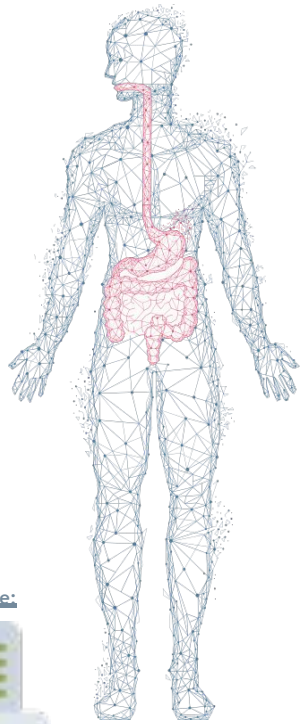
L12:

Liver function tests

GNT Block



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Editing file:

Objectives:

- 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.

Lecture presented by :

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Alila Medical Media Video
(3 min)

Dr Matt Video
(20 min)

Major metabolic functions of the liver

Synthetic function:	• endogenous 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_{12}
Production of bile salts	• Helps in digestion

Some examples of liver dysfunction

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

Liver function tests (LFTs)

Noninvasive methods for screening of liver dysfunction
or minimally invasive because we need to draw blood

Help in identifying general types of disorder

Assess severity and allow prediction of outcome

Disease and treatment follow up

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

Here we usually check synthetic & clearance functions

Group II: Markers of hepatocellular injury

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

Here we look for enzymes that are usually (inside) the cell, because when there is injury → it will be released out

Group III: Markers of cholestasis

- Alkaline phosphatase (**ALP**)
- γ-glutamyltransferase (**GGT**)

The epithelial cells of the bile canaliculi release these enzymes when they're damaged

Limitations Of LFTs

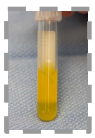
- Normal LFT values do not always indicate absence of liver disease
  - Liver a has very large reserve capacity
- Asymptomatic people may have abnormal LFT results
  - Diagnosis should be based on clinical examination

Common serum liver chemistry tests

Important

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

Bilirubin



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

Serum bilirubin levels: Dr. you need to know the values for the practical

- Normal
  - **0.2 - 0.8** mg/dL
  - Unconjugated (indirect): 0.2 – 0.7 mg/dL
  - Conjugated (direct): 0.1 – 0.4 mg/dL (When we do the lab test, we directly obtain both the conjugated and total values. This is why we refer to the conjugated as 'direct.' For the unconjugated value, we subtract the conjugated from the total.)
- Latent jaundice: no symptoms
  - Above 1 mg/dL
- Jaundice:
  - Above 2 mg/dL

Bilirubin levels & jaundice

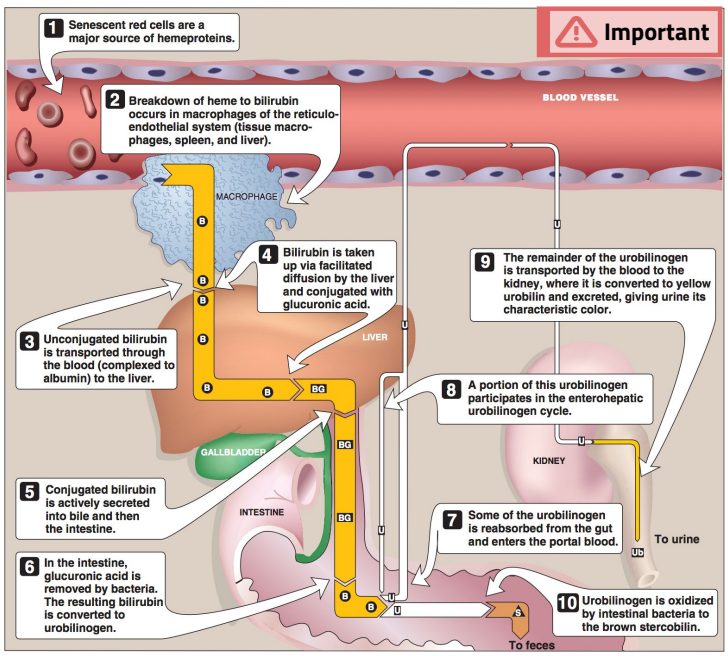
Class of Jaundice	Causes
Pre-hepatic or hemolytic (Unconjugated bilirubin)	**Abnormal red cells**; antibodies; drugs and toxins; thalassemia Hemoglobinopathies
Hepatic or Hepatocellular (Mix bilirubin)	Viral hepatitis, toxic hepatitis, intrahepatic cholestasis **Gilbert's, Crigler-Najjar syndrome**
Post-hepatic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

