



LIVER FUNCTION TESTS AND THEIR CLINICAL INTERPRETATION

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INTRODUCTION

- Liver performs a multitude of functions
- The functions get deranged when liver is diseased
- Assessment of functional status of liver generally requires laboratory tests.

THE MULTIPLE FUNCTIONS OF THE LIVER INCLUDE:

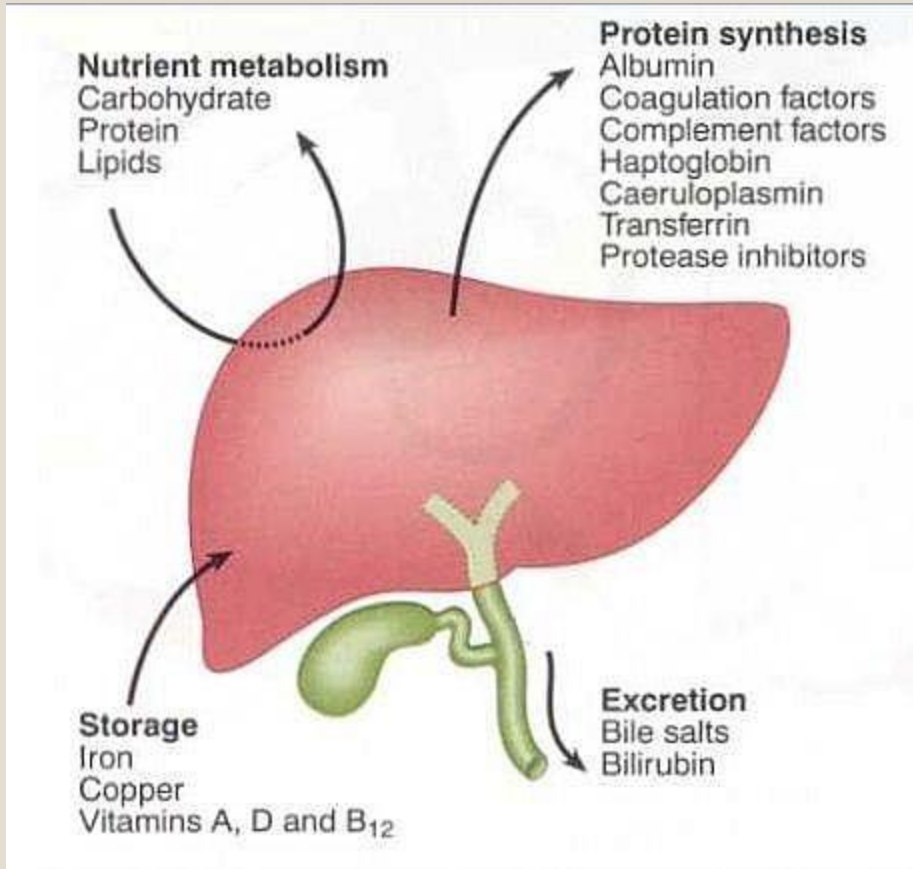
Metabolic functions

Synthetic functions

Excretory functions

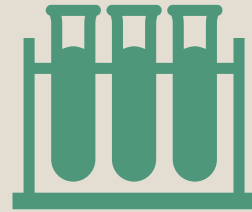
Detoxifying functions

