

FUNCTIONAL EXPLORATION OF THE LIVER

The liver is located in the upper right-hand portion of the abdominal cavity, beneath the diaphragm, and on top of the stomach, right kidney and intestines. The liver consists of two main lobes, both of which are made up of thousands of lobules. These lobules are connected to small ducts that connect with larger ducts to ultimately form the hepatic duct. The hepatic duct transports the bile produced by the liver cells to the gallbladder and duodenum (the first part of the small intestine).

The liver regulates most chemical levels in the blood and excretes bile, which helps carry away waste products from the liver. All the blood leaving the stomach and intestines passes through the liver. The liver processes this blood and breaks down the nutrients and drugs into forms that are easier to use for the rest of the body. More than 500 vital functions have been identified with the liver. The most important functions include the following:

- Production of bile, which helps carry away waste and break down fats in the small intestine during digestion
- Production of certain proteins for blood plasma
- Production of cholesterol and special proteins to help carry fats through the body
- Conversion of excess glucose into glycogen for storage (glycogen can later be converted back to glucose for energy)
- Regulation of blood levels of amino acids, which form the building blocks of proteins
- Processing of hemoglobin for use of its iron content (the liver stores iron)
- Conversion of poisonous ammonia to urea (urea is an end product of protein metabolism and is excreted in the urine)
- Clearing the blood of drugs and other poisonous substances
- Regulating blood clotting
- Resisting infections by producing immune factors and removing bacteria from the bloodstream.

The liver may be affected by many factors: infections, toxins, ischemia, drugs, and autoimmune diseases. All these factors determine lesions and functional degeneration of hepatocytes followed by symptoms or/and changes in hepatic tests. These changes reflect the intensity and complexity of certain lesions. The liver can lose three-quarters of its cells before it stops functioning. In addition, the liver is the only organ in the body that can regenerate itself. Most diseases that affect the liver show very mild symptoms in the initial phases and it is important for you to get tested for these diseases before the symptoms get worse or unmanageable. These tests can also distinguish between acute and chronic liver disorders and between hepatitis and cholestasis.

1. Exploration of hepatic cell necrosis syndrome

Hepatic cytolysis syndrome represents the disturbance in membrane function due to hepatic cells injuries (replacement of active transport with passive diffusion and increased cell permeability). The following enzymes are released into the blood in greater amounts.

Alanine aminotransferase (ALT) is a cytoplasmic enzyme, present mostly in liver, but also in the heart and muscles. Its concentration is bigger in liver; therefore a plasma increase is more specific for hepatic diseases than AST increase.

Aspartate aminotransferase (AST) is a mitochondrial enzyme that can be found in the liver, kidneys, pancreas, heart, skeletal muscle, and red blood cells. Acute tissue destruction releases the enzyme from the cells leading to an increased plasma level.

Normal values: 0-35 IU/L.

Increased values of ALT and AST: liver diseases (acute hepatitis, intoxications, ischemia, hepatic steatosis), cholestasis (choledocholithiasis), alcohol abuse, myocardial infarction heart failure, muscle diseases. Early increasing of transaminases in acute hepatitis is proportional to tissue destruction intensity, without having a prognostic significance. Their value can increase up to 100

fold. In chronic liver disease transaminases can be normal or elevated (only in acute episodes). Normal values in advanced cirrhosis are due to increased liver fibrosis.

AST/ALT ratio is called Ritis index and has a normal value of 1.3. Values over 2 suggest hepatitis and alcoholic cirrhosis.

Glutamatedehydrogenase is a mitochondrial enzyme, involved in urea synthesis. Normal values: below 1, 5 mIU/ml. Increased values: severe acute hepatitis, acute episodes of chronic hepatitis and cirrhosis, biliary duct obstructions.

Lactatdehydrogenase (LDH) transforms lactic acid in piruvic acid. There are five known isoenzymes, number 5 being characteristic to the liver. Normal values: 100 -190 IU/L. Increased values for LDH 5: acute hepatitis, chronic hepatitis, cirrhosis, liver cancer.

2. Cholestasis syndrome evaluation

Cholestasis syndrome is defined as disturbances in biliary function of the liver and it can be intrahepatic or extra hepatic. It is characterized by increased values of the above mentioned enzymes associated with elevated conjugated bilirubin.

