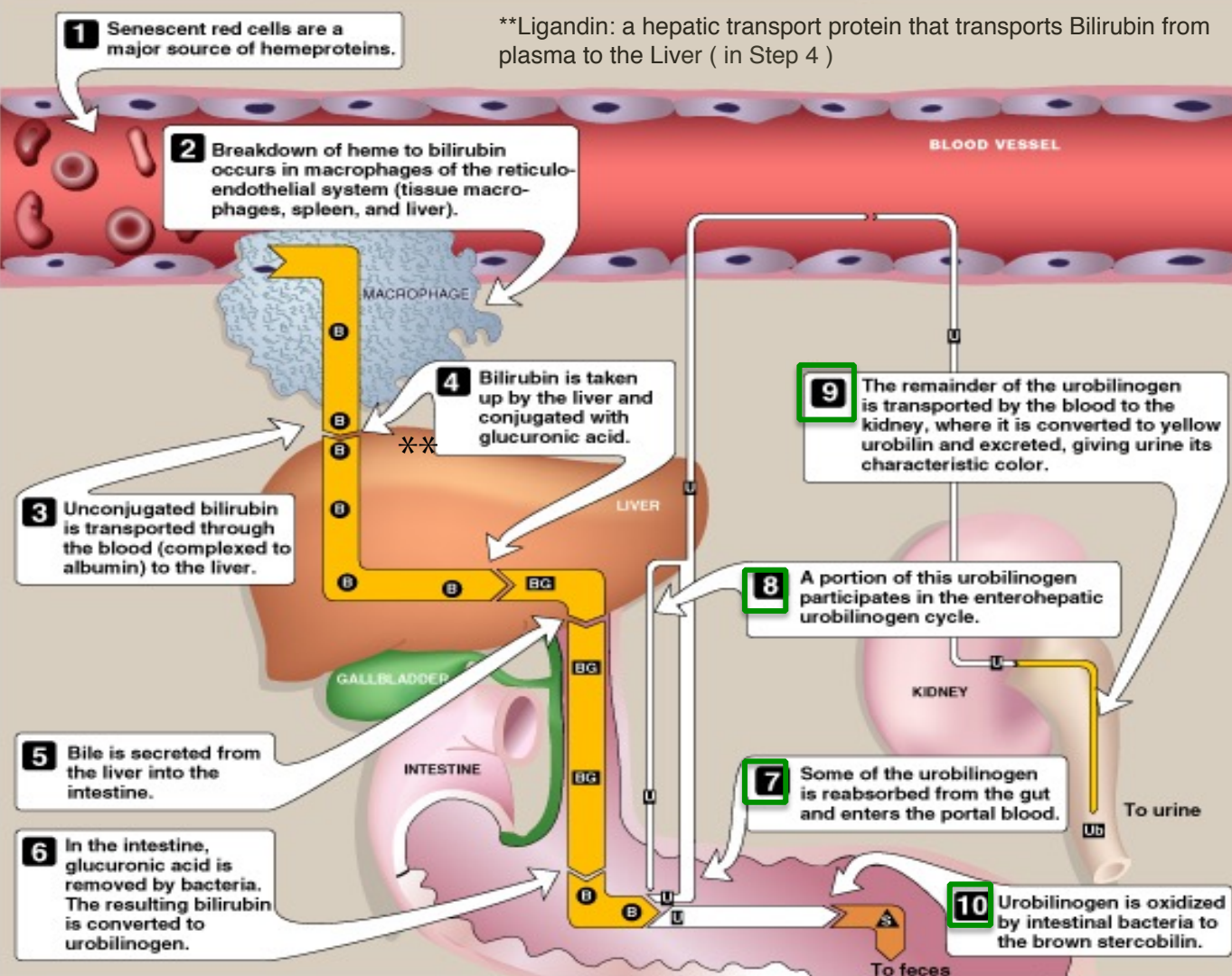
Production of Bile Salts

- Helps in Digestion

* Genetic Disorder

Note** if one enzyme is raised it doesn't mean that there is liver damage, more than one enzyme are required for accurate diagnosis of Liver Damage

Bilirubin



**Ligandin: a hepatic transport protein that transports Bilirubin from plasma to the Liver (in Step 4)

- A byproduct of RBC breakdown
- It is the yellowish pigment observed in Jaundice
- High levels in Gallstones, Acute and Chronic Hepatitis
- Normal → 0.2 - 0.8 mg/dL
- Unconjugated/Free/Indirect (bilirubin-albumin complex) → 0.2 - 0.7 mg/dL
- Conjugated/direct: 0.1- 0.4 mg/dL
- Latent Jaundice → > 1 mg/dL
- Jaundice → > 2 mg/dL

1. Hb (in senescent RBC) => (RES)
2. In RES (Heme) → bilirubin
3. Bilirubin-albumin complex => (blood) => Liver.
4. Bilirubin + glucuronic acid => Bile => Intestine
5. Bacteria removes Glucuronic acid => Bilirubin becomes unconjugated(free) & Bacteria convert it to Urobilinogen
6. 4 ways to consume Urobilinogen in Intestine. (Green-labeled)

=> Means (will be transported to)
 → Means (Will be converted to)

3. Occur in RES 4. Occur in Liver
 5. Occur in intestine

Urinary Urobilinogen & Urine Bile Salts

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

Prothrombin Time

- Prothrombin is a marker of liver function
 - Its half-life is 6 hrs. (indicates the current function of the liver)
 - Dosage of Vitamin K doesn't affect PT in Liver disease
- Causes of Prolonged PT:**
1. **Loss of >80% of Liver reserve capacity**
 2. **Vitamin K Deficiency**

