



Blood is the liquid internal environment of the body. The total blood volume of an adult is 5-6 liters. Blood consists of a liquid part-plasma, which makes up 55% of its total volume, and shaped elements, which include red blood cells, white blood cells and platelets.

Thanks to the work of the heart, blood circulates through a closed system of blood vessels and carries out the transport of various chemicals.

It transfers oxygen from the lungs to the tissues and carbon dioxide from the tissues to the lungs as part of red blood cell hemoglobin (respiratory function);

-delivers food digestion products from the intestines to the tissues (trophic function);

-carries the final products of metabolism from the tissues to the excretory organs (excretory function);

- moves intermediate metabolic products, the synthesis and use of which occurs in different organs.

Blood participates in the regulation of metabolism, delivering signal molecules from the organs of internal secretion to the target tissues.

The protective function of blood has two sides. First, it contains cellular (white blood cells) and humoral (antibodies) elements of the immune response that protect the body from any foreign molecule. Second, it is the ability of blood to clot. If the vessel is damaged, the closed blood circulation is interrupted, and a decrease in the

amount of blood can lead to serious violations of cell functions, up to their death. The blood of a healthy person forms a blood clot at the site of injury, which clogs the lumen of the damaged vessel and stops bleeding.

Blood supports the body's acid-base and water balance. Normally, the pH of the blood is 7.36 — 7.4. Maintaining a constant pH is an important task, since a large number of acidic (for example, lactate, ketone bodies, carbonic acid), as well as the main (ammonia) products of metabolism are released into the blood. PH is regulated by blood buffer systems, which are discussed in detail in the course of physiology.

Performing a thermoregulatory function, the blood maintains a constant body temperature in different parts of it.

The chemical composition of substances soluble in blood plasma is relatively constant, since there are powerful neural and humoral mechanisms that support homeostasis (constancy of the internal environment). Soluble plasma substances make up about 10% of the blood mass, of which proteins account for about 7%, the share of inorganic salts-0.9%, the rest is formed by non-protein organic compounds. The range of concentrations of different blood plasma substances in a healthy person is presented in special biochemical reference books and is the most important material for medical biochemistry.

Blood is connected to all tissues of the body, so the occurrence of a pathological process in any organ leads to changes in the biochemical parameters of blood. This information can be valuable when making a diagnosis and evaluating the effectiveness of treatment measures.

### **Proteins of blood plasma**

The blood plasma contains 7% of all body proteins at a concentration of 60-80 g / l. plasma Proteins perform many functions. One of them is to maintain osmotic pressure, since proteins bind water and keep it in the bloodstream.

\* Plasma proteins form the most important buffer system of the blood and maintain the pH of the blood in the range of 7.37 — 7.43.

• Albumin, transthyretin, transcortin, transferrin and some other proteins perform transport function.

\* Plasma proteins determine the viscosity of blood and, therefore, play an important role in the hemodynamics of the circulatory system.

\* Plasma proteins are a reserve of amino acids for the body.

\* Immunoglobulins, blood clotting system proteins,  $\alpha$ 1-antitrypsin and complement system proteins perform a protective function.

By electrophoresis on acetylcellulose or agarose gel, plasma proteins can be divided into albumins (55 — 65%),  $\alpha$ 1-globulins (2 — 4%),  $\alpha$ 2-globulins (6 — 12%),  $\beta$ -globulins (8 — 12%) and h-globulins (12 — 22%) .

The use of other media for electrophoretic separation of proteins allows detecting a larger number of fractions. For example, during electrophoresis in polyacrylamide or starch gels, 16 — 17 protein fractions are isolated in the blood plasma. The method of immunoelectrophoresis, combining electrophoretic and immunological

methods of analysis, allows you to divide plasma proteins into more than 30 fractions.

Most serum proteins are synthesized in the liver, but some are formed in other tissues. For example, h-globulins are synthesized by B-lymphocytes, peptide hormones are mainly secreted by cells of the endocrine glands, and the peptide hormone erythropoietin — by kidney cells.

Many plasma proteins, such as albumin,  $\alpha$ 1-antitrypsin, haptoglobin, transferrin, ceruloplasmin,  $\alpha$ 2-macroglobulin and immunoglobulins, are characterized by polymorphism .