Storage functions





Number of tests are required to assess hepatic functions

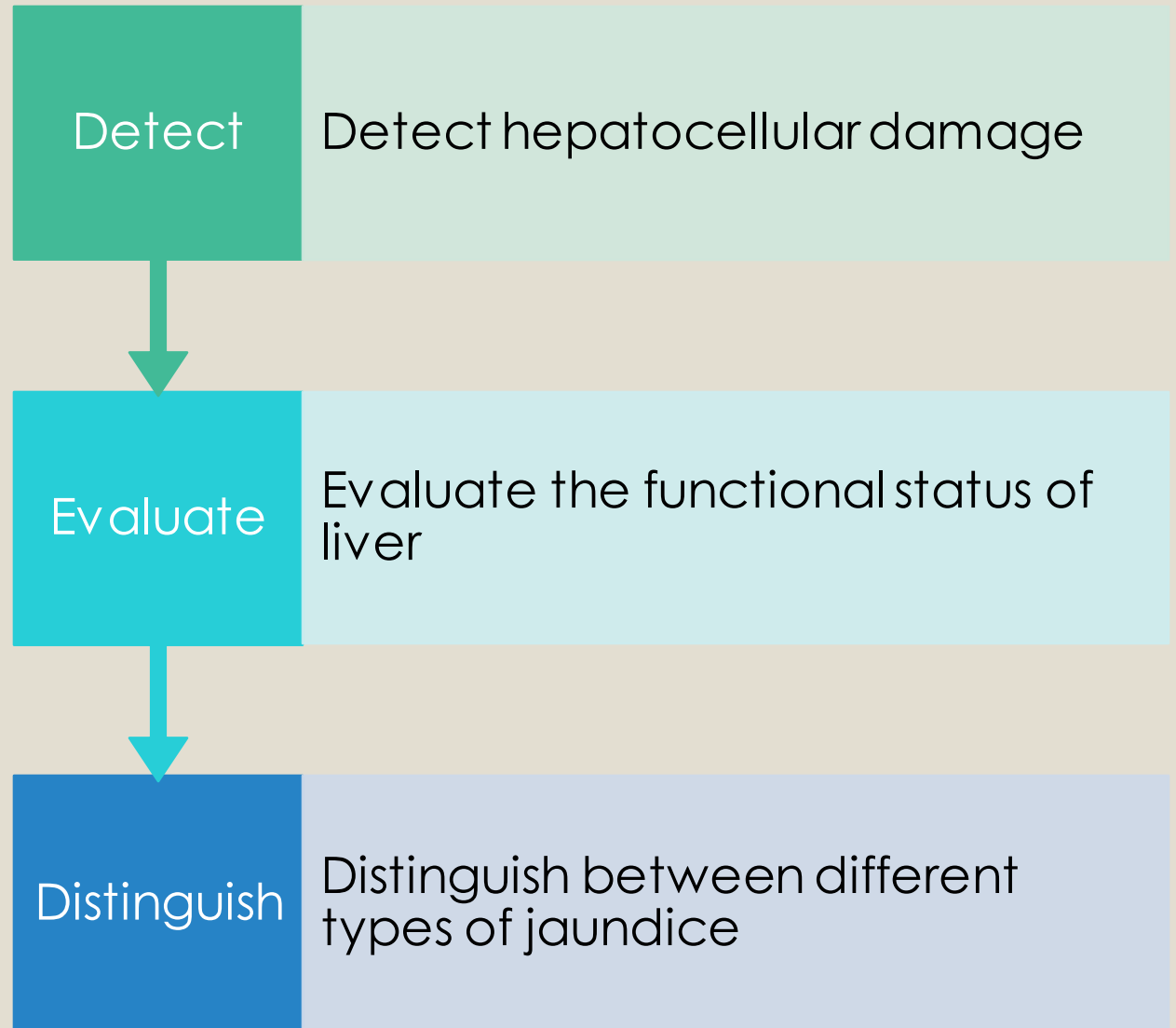


All the tests need not be performed in every patient.



The tests should be selected according to the symptoms and signs

LIVER
FUNCTION
TESTS ARE
PERFORMED
USUALLY TO





Many tests, used earlier are now obsolete such as;

- Icterus index
- Vanden Bergh test
- Thymol turbidity
- Zinc sulphate turbidity
- Cholesterol-cephalin flocculation
- Serum cholesterol : cholesterol ester ratio



