# LIVER BIOCHEMISTRY. NEUTRALIZATION OF TOXIC SUBSTANCES IN THE BODY. THE ROLE OF THE LIVER IN METABOLISM

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***Abstract.*** *The liver is the largest parenchymal organ. It performs a number of key functions in the body. Accepts and distributes substances entering the body from the digestive tract, which are brought with blood through the portal vein. These substances penetrate into hepatocytes, undergo chemical transformations and, in the form of intermediate or final metabolites, enter the blood and are carried to other organs and tissues. It serves as a place of bile formation. Synthesizes substances that are used in other tissues. Inactivates exogenous and endogenous toxic substances, as well as hormones.*

***Keywords:*** *metabolites, foreign substances in the liver, conjugations in the liver, carbohydrates, lipids, proteins, heme, jaundice.*

Different diverse functions are due to the peculiarities of the structure of the liver and its individual cells. The hepatocyte has a well-developed endoplasmic reticulum (ER) system, both smooth and rough. One of the main functions of ER is the synthesis of proteins that are used by other organs and tissues (albumins), or enzymes that work in the liver. In addition, phospholipids, triglycerides and cholesterol are synthesized in the ER. Smooth ER contains xenobiotic detoxification enzymes.

The role of the liver in carbohydrate metabolism. The liver plays a leading role in maintaining the physiological concentration of glucose in the blood. Of the total amount of glucose coming from the intestine, the liver extracts most of it and spends: 10-15% of this amount on glycogen synthesis, 60% on oxidative decomposition, 30% on fatty acid synthesis. With physiological hypoglycemia, glycogen breakdown is activated in the liver. The first stage of this process is the cleavage of the glucose molecule and its phosphorylation (enzyme phosphorylase). Further, Glu-5-F can be spent in three directions:

1. along the path of glycolysis with the formation of pyruvic acid and lactate;
2. by the pentose phosphate pathway;
3. split under the action of phosphatase into glucose and phosphorus.

The latter pathway prevails, which leads to the release of free glucose into the general bloodstream.

Gluconeogenesis is active in the liver, in which glucose precursors are pyruvate and alanine (coming from muscles), glycerol - from adipose tissue and a number of glucogenic substances with food. Excessive intake of glucose from food increases the intensity of all the ways of its transformation in the hepatocyte. This activates its oxidation with the formation of a large amount of pyruvate. For its further oxidation, a large amount of CoA is also needed, which is also used for

the oxidation of fatty acids. As a result, the oxidation of fatty acids and the breakdown of lipids in fat depots slows down.

Lipid metabolism. Bile acids are synthesized in the liver, with a deficiency of which fat digestion practically does not occur. The leading role belongs to the regulation of liver lipid metabolism. Thus, with a deficiency of the main energy material - glucose, fatty acid oxidation is activated in the liver. In conditions of excess glucose in hepatocytes, triglycerides and phospholipids are synthesized from fatty acids that enter the liver from the intestine. The liver plays a leading role in the regulation of cholesterol metabolism. The starting substance in its synthesis is acetyl-CoA. I.e. Excessive nutrition stimulates the formation of cholesterol. Transport forms of lipoproteins are synthesized in the liver. In addition, ketone bodies are synthesized in the liver, in particular acetoacetate and hydroxybutyric acid, which are carried by blood throughout the body. The heart muscle and the cortical layer of the adrenal glands prefer to use these compounds as an energy source, rather than glucose.

Protein metabolism. The liver uses the AK coming from the digestive tract to synthesize its own proteins, but most of them go to the synthesis of plasma proteins. Fibrinogen, albumins, a- and b-globulins, lipoproteins are synthesized in the liver. The liver also synthesizes the so-called labile reserve protein, which is like a stock of AK, which can then be used by various organs and tissues as needed. The liver occupies a central place in the exchange of AK, because the processes of their chemical modification are actively taking place in it. In addition, it is in the liver that the synthesis of urea occurs.