Metabolism of bilirubin

01. Rupture of RBCs lead to release of heme.
02. Heme is converted to biliverdin (Catalyzed by microsomal heme oxygenase) which is reduced to bilirubin.
03. bilirubin is complexed with albumin and released at entrance to the liver (unconjugated bilirubin).
04. Bilirubin is conjugated with UDP-glucuronic acid. (dr.Sumbul: the only enzyme name you have to memorize here is UDP-glucuronic transferase)
05. Conjugated bilirubin is secreted into bile and then into the intestine.
06. Bacteria utilize glucuronic acid so it remove it from bilirubin converting it into urobilinogen.

★ **Fate of urobilinogen:**

07. Some enter the portal circulation where:
08. Returns back to the liver.
09. filtered by the kidney as urobilin.
10. majority is excreted with feces as stercobilin (gives the feces its characteristic color).



Metabolism of bilirubin

Dr.sumbul questions on the picture

Important

Q1:If there's a problem at level of liver what kind of bilirubin you will find in circulation?

In severe cases you will find unconjugated bilirubin, because the liver is damaged and unable to conjugate it. In milder cases, both unconjugated and conjugated bilirubin may be present, because the liver in this case is doing it work but not in the perfect way.

Q2:if there is increase in RBCs breakdown for any reason what will happen ?

A lot of unconjugated bilirubin is present due to increased bilirubin production.

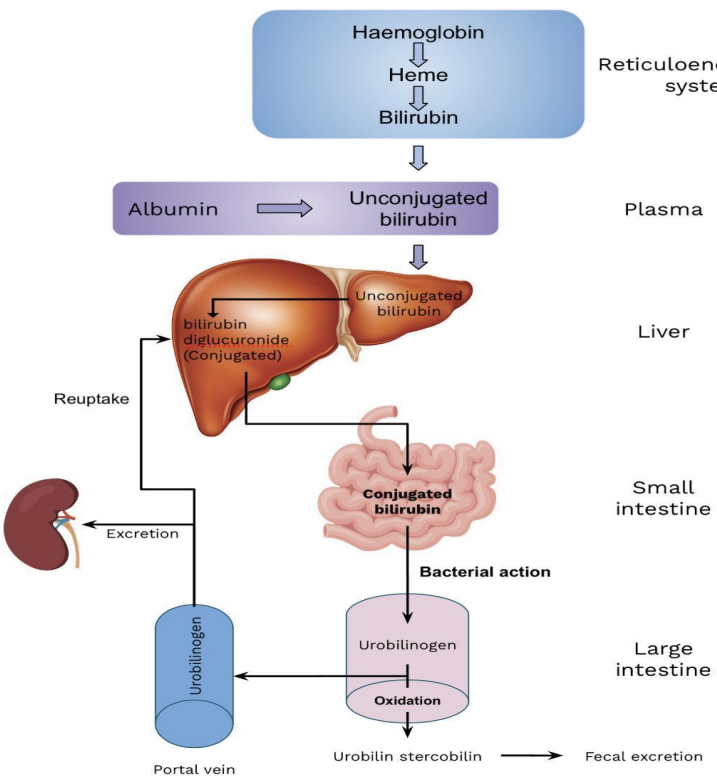
Q3:if the problem is after the liver like obstruction what will happen?

The liver functions properly so there will be an accumulation of conjugated bilirubin. Since bilirubin isn't reaching the intestines, pale stools occur and bilirubin leaks into blood reaching the kidneys resulting in dark urine.

Important

Conjugating enzyme: Uridine-Diphosphoglucuronic Glucuronosyltransferase (UDPGT)