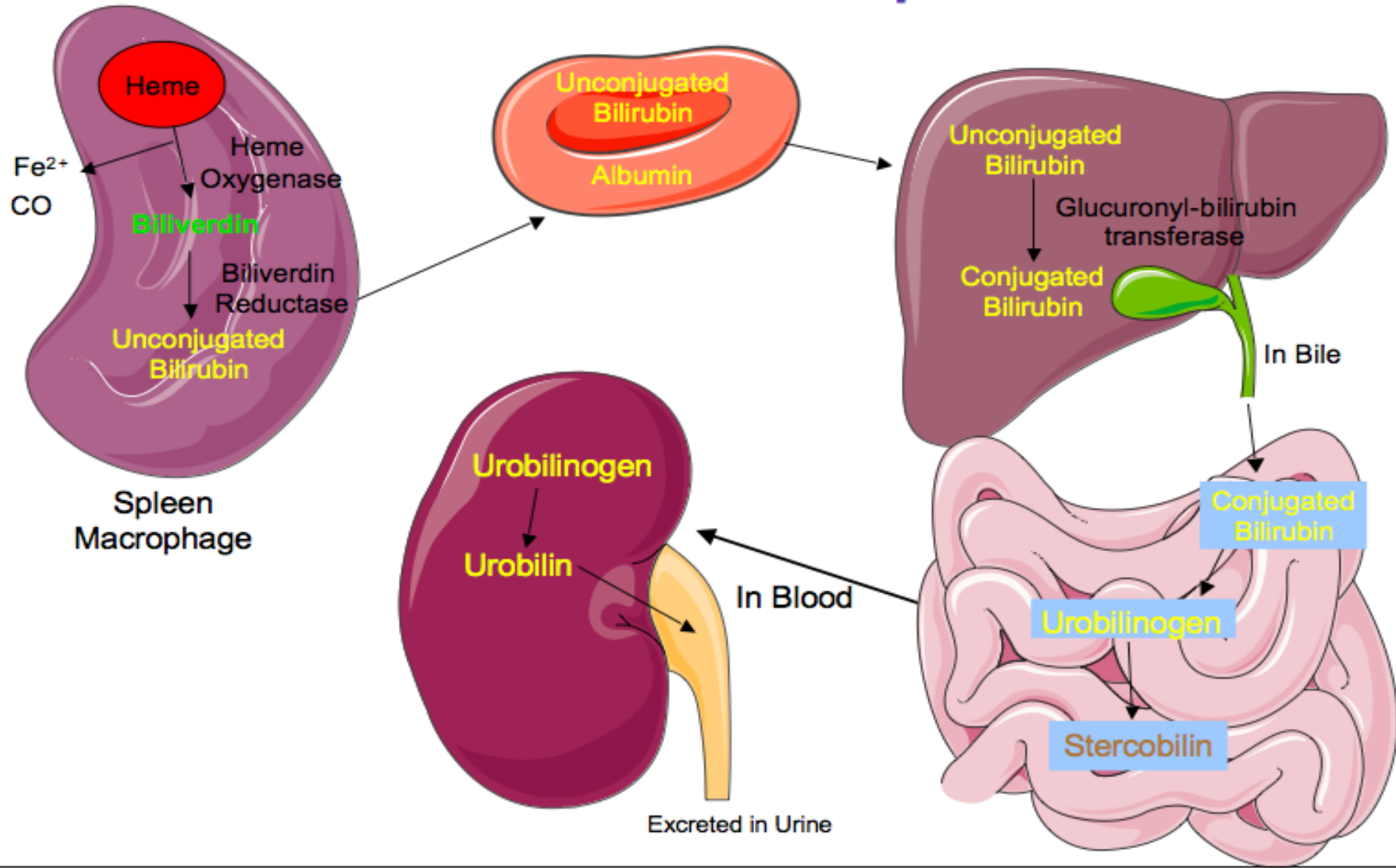
Liver functions tests commonly done now are,

- Serum bilirubin
- Bile pigments, bile salts and urobilinogen in urine.
- Serum proteins and albumin: globulin ratio
- Serum enzymes
- Prothrombin time

SERUM BILIRUBIN

- ❑ Bilirubin is formed from haem in reticuloendothelial cells
- ❑ It is conjugated with glucuronic acid in liver
- ❑ Conjugated bilirubin is excreted by liver in bile

Bilirubin Transport



Plasma bilirubin comprises unconjugated bilirubin and conjugated bilirubin

Normal concentration of bilirubin in plasma is:

Unconjugated:
0.1-0.6 mg /dl

Conjugated:
0.1-0.4 mg/dl

Total:
0.2-1.0mg/dl

- ❖ A rise in serum bilirubin above 2mg/dl leads to yellow staining of tissues.
- ❖ The yellow staining is usually first seen in sclera
- ❖ This yellow staining is known as jaundice



JAUNDICE MAY BE :

Haemolytic (prehepatic)

hemolytic

Anemia

Hemoglobinopathy,

Mismatched blood
transfusion

Hepatocellular (hepatic)

Alcoholic hepatitis,

Viral hepatitis,

Drug induced intra
hepatic cholestasis

Obstructive (post-hepatic)

Biliary duct
obstruction due to
gall stones, tumor in
bile duct,
carcinoma head of
pancreas, lymph
node enlarged in
porta hepatis