Almost all plasma proteins, with the exception of albumin, are glycoproteins. Oligosaccharides attach to proteins by forming glycosidic bonds with the hydroxyl group of serine or threonine, or interacting with the carboxyl group of asparagine. The terminal residue of oligosaccharides in most cases is N-acetyl-neuramic acid, combined with galactose. The vascular endothelial enzyme neuraminidase hydrolyzes the bond between them, and galactose becomes available to specific hepatocyte receptors. By endocytosis, " aged " proteins enter the liver cells, where they are destroyed. T1 / 2 of plasma proteins is from several hours to several weeks.

In a number of diseases, there is a change in the ratio of the distribution of protein fractions in electrophoresis compared to the norm.

Such changes are called dysproteinemias, but their interpretation often has relative diagnostic value. For example, a decrease in albumins,  $\alpha$ 1 - and  $\gamma$ -globulins and an increase in  $\alpha$ 2 - and  $\beta$ -globulins characteristic of nephrotic syndrome is also noted in some other diseases accompanied by loss of proteins. With a decrease in humoral immunity, a decrease in the  $\gamma$ -globulin fraction indicates a decrease in the content of the main component of immunoglobulins — IgG, but does not reflect the dynamics of changes in IgA and IgM.

The content of certain proteins in the blood plasma can dramatically increase in acute inflammatory processes and some other pathological conditions (injuries, burns, myocardial infarction). These proteins are called acute phase proteins, since they are involved in the development of an inflammatory response of the body. The main inducer of the synthesis of most acute phase proteins in hepatocytes is the polypeptide interleukin-1, which is released from mononuclear phagocytes. Acute phase proteins include C-reactive protein, so called because it interacts with the C-polysaccharide of pneumococci,  $\alpha$ 1-antitrypsin, haptoglobin, acid glycoprotein, fibrinogen. It is known that C-reactive protein can stimulate the complement system, and its concentration in the blood, for example, with an exacerbation of rheumatoid arthritis can increase by 30 times compared to the norm. The plasma protein  $\alpha$ 1-antitrypsin can inactivate certain proteases that are released in the acute phase of inflammation.

Albumin.

The concentration of albumin in the blood is 40-50 g/l. Per day, the liver synthesizes about 12 g of albumin, T1/2 of this protein-about 20 days. Albumin consists of 585 amino acid residues, has 17 disulfide bonds. The albumin molecule

contains many dicarboxylic amino acids, so it can retain  $\text{Ca}^{2+}$ ,  $\text{Si}^{2+}$ , and  $\text{Zn}^{2+}$  cations in the blood. About 40% of albumin is contained in the blood and the remaining 60% in the intercellular fluid, but its concentration in plasma is higher than in the intercellular fluid, since the volume of the latter exceeds the volume of plasma by 4 times.

Due to its relatively small molecular weight and high concentration, albumin provides up to 80% of the plasma osmotic pressure. With hypoalbuminemia, the osmotic pressure of blood plasma decreases. This leads to an imbalance in the distribution of extracellular fluid between the vascular bed and the intercellular space. Clinically, this manifests as edema. The relative decrease in blood plasma volume is accompanied by a decrease in renal blood flow, which causes the stimulation of the renin-angiotensin-aldosterone system, which ensures the restoration of blood volume. However, if there is a lack of albumin, which should hold  $\text{Na}^+$ , other cations and water, the water goes into the intercellular space, increasing edema.

Hypoalbuminemia can also be observed as a result of reduced albumin synthesis in liver diseases (cirrhosis), increased capillary permeability, protein loss due to extensive burns or catabolic conditions (severe sepsis, malignant neoplasms), nephrotic syndrome accompanied by albuminuria, and starvation. Circulatory disorders, characterized by slowing blood flow, lead to an increase in the flow of albumin into the intercellular space and the appearance of edema. A rapid increase in capillary permeability is accompanied by a sharp decrease in blood volume, which leads to a drop in blood PRESSURE and is clinically manifested as a shock. Albumin is the most important transport protein. It transports free fatty acids, unconjugated bilirubin,  $\text{Ca}^{2+}$ ,  $\text{Si}^{2+}$ , tryptophan, thyroxine, and triiodothyronine. Many medications (aspirin, dicumarol, sulfonamides) bind to albumin in the blood. This fact should be taken into account in the treatment of diseases accompanied by hypoalbuminemia, since in these cases the concentration of free medication in the blood increases. In addition, it should be remembered that some drugs can compete for binding centers in the albumin molecule with bilirubin and among themselves. Transthyretin (prealbumin) is called thyroxine binding by prealbumin. This is an acute phase protein. Transthyretin relates to the fraction of albumin, it has a tetrameric molecule. It is able to attach a retinol — binding protein in one binding center, and up to two molecules of thyroxine and triiodothyronine in the other. The connection to these ligands occurs independently of each other. In the transport of the latter, transthyretin plays a significantly smaller role compared to thyroxine-binding globulin.

