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RHEOLOGICAL PROPERTIES OF BLOOD AND ITS BIOPHYSICAL ROLE IN HEMODYNAMIC PROCESSES

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Annotatsiya: Qonning reologik xususiyatlari (viskozite, eritrotsitlarning deformatsiyalanishi va agregatsiyasi) gemodinamik jarayonlarda muhim biofizik rol o‘ynaydi. Ushbu maqolada qonning Nyuton bo‘lmagan suyuqlik sifatidagi oqish xossalari, Puazeyl qonuni asosida makro- va mikrosirkulyatsiyadagi ta’siri, Fahraeus-Lindqvist effekti hamda “sladj” fenomeni kabi reologik o‘zgarishlar tahlil qilinadi. Qon reologiyasining buzilishi yurak-qon tomir kasalliklari, shok holatlari va mikrosirkulyatsiya buzilishlarida qanday mexanizmlar orqali to‘qima gipoksiyasiga olib kelishi ko‘rsatilgan. O‘zbek tibbiyot adabiyotlari va patofiziologiya manbalariga asoslanib, reologik ko‘rsatkichlarning klinik ahamiyati yoritiladi.

Kalit so‘zlar : qon reologiyasi, gemoreologiya, gemodinamika, qon viskozitesi, eritrotsit agregatsiyasi, mikrosirkulyatsiya, Puazeyl qonuni, sladj fenomeni.

Аннотация: Реологические свойства крови (вязкость, деформируемость и агрегация эритроцитов) играют важную биофизическую роль в гемодинамических процессах. В статье анализируются реологические характеристики крови как неньютоновской жидкости, её влияние на макро- и микрогемодинамику на основе закона Пуазейля, эффект Фареуса-Линдквиста, а также феномен «сладж». Показано, как нарушения реологии крови приводят к тканевой гипоксии при сердечно-сосудистых заболеваниях, шоке и расстройствах микроциркуляции. На основе узбекской медицинской литературы и источников по патофизиологии освещается клиническое значение реологических показателей.

Ключевые слова : реология крови, гемореология, гемодинамика, вязкость крови, агрегация эритроцитов, микроциркуляция, закон Пуазейля, феномен сладж.

Abstract: The rheological properties of blood (viscosity, erythrocyte deformability and aggregation) play a significant biophysical role in hemodynamic processes. This article analyzes the flow characteristics of blood as a non-Newtonian fluid, its influence on macro- and microcirculation based on Poiseuille’s law, the Fahraeus-Lindqvist effect, and the “sludge” phenomenon. It demonstrates how disturbances in blood rheology lead to tissue hypoxia in cardiovascular diseases, shock states, and microcirculatory disorders. Based on Uzbek medical literature and pathophysiology sources, the clinical significance of rheological parameters is highlighted.

Keywords : blood rheology, hemorheology, hemodynamics, blood viscosity, erythrocyte aggregation, microcirculation, Poiseuille’s law, sludge phenomenon.

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Introduction

The main goal of the science of medical biological physics is to explain biological processes occurring in a living organism based on physical laws and to apply them in medical practice. The human organism is a complex open system in which the constant exchange of matter, energy and information occurs. The effective course of these processes is especially directly related to the proper functioning of the circulatory system. Therefore, the study of the physical properties of blood, its flow mechanisms, and its movement in the vascular system is one of the most important areas of biophysics. Blood is a special fluid tissue in the body that performs a transport function, participating in the transport of oxygen and carbon dioxide, nutrients, hormones, and metabolic waste. This function of blood is provided by the pumping activity of the heart and the complex structure of the vascular system. The energy emanating from the heart is distributed through the blood vessels throughout the body, and this process is carried out on the basis of physical laws, in particular the principles of hydrodynamics and rheology. The most important peculiarity of blood is that it has a complex structure in contrast to ordinary physical fluids, being a heterogeneous system. Its composition includes plasma and shaped elements — Erythrocytes, Leukocytes and platelets. It is these shape-forming elements that significantly change the flow properties of blood. Therefore, the movement of blood does not fully comply with the laws of classical Newtonian fluids, and it is considered a non-Newtonian fluid. From a rheological perspective, the main properties of blood are determined by its viscosity, elasticity, resistance to flow, and ability to deform. Blood viscosity represents the degree of its internal friction, and this indicator depends on the hematocrit level, the amount of plasma proteins, and the deformability of erythrocytes. As viscosity increases, blood flow slows, resistance within the vessels increases, and the heart's workload increases.