- Alkaline phosphatase (AP) hydrolyses phosphoric acid esters. It has three permanent isoenzymes: liver, bone and intestinal, and a temporary one during pregnancy. The liver isoenzyme is involved in transports from the biliary and sinusoidal pole of hepatocytes and biliary ducts. Normal values: 30-120 IU/L. The levels of ALP in plasma are high when there is a large obstruction of the bile duct, infiltrative diseases of the liver or intrahepatic cholestasis.
- Gamaglutamiltranspeptidase (GGT) is a microsomal enzyme nonspecific for the liver (produced in the liver, pancreas, and biliary tract). Normal values: 1-94 IU/L. Increased values: cholestasis, alcohol abuse, pancreatic diseases, and diabetes mellitus.
- Cholinesterase is a ribosomal enzyme, with several isoenzymes, nonspecific for the liver. Normal values: 5-12 IU/ml. Decreased values: acute and chronic hepatitis, cirrhosis, malnutrition.

3. Exploration of excrete-biliary function of the liver

Bile is the secretion product of the hepatocytes. It is continuously produced and collected into the gallbladder between meals. The main bile components are: water, mucin, biliary pigments, biliary salts, lecithin and cholesterol. Bilirubin is the main biliary pigment, generated from hem degradation (a non-protein group that contains iron and belongs to hem proteins). Hem proteins represent a class of proteins involved in oxygen transport and metabolism (i.e. Hemoglobin and mioglobin). 70 to 90% of bilirubin comes from red blood cells hemoglobin, destroyed in the reticule-endothelial system (spleen, liver and bone marrow). The difference up to 100% comes from the degradation of myoglobin, P- 450 cytochrome, catalase and peroxidase especially in the liver and also from inefficient erythropoiesis. The generated bilirubin is called unconjugated, is not soluble in water and transported in plasma bonded to albumin. Unconjugated bilirubin enters the hepatocyte through facilitated diffusion, and then it is conjugated with glucuronic acid resulting conjugated bilirubin. It is water soluble and is excreted in the bile. In the large intestine under the influence of bacteria conjugated bilirubin is transformed in urobilinogen (UBG), 20% of it being reabsorbed in blood. A part of urobilinogen is eliminated in urine by kidney filtration and the other part reaches the liver from where it will be excreted into the bile. Unabsorbed UBG (80%) will be eliminated into the faeces as stercobilin.

Plasma concentration of bilirubin is determined through van den Bergh reaction. Bilirubin that directly reacts is the conjugated bilirubin, the difference being represented by the indirect fraction (unconjugated bilirubin). The total amount of bilirubin is called total bilirubin.

Normal values:

Total Bilirubin	0, 3-1 mg %
Conjugated Bilirubin (CB)	0, 1-0, 3 mg %
Unconjugated Bilirubin (UB)	0, 2-0,7 mg %

4. Exploration of metabolic function of the liver

1. Metabolism of proteins

Liver maintains the normal plasma concentration of proteins through de novo synthesis of proteins from amino acids and by food and tissue proteins metabolism. A decrease in proteins plasma level signs a decrease of liver function. Evaluation of liver function in proteins metabolism is realized through the following determinations:

- Total serum proteins (NV: 55 - 80 g/l)

Plasma proteins types:

Albumins 35 - 55 g/l

Globulins 20 - 35 g/l

Fibrinogen 2 - 4 g/l in chronic liver disease, cirrhosis

- Prothrombin time (PT) test. The prothrombin time test measures how long it takes for blood to clot. Blood clotting requires vitamin K and a protein that is made by the liver. Prolonged clotting may indicate liver disease or other deficiencies in specific clotting factors. NV: 11.1-13.1 sec. It increases in cirrhosis.

2. Metabolism of lipids

Liver has an essential role in cholesterol metabolism, in biliary acids synthesis, but also in the metabolism of triglycerides, phospholipids and lipoproteins. The following tests are used:

Test	Normal values	Increase in:	Decrease in:
Total cholesterol	<200 mg%	cholestasis , PBC, steatosis	cirrhosis
Triglycerides	<150 mg%	cholestasis, hepatitis	cirrhosis
LDL cholesterol	<115 mg%	cholestasis	cirrhosis
HDL cholesterol			cirrhosis
women	>40 mg%		
men	> 50 mg%		

3. Carbohydrates metabolism

a) Blood glucose (NV:70-110 mg%). Its blood level decreases in cirrhosis due to increased tissue degradation of glucose as source of energy.

b) Oral glucose tolerance test (OGTT). 75 g of glucose is administered, a jeun, in 250 ml of water and after 2 hours we determine the blood glucose. The test is modified (>140 mg %) in cirrhosis due to the decreased capacity of liver to regulate glucose homeostasis.

Other tests include disease specific markers: viral hepatitis serology, Iron studies, ceruloplasmin (Wilson's disease), and alpha-1 antitrypsin.