The most prominent representative of  $\alpha_1$  globulins is an  $\alpha_1$ -antiprotease inhibitor — normally contains 2.5-4.0 g/l. Inhibits proteinases-trypsin, chymotrypsin, elastase, collagenase, thrombin, plasmin, renin, etc. Its activity accounts for 90-95% of all proteolytic activity. The concentration of these proteins increases in inflammatory processes, in pregnant women, and in a number of other pathological conditions.

The  $\alpha_1$  globulin fraction also includes:

$\alpha$ 1-fetoprotein-an embryonic protein synthesized in the fetus in hepatocytes, after birth can be detected in the child in the first days to a year. Normally, it is absent. It is detected with prolonged jaundice of newborns, in adults - with liver pathology, its cancer

$\alpha$ 1-acidic glycoprotein-orosomucoid-acidic protein, contains up to 40% of the carbohydrate component. Its blood contains 0.6-0.9 g/l. Normally, it inhibits cathepsin C, increases its concentration in acute inflammatory processes and injuries.

the  $\alpha$ 2-globulin fraction includes:

Haptoglobin-it binds plasma hemoglobin and protects the body from iron loss, preserving it for heme synthesis, binds iron to hemoglobin to form a hemoglobin-haptoglobin complex, performs a non-specific protective function, is a natural inhibitor of cathepsin B, participates in the transport of vitamin B12 Has peroxidase activity, so it has a bactericidal effect. Heterogeneous in structure: there are 3 types of haptoglobin Hp-1-1, Hp-2-1, Hp-2-2. Normally, it contains 0.6-1.8 g/l.

Ceruloplasmin belongs to the  $\alpha$ 2-globulin fraction. The norm contains 0.3-0.6 g/l. This is a glycoprotein, copper oxidase, one of the main regulators of copper metabolism in the body. 1 molecule of ceruloplasmin contains 6-8 copper atoms. It performs a transport function: it transports copper and delivers it to the liver. It has oxidase activity. Performs the role of an enzyme. It participates in the oxidation and metabolism of iron, biogenic amines (epinephrine, norepinephrine, serotonin), ascorbic acid, and other substances. A decrease in the content of ceruloplasmin in the blood is noted in patients with hepatolenticular degeneration (Wilson-Konovalov disease), there is an accumulation of copper in the nervous system and liver.

$\alpha$ 2-macroglobulin-regulates the activity of thrombin and kininogen. It is formed in the liver.

In the blood plasma, there is a protein that can bind iron heme-hemopexin and transport substances containing the gemin group.

Transferrin and its content in the plasma is 2.0-3.2 g/L.  $\beta$ -globulin. It easily forms a complex compound with iron, which is easily broken down. It converts plasma iron into a deionized form and delivers it to the bone marrow, where iron is used for the hematopoietic process.

The main part of  $\beta$ -globulins is represented by  $\beta$ -lipoproteins. The content of the latter varies between 2.5-8 g/l.

The  $\alpha$  and  $\beta$ -globulins are proteins of the coagulating system: prothrombin-a precursor of thrombin, proconvertin, antihemophilic globulin-are synthesized in the liver. Their synthesis depends on the presence of vitamin K. the gamma-globulin fraction is represented by immunoglobulins

All of them have the activity of antibodies formed by contact with antigens of viral, bacterial and other etiology.

There are 5 classes of immunoglobulins: IgG, IgM, IgA, IgE, IgD.

The basis of the molecular structure consists of 4 polypeptide chains — 2 heavy (H-chains) and 2 light (L-chains) connected by three disulfide bridges. Light

chains in all classes of Ig are similar and can be represented by 2 subclasses-Kappa and lambda. Heavy chains determine IG specificity and differ in amino acid composition and antigen specificity. The division of Ig into classes is based on the differences in their heavy chains. Distinguish between  $\mu$ ,  $\alpha$ ,  $\gamma$ ,  $\epsilon$ ,  $\delta$  (Structure).