Albumin

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

Globulin

- Normal serum levels: **2.5 - 3.5 g/dL**
- α & β globulins synthesized mainly by liver.
- Constitute Immunoglobulin (antibodies) produced by B cells.
- High serum γ -globulins in Chronic Hepatitis and Cirrhosis:
- **IgG in autoimmune hepatitis**
- **IgA in alcoholic liver disease**

A/G Ratio

Normal A/G ratio: **1.2/1 – 1.5/1**

Globulin levels increase in Hypoalbuminemia for compensation

Bilirubin levels & Jaundice

Class of Jaundice	Type of Bilirubin raised	Causes
Pre-hepatic or hemolytic	Unconjugated	Abnormal RBCs, Antibodies, Drugs & Toxins, Thalessemia, Hemoglobinopathies
Hepatic or Hepatocellular	Unconjugated & Conjugated	Viral Hepatitis, Toxic Hepatitis, Intrahepatic Cholestasis, Gilbert's, Crigler-Naajjar syndrome
Post-hepatic	Conjugated	Extrahepatic Cholestasis; Gallstones; Tumors of the Bile Duct, Carcinoma of Pancreas

PT: Time it takes for blood to clot ← From clotting factors in liver

Markers of Hepatocellular Injury

	Aspartate Aminotransferase (AST)	Alanine Aminotransferase (ALT) * <u>more Liver specific</u>	
Normal Range (U/L)	8 – 20	Female: 10 – 30	Male: 13 – 35
Change in Serum Level lead to:	High → Chronic Hepatitis Cirrhosis Liver Cancer	High (300-1000 U/L):	Acute Hepatitis
		Moderate (100-300U/L):	Alcoholic Hepatitis
		Minor (50-100U/L):	Cirrhosis Non-Alcoholic Steatohepatitis (NASH) Hepatitis C
		<u>Appear in plasma many days before clinical signs appear.</u> <u>Elevated in Obese but otherwise healthy individuals</u>	

Markers of Cholestasis

	γ- Glutamyltransferase (GGT)	Alkaline Phosphatase (ALP) * Not specific to Liver Disease	
Normal Range (U/L)	10 – 30	40 – 125	
Change in Serum Levels lead to:	Moderate → Infective Hepatitis Prostate Cancers *Note: <u>increased in Alcoholics even if LFTs is Normal.</u> → <u>Highly Sensitive in detecting alcohol abuse</u>	Very High	Bone Disease
		High	Extrahepatic Obstruction (Obstructive Jaundice), Cholestasis
		Moderate	Infective Hepatitis, Alcoholic Hepatitis, Hepatocellular Carcinoma
	Used for Glutathione Synthesis	Produced by Bone Osteoblasts (for bone calcification)	

- 1. Which ONE of the following is NOT a marker of Cholestasis :**
 - A. Alkaline phosphatase**
 - B. Gamma-Glutamyltransferase**
 - C. ALT**
 - D. 5'-Nucleotidase**
- 2. Which ONE of the following statements explain the fact that normal LFTs don't always indicate absence of liver disease ?**
 - A. The liver is the largest gland in the body**
 - B. LFTs aren't specific for liver function**
 - C. The liver has a large reserve capacity**
 - D. Because normal LFTs always correlate with normal abdominal examination**
- 3. Bilirubin leaves the liver in the form of :**
 - A. Free (unconjugated) bilirubin**
 - B. Bilirubin + Glucuronic acid**
 - C. Urobilinogen**
 - D. Urobilin**

- 4. Conversion of Heme into bilirubin takes place in :**
 - A. Kidneys**
 - B. Reticulo-endothelial system**
 - C. Beta cells of pancreas**
 - D. Hepatocytes.**
- 5. Which ONE of the following types of bilirubin will be raised in case of pre-hepatic jaundice:**
 - A. Conjugated bilirubin**
 - B. Unconjugated bilirubin**
 - C. Both (conjugated & Unconjugated) bilirubin**
 - D. All types will spike**
- 6. Where is Prothrombin synthesized?**
 - A. Liver**
 - B. Pancreas**
 - C. B Cells**
 - D. Kidney**

Answers: 1) C 2) C 3) B 4) B 5) B 6) A

7. **58-year old male presented with classical presentation of cancer. Following physical and lab examination, the diagnosis of pancreatic carcinoma was confirmed. Which ONE of the following markers is expected to be high in the patient's serum :**
- A. Pre-hepatic bilirubin
 - B. Post-hepatic bilirubin
 - C. Hepatic bilirubin
 - D. ALT
8. **The underlying cause of increased Globulin levels in patients with Hypoalbuminemia is:**
- A. Autoimmune reaction
 - B. Increased Osmotic pressure
 - C. Protective mechanism against infections
 - D. Compensatory mechanism
9. **Which ONE of the following markers is more liver- specific in cases of hepatocellular injury:**
- A. AST
 - B. Bilirubin
 - C. ALT
 - D. Prothrombin time

10. **In which ONE of the following conditions Prothrombin Time (PT) is increased?**
- A. Complete Liver resection
 - B. Infusion of Vitamin K
 - C. Vitamin K Deficiency
 - D. When liver loses about 10% of its reserve capacity.
11. **The best marker to determine if someone is drinking alcohol or not is :**
- A. ALT
 - B. Alkaline phosphatase
 - C. Gamma-glutamyltransferase
 - D. Beta-globulin



Thank You!

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