Inborn errors

- ❑ **Gilbert syndrome** : is the most common hereditary cause of increased bilirubin
- ❑ It is characterised by elevated levels of unconjugated bilirubin in the bloodstream
- ❑ Enzyme glucuronyl transferase deficiency
- ❑ **Crigler Najjar syndrome** : rare, AR disorder with high levels of unconjugated hyperbilirubinemia affecting brain
- ❑ UDP- glucuronyl transferase enzyme is defective.
- ❑ **Dubin Johnson syndrome** : AR disorder, increased conjugated bilirubin in the serum without elevation of liver enzymes (ALT, AST)
- ❑ Defective secretion of conjugated bilirubin into the bile. Liver cells **are pigmented**
- ❑ **Rotor syndrome**: Rare, AR disorder with increase in conjugated bilirubin
- ❑ Similar to Dubin Johnson syndrome except that the liver cell are **not pigmented**

Measurement of total, unconjugated and conjugated bilirubin in serum helps in:

- Detection of jaundice
- Distinction between different types of jaundice

- in **haemolytic jaundice**, total and unconjugated bilirubin are raised
- In **hepatocellular jaundice**, total, unconjugated and conjugated bilirubin are raised
- In **obstructive jaundice**, total and conjugated bilirubin are raised

- Bilirubin is the major bile pigment in human beings
- Normally it is not present in urine
- Only conjugated bilirubin is soluble in water and can be excreted in urine
- Conjugated bilirubin in serum is raised in hepatocellular and obstructive jaundice
- Therefore, bilirubin is present in urine, in hepatocellular and obstructive jaundice

Bile pigments
in urine

- ❖ Urobilinogen is formed from bilirubin in the intestine
- ❖ It is absorbed into portal circulation and is mostly re-excreted by the liver in bile
- ❖ Some of it escapes from liver into systemic circulation and is excreted in urine
- ❖ Normal urine contains a very small amount of urobilinogen

UROBILINOGEN IN URINE

In haemolytic jaundice, formation of bilirubin is increased

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graph TD; A[In haemolytic jaundice, formation of bilirubin is increased] --> B[Hence, there is increased formation of urobilinogen]; B --> C[Consequently, urinary urobilinogen is increased];
```

Hence, there is increased formation of urobilinogen

Consequently, urinary urobilinogen is increased

In obstructive jaundice, bilirubin doesn't reach the intestine

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graph TD; A[In obstructive jaundice, bilirubin doesn't reach the intestine] --> B[Hence, no urobilinogen is formed in the intestine]; B --> C[Therefore, no urobilinogen is present in urine];
```

Hence, no urobilinogen is formed in the intestine

Therefore, no urobilinogen is present in urine

In hepatocellular jaundice, urinary urobilinogen is:

Normal or

decreased

BILE SALTS IN URINE

- ❖ Bile salts are formed in the liver from cholesterol
- ❖ They are excreted in bile

- ❖ In **obstructive jaundice**, bile salts cannot reach intestine due to biliary obstruction
- ❖ They are regurgitated from liver into systemic circulation
- ❖ Since they are water-soluble, they are excreted in urine

❖ In **hepatocellular jaundice**, swollen liver cells compress biliary canaliculi

❖ Hence, there is intrahepatic obstruction of biliary canaliculi

❖ Bile salts cannot reach intestine and appear in urine.

❖ In **haemolytic jaundice** there is no obstruction to the flow of bile

❖ Therefore, the bile salts are not present in urine

	Hemolytic jaundice	Hepatic jaundice	Obstructive jaundice
SERUM BILIRUBIN (TOTAL)	Raised	Raised	Raised
SERUM BILIRUBIN (UNCONJUGATED)	Raised	Raised	Normal
SERUM BILIRUBIN (CONJUGATED)	Normal	Raised	Raised
BILE PIGMENTS IN URINE	Absent	Present	Present
UROBILINOGEN IN URINE	Raised	Normal or decreased	Absent
BILE SALTS IN URINE	Absent	Present	Present

SERUM PROTEINS AND ALBUMIN : GLOBULIN RATIO

Liver is the only site of albumin synthesis

Albumin synthesis decreases in liver diseases like cirrhosis

Hence, serum albumin level is decreased (normal 3.5-4.5 gm/dl)

Globulin synthesis may be increased, specially in infective diseases (normal 2.5-3.5gm/dl)

So, the albumin : globulin ratio in serum is decreased or reversed in liver disease

However, this may happen in some non hepatic diseases also

- In viral hepatitis, there is acute necrosis of liver cells
- Enzymes present in hepatic cells are released in blood
- This raises the concentration of several enzymes in serum