IgG-make up 70-75% of the total amount of Ig. They carry antibodies against most antigens. IgG-secondary response immunoglobulins. They are actively transported through the placenta and play an important role in protecting the newborn from infections. Molecular weight 160,000 da, blood content 8-18 g/l.

IgM-primary response immunoglobulins — a powerful activator of the complement system. The antibodies of this class include antibodies of the blood test, rheumatoid factor, cold agglutinins. Molecular weight-960,000, plasma content 0.6-2.8 g/l.

IgA-makes up 20% of the total mass of plasma immunoglobulins and plays an important role in the formation of local immunity and mucous membranes. It is synthesized in plasma cells, is found mainly in submucosal tissues, on the mucous surface of the respiratory tract and intestinal tract, and in almost all excretory glands. Part of the IgA enters the bloodstream, but most of it remains on the mucous membranes and serves as a protective immune barrier. The molecular weight of 160000, a concentration of 0.9-4.5 g/L.

IgAs — provides immune protection of the mucous membranes of the mouth.

IgE-contained in the blood in very low amounts-0.0001-0.0005 g/l — However, the importance for the body is great, it is associated with allergic reactivity, plays the role of a trigger mechanism for allergic reactions of an immediate type.

IgD — the role is not clear. First isolated from the blood in myeloma.

There is also a group of proteins called "acute phase proteins". Proteins of this group are normally contained in the blood in very small amounts or are not present at all (not defined), and in acute inflammation or exacerbation of chronic appear in the plasma as newly synthesized proteins (this is C-reactive protein, cryoglobulin,  $\alpha$ 1 glycoprotein (orosomuroid),  $\alpha$ 1-antiprotease inhibitor, haptoglobin, hemopexin, ceruloplasmin, etc.). Proteins of this group are normally contained in the blood in very small amounts or are not present at all (not defined), and in acute inflammation or exacerbation of chronic appear in the plasma as newly synthesized proteins. The inflammatory process in the human body consists of two components that are related to each other and determine its course: This is a local tissue reaction caused by the release of inflammatory mediators, lysosomal enzymes and prostaglandin, which leads to microcirculatory disorders, exudation, infiltration by white blood cells, immune response and reparative processes. And the general reaction of the body, which is expressed in the appearance of pain, fever, leukocytosis and an increase in the concentration of glycoproteins in the blood plasma . Early inflammatory response to tissue damage includes the formation of inflammatory mediators (biogenic amines — histamine, serotonin, kinins). This causes vasodilation, increases the permeability of the vascular wall, hyperemia and edema, there is exudation of white blood cells, the release of enzymes from the lysosomes of white blood cells: elastase and collagenase, which provides tissue damage. Damage to the lysosomes of cells or the release of their contents from

white blood cells during phagocytosis is the trigger for the synthesis of APP. They begin to synthesize by the end of 3 hours after damage. The appearance of the first portions of APP in the plasma can be noted at the end of the fifth or beginning of the sixth hour after damage. The maximum synthesis time is between 12 and 48 hours. The development of large amounts of matrices for the synthesis of acute phase proteins in hepatocytes leads to a deficit of factors of protein biosynthesis and protein-synthesis structures of the cell. Liver cells reduce the synthesis of their usual proteins, as a result, the level of albumin and other plasma proteins that are not related to APP is reduced. C-reactive protein-0.1 g / l — It's not normal. C-reactive protein is an integral test of the biological function of inflammation. The name is associated with the property to react precipitation with C-polysaccharide pneumococcus. It participates in the activation of complement and together with its components is responsible for the formation of amyloid protein and its deposition in the vascular membrane. The concentration of C-reactive protein increases in bacterial infections, in diffuse connective tissue diseases (rheumatoid arthritis, ankylosing spondylitis, systemic lupus erythematosus, rheumatic polyarthritis; when tissue destruction — peritonitis, injuries, surgical interventions).

Cryoglobulin — it is not normal. it appears in pathology, it is able to precipitate or gelatinize at a temperature below 37 oC. It can be found in serum for myeloma, nephrosis, liver cirrhosis, rheumatism, lymphosarcoma, leukemia, and other diseases. Fibrinogen is a plasma protein that can turn into insoluble fibrin under the action of thrombin. Its concentration increases above 4 g / l in infectious processes (ESR is increased), in neoplasms, postoperative period, after injuries, participates in the formation of a blood clot and stopping bleeding.