Stages of neutralization of substances in the liver:

1. increasing the hydrophilicity of foreign substances. It includes reactions of their hydrolysis, oxidation, hydroxylation, reduction, etc. The most frequent modification of a hydrophobic substance at stage 1 is hydroxylation.

2. conjugation of unchanged or chemically modified substances at stage 1 with a number of metabolites.

Detoxification of toxic metabolites and foreign compounds (xenobiotics) occurs in hepatocytes in two stages. The reactions of the first stage are catalyzed by a monooxygenase system, the components of which are embedded in the membranes of the endoplasmic reticulum. Oxidation, reduction or hydrolysis reactions are the first stage in the system of excretion of hydrophobic molecules from the body. They convert substances into polar water-soluble metabolites.

The main enzyme is cytochrome P-450 hemoprotein. To date, many isoforms of this enzyme have been identified and assigned, depending on their properties and functions performed, to several families. 13 subfamilies of cx P-450 have been identified in mammals, it is conventionally believed that enzymes of the I-IV family participate in the biotransformation of xenobiotics, the rest metabolize endogenous compounds (steroid hormones, prostataglandins, fatty acids, etc.). An important property of cx P-450 is the ability to induce under the action of exogenous substrates, which formed the basis for the classification of isoforms depending on the inducibility of a particular chemical structure by a substance. At the first stage of biotransformation, the formation or release of hydroxy, carboxyl, thiol and amino groups occurs, which are hydrophilic, and the molecule can undergo further transformation and excretion from the body. NADPH is used as a coenzyme. In addition to cx P-450, cx b5 and cytochrome reductase participate in the first stage of biotransformation.

Many medicinal substances, entering the body, turn into active forms at the first stage of biotransformation and have the necessary therapeutic effect. But often a number of xenobiotics are not detoxified, but on the contrary are toxified with the participation of the monooxygenase system and become more reactive. The metabolic products of foreign substances formed at the first stage of biotransformation are further detoxified by a series of reactions of the second stage. The compounds formed in this case are less polar and, therefore, are easily removed from the cells. The zonality of the metabolic complexes of the liver, the main organ of maintaining chemical homeostasis, determines the difference in the enzyme composition between hepatocytes of the perivenous (central) and periportal (peripheral) zones of acinus. This is due to their unequal oxygen demand of different enzyme systems. Thus, the highest concentration of CTK enzymes, amino and fatty acid catabolism, urea cycle, gluconeogenesis was noted in the periportal zone receiving more oxygenated blood. Since the components of the reactions of the second phase of biotransformation are localized in the cells of this acinus zone, they are more protected from the action of toxic products. Glycolysis and the first stage of xenobiotic biotransformation are more active in hepatocytes of the pericentral zone. When liver cells are damaged, there is a communication between the bile ducts, blood and lymph vessels, through which bile enters the blood and partially into the biliary tract. Edema of the periportal space can also contribute to the reabsorption of bile from the bile ducts into the blood. Swollen cells squeeze the bile ducts, creating a mechanical obstruction to the outflow of bile. The metabolism and functions of liver cells are disrupted. With hepatocellular and cholestatic varieties of hepatic jaundice, the excretion of conjugated bilirubin into the bile sharply decreases, and it enters the blood from pathologically altered hepatocytes, direct hyperbilirubinemia occurs. At the same time, the level of free bilirubin increases in the blood — indirect hyperbilirubinemia, which is associated with a decrease in such functions of the hepatocyte as capture, intracellular transport of free bilirubin and its binding to glucuronides. The ingestion of bile acids into the blood along with bile causes the development of cholemic syndrome. A decrease in the flow of bile into the intestine (hypocholia, acholia) leads to a decrease in the formation of bilirubin metabolites and their excretion with feces and urine (traces of sterkobilin), as well as the appearance of symptoms of acholic syndrome.

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