Dr sumbul: it is enough to write it as UDP-glucuronic transferase



Markers of liver dysfunction

	Normal value No Need to memorize the numbers	Features	Disease	Notes
Urobilinogen	Most UBGs are metabolized in the large intestine (by bacteria) but a fraction is excreted in urine (less than 4 mg/day)	-	-	-
Bile salts	Normally bile salts are **NOT present in urine**	-	**Obstruction** in the biliary passages → Leakage of bile salts into circulation → **Excretion in urine**	-
Serum Albumin	3.5 - 5 g/dL (measured from serum)	-The most abundant protein synthesized by the liver. -its Synthesis depends on the extent of functioning liver cell mass. -Longer half-life: 20 days	Its levels **decrease in all chronic liver diseases.**	Albumin to globulin (A/G) ratio: -**Normal A/G ratio: 1.2/1 - 1.5/1** -hypoalbuminemia: Globulin levels increase as a compensation mainly γ because α and β are synthesized by the liver which is already damaged.
Serum Globulin	2.5 - 3.5g/dL (Normally less than albumin)	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.	
Prothrombin Time	-Specific to the liver -The difference between PT and albumin is that PT gives an idea about the acute function due to its short half-life	- synthesized by the liver, a **marker of liver function**. -Half-life: 6 hrs. (indicates the present function of the liver)	It 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

Markers for cholestasis

	Alkaline phosphatase (ALP)	ɣ Glutamyltransferase (GGT)
Normal value No Need to memorize them	40 - 125 U/L	10 - 30 U/L
Features	‣ Non-specific marker of liver disease. ‣ Produced by bone osteoblasts (for bone calcification). "Bone = ALP" ‣ Present on hepatocyte membrane. ‣ Enters biliary duct so elevation in case of obstruction.	‣ Used for glutathione synthesis ‣ **Highly sensitive to detecting alcohol abuse**; it is increased in alcoholics despite normal liver function tests. ‣ The most specific for alcoholic hepatitis More to less specific: GGT > ALT > ALP
Disease	‣ **Moderate elevations** observed: - infective hepatitis. - alcoholic hepatitis. - hepatocellular carcinoma. ‣ **High elevations** observed in: - Extrahepatic obstruction (obstructive jaundice). - Intrahepatic cholestasis. ‣ **Very high levels** observed in: - Bone diseases.	‣ **Moderate elevations** observed in: - Infective hepatitis. - Prostate cancers.

Markers for hepatocellular injury

	Aspartate aminotransferase (AST)	Alanine aminotransferase (ALT)
Normal value	8-20 U/L	‣ Male: **13-35** U/L. ‣ Female: **10-30** U/L.
Features	‣ Marker for hepatocellular damage. ‣ Less specific.	‣ **More liver-specific than AST.** ‣ 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. ‣ It's more specific to the liver and moderate elevation is seen in alcoholic hepatitis.
Disease	‣ **High serum levels** are observed in: - Chronic hepatitis. - Cirrhosis. - Liver cancer.	‣ **Minor elevations** (**50 - 100 U/L**): - Cirrhosis. - hepatitis C. - Non-alcoholic steatohepatitis (NASH). ‣ **Moderate elevations** (**100 - 300 U/L**): - alcoholic hepatitis. ‣ **High serum levels** (**300 - 1000 U/L**): - acute hepatitis.

443:
Dr: you need to know the ALT values for the Practical
Dr: Ranges for diseases of ALT are important

Quiz

MCQs

Q1: Which of the following is NOT a major metabolic function of the liver?
A- Synthesis of plasma proteins
B- Detoxification of ammonia
C- Storage of vitamins A, D, E, K,
D- Production of insulin

Q2: Which marker of liver function tests are most accurate diagnose hepatocellular injury?
A- Serum bilirubin
B- Prothrombin time
C- Alanine aminotransferase (ALT)
D- Alkaline phosphatase (ALP)

Q3: In liver dysfunction, which of the following markers is typically elevated in urine?
A- Serum albumin
B- Serum globulin
C- Prothrombin time
D- Bile salts

Q4: Which condition is characterized by the accumulation of excessive fat in the liver?
A- Cirrhosis
B- Hepatitis
C- Steatosis
D- Liver cancer

Q5: What is the normal range for serum bilirubin levels?
A- 0.1 - 0.4 mg/dL
B- 0.2 - 0.7 mg/dL
C- 0.2 - 0.8 mg/dL
D- Above 2 mg/dL

Q6: Which type of jaundice is caused by abnormal red cells or hemoglobinopathies?
A- Pre-hepatic
B- Hepatic
C- Post-hepatic jaundice
D- Latent jaundice

Answers: 1. D 2.C 3.D 4.C 5.C 6.A

SAQ

Q: Explain the role of serum bilirubin in diagnosing liver dysfunction and discuss the different types of jaundice based on bilirubin levels?

Answer: Serum bilirubin is a marker for liver dysfunction. Elevated levels indicate liver disease. Types of jaundice based on bilirubin levels include pre-hepatic (hemolytic), hepatocellular, and post-hepatic (obstructive) jaundice.

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