The protein substances contained in the blood plasma, which are of great diagnostic value, include plasma enzymes. They are divided into three large groups: - secretory, – excretory,-indicator. Secretory-synthesized in the liver, normally isolated in the blood plasma (serum cholinesterase, enzymes involved in the process of blood clotting). Excretory — synthesized mainly in the liver (alkaline phosphatase, leucinaminopeptidase, etc.) and isolated with bile in the intestine. The Greatest interest in the diagnosis of diseases are indicator (organ-specific) enzymes. Normally, their concentration in the blood is low, and increases with diseases of a particular organ. The reasons for the increase may be: increased permeability of the cell membrane; viral or bacterial beginnings (by cytolysis, the cell membrane is damaged); toxic beginnings; the action of drugs. These include: aminotransferases (ALAT, ASAT), LDH, creatine phosphokinase, alkaline phosphatase, and others. Thus, with rickets in the blood serum, the activity of the enzyme alkaline phosphatase increases, with pancreatic damage-amylase, with myocardial infarction-creatine kinase (isoenzyme MB fraction), ASAT, LDH, with diseases of skeletal muscles — creatine kinase (isoenzyme MM).In prostate cancer, the activity of acid phosphatase increases in the blood serum, in the case of salivary gland damage — amylase, in liver diseases — ALAT, LDH5, ornithine carbomailtransferase, etc., in kidney pathology — glycinamidinotransferase. A large group in the blood are non-protein nitrogen-containing substances. The content of non-protein nitrogen in whole blood and plasma is almost the same and

is 15-25 mmol/l in the blood. Non-protein nitrogen of blood includes urea nitrogen (50% of the total amount of non-protein nitrogen), amino acids (25%), ergothionine (8%), uric acid (4%), creatine (5%), creatinine (2.5%), ammonia and indican (0.5%) and other non-protein substances containing nitrogen (polypeptides, nucleotides, nucleosides, glutathione, bilirubin, choline, histamine, etc.). thus, the composition of non-protein nitrogen in the blood consists mainly of nitrogen from the end products of simple and complex proteins. Non-protein blood nitrogen is also called residual nitrogen. In a healthy person, fluctuations in the content of non-protein, or residual nitrogen in the blood are insignificant and mainly depend on the amount of proteins coming from food. In a number of pathological conditions, the level of non-protein nitrogen in the blood increases. This condition is called azotemia. Azotemia, depending on the causes that caused it, is divided into retention and production. Retention azotemia occurs as a result of insufficient excretion of nitrogen-containing products in the urine when they normally enter the bloodstream. It in turn can be renal and extrarenal. In renal retention azotemia, the concentration of residual nitrogen in the blood increases due to a weakening of the purifying (excretory) function of the kidneys. A sharp increase in the content of residual nitrogen in re-tensionable renal azotemia occurs mainly due to urea. In these cases, urea nitrogen accounts for 90% of non-protein blood nitrogen, instead of 50% in the normal range. Extrarenal retention azotemia can occur as a result of severe circulatory failure, decreased blood pressure, and decreased renal blood flow. Often extrarenal retention azotemia is the result of the presence of an obstacle to the outflow of urine after its formation in the kidney. Production azotemia is observed when excessive intake of nitrogen-containing products into the blood, as a result of increased breakdown of tissue proteins. Mixed-type azotemias are often observed. A significant amount of urea is contained in the blood plasma, urea is 18 times less toxic than other nitrogenous substances. In acute renal failure, the concentration of urea in the blood reaches 50-83 mmol/l (the norm is 3.3-6.6 mmol / l). An increase in urea content in the blood to 16.6-20.0 mmol/l (based on urea nitrogen) is a sign of moderate renal impairment, up to 33.3 mmol/l-severe and over 50 mmol/l — very severe violation with an unfavorable prognosis. Uric acid is also an important protein-free nitrogenous substance in the blood. Normally, the concentration of uric acid in whole blood is 0.18-0.24 mmol/l (in serum-about 0.29 mmol/l). The elevated levels of uric acid in the blood (hyperuricemia) is the main symptom of gout. In gout, the level of uric acid in the blood serum increases to 0.47-0.89 mmol/l and even to 1.1 mmol/l. The residual nitrogen also includes nitrogen of amino acids and polypeptides. Various diseases are accompanied by changes in the content of certain substances in the blood. The study of normal blood parameters is the basis for correct diagnosis in various pathological conditions, establishing the prognosis of the disease and evaluating the effectiveness of treatment.