SERUM ENZYMES

The following serum enzymes are raised in viral hepatitis

Glutamate oxaloacetate transaminase (SGOT)

Glutamine pyruvate transaminase (SGPT)

Lactate dehydrogenase (LDH)

- The rise in SGPT is generally greater than that in SGOT in liver disease
- Determination of isoenzymes of LDH may be more informative than that of total LDH
- Serum gamma glutamyl transferase (GGT) is increased in many liver diseases.
- Rise in serum GGT is a sensitive indicator of alcoholic hepatitis
- 5'-Nucleotidase is also raised in many diseases
- Alkaline phosphatase (ALP) is synthesized by parenchymal cells as well as epithelial cells of biliary canaliculi

PROTHROMBIN TIME



Prothrombin is synthesized in liver



Prothrombin synthesis is decreased in hepato-cellular disease



This leads to a decrease in prothrombin concentration in plasma which prolongs prothrombin time (normal 10-14 sec)



Newly synthesized prothrombin is inactive



It becomes active only after some post translational modification

- Vitamin K is required for the post translational modification
- Hence prothrombin time is prolonged in vitamin K deficiency also
- Injection of vitamin K restores the prothrombin time in vitamin K deficiency but not in hepatocellular disease

◦ Some uncommon liver functions tests done in special situations are:

- Galactose tolerance test
- Hippuric acid test
- Bromsulphthalein test
- Anti-mitochondrial antibody test
- Anti-smooth muscle antibody test
- Blood ammonia

GALACTOSE TOLERANCE TEST

- Liver converts the dietary galactose into glucose
- Capacity of liver to convert galactose into glucose is decreased in liver disease
- So, blood galactose remains elevated for along time after ingestion of galactose
- Oral galactose tolerance test is preferable and is done after overnight fasting
- Forty gm of galactose dissolved in water, is given by mouth to the subject
- Blood galactose is measured 60 minutes later
- A blood galactose level above 60mg /dl indicates impairment of hepatic functions

HIPPURIC ACID TEST

- This is a test of conjugating function of liver
- Benzoic acid is given to the subject
- Liver conjugates benzoic acid with glycine to form hippuric acid.
- Hippuric acid is excreted in urine
- If liver function is normal, all the benzoic acid is conjugated to form hippuric acid
- All the hippuric acid is excreted in urine
- If liver function is impaired, formation and excretion of hippuric acid is decreased

- Hippuric acid test may be done orally or intravenously
- The oral test is done after an overnight fast or 2-3 hours after light breakfast
- The subject is asked to void and is given 6gm of sodium benzoate dissolved in water
- The urine passed over the next four hours is collected
- The total amount of hippuric acid present in urine is measured
- Excretion of less than 4 gm of hippuric acid shows impairment of hepatic function

- In the intravenous hippuric acid test, the subject is asked to void
- 1.77 gm of sodium benzoate dissolved in 2 ml of water is injected intravenously
- The urine passed over the next one hour is collected
- Total hippuric acid present in urine is measured
- Excretion of less than 0.8 gm of hippuric acid shows impairment of hepatic function

BROMSULPHTHALEIN (BSP) TEST

- BSP dye (5mg/kg 5%w/w solution) is injected intravenously in this test
- It is conjugated in the liver and is excreted in bile
- BROMSULPHTHALEIN (BSP) is a dye which is taken up from circulation by liver
- Rate of removal of BSP from blood is a sensitive indicator of hepatobiliary function
- BSP test is done after overnight fasting

- 5% BSP solution is injected intravenously in the dose of 5mg /kg body weight
- Blood samples are collected 3 and 45 minutes after the injection
- BSP level is measured in both the blood samples
- If the level at 45 minutes is more than 6% of the level at 3 minutes, it indicates impairment of hepatic –biliary functions

- Detection of anti-mitochondrial antibody helps in the diagnosis of primary biliary cirrhosis
- Detection of anti-nuclear and / or anti smooth muscle antibodies helps in the diagnosis of autoimmune hepatitis

IMMUNOLOGICAL TESTS

BLOOD AMMONIA

- In advanced liver disease, liver may fail to convert ammonia into urea
- This can cause hepatic encephalopathy
- Measurement of blood ammonia helps in its diagnosis and monitoring



Thank you!

The text "Thank you!" is written in a black, cursive font. It is surrounded by several gold stars of varying sizes and a thick, gold brushstroke underline that curves under the text.