From a hemodynamic perspective, blood flow is determined by the pressure difference, the radius of the vessels, and the rheological properties of the blood. Laminar and turbulent flows play an important role in these processes. Under normal conditions, blood flows in a laminar flow, that is, in a layered, orderly manner. However, turbulent flow can occur when blood vessels narrow or pathological conditions occur, leading to energy loss and disruption of the cardiovascular system. The rheological properties of the blood are of great importance, especially at the level of microcirculation, that is, in the capillaries. At this level, the exchange of gases and substances occurs. The elasticity of erythrocytes allows them to pass through even very narrow capillaries, which ensures the oxygen supply to the tissues. If the rheological properties of blood are impaired, microcirculation is disrupted and pathological conditions such as hypoxia and ischemia may develop in the tissues. However, the rheological properties of the blood also determine the general hemodynamic state of the body. Their changes can cause increased heart function, increased or decreased blood pressure, and the development of various cardiovascular diseases. Therefore, the study of the physical properties of blood is important not only for theoretical biophysics, but also for clinical medicine. To understand the basic laws of blood rheology, it is first necessary to correctly select its physical model. In Newtonian fluids (such as water or plasma), viscosity does not depend on shear rate. However, blood exhibits a completely different behavior: at low shear rates, its viscosity increases sharply, while at high shear rates, it decreases. This phenomenon is called Creamy thinning (shear-thinning). The reason for it is the ability of erythrocytes to aggregate and break down aggregates. This property plays a very important role in the movement of blood through the vessels, as it relatively smooths out the load on the heart and prevents the flow from becoming turbulent.

Another important parameter that characterizes blood flow is the leakage limit (yield stress). Blood does not flow to a certain minimum tension, but deforms like an elastic body. Only at a

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voltage exceeding this marginal value does blood begin to flow. This property is especially important in capillaries and venules, where blood pressure is low. If the threshold for blood flow increases due to pathological causes (for example, an increase in fibrinogen concentration or increased erythrocyte aggregation), microcirculation is severely impaired and tissue ischemia may develop. The deformability properties of erythrocytes deserve special attention. Under normal conditions, erythrocytes can change their shape and pass through capillaries with a diameter of 2-3 microns. Their membrane is very flexible, which, together with the internal viscosity of the cell (depending on the hemoglobin concentration), determines the ability to deform. A decrease in the ability of erythrocytes to deform – for example, in diabetes mellitus, sickle cell anemia, thalassemia or old age – increases the overall viscosity of the blood, increases hemodynamic resistance and worsens the oxygen supply of tissues. Leukocytes and platelets also have an effect on blood rheology. Leukocytes are much larger and less deformable cells than erythrocytes. Although their number is relatively small, their adhesion and attachment to the vascular wall in inflammatory processes can dramatically reduce the permeability of capillaries. Platelets, when activated, change their shape, form protrusions, and their aggregation significantly affects the rheological properties of blood. In the microcirculatory stream, the rheological properties of blood become even more complex. The phenomenon of the "marginal plasma layer" - the presence of a layer of pure plasma without erythrocytes near the vessel wall - reduces the overall viscosity of the blood. The thickness of this layer depends on the diameter of the vessel, the rate of blood flow, and the hematocrit. In small vessels, erythrocytes move in the central axis, while near the wall the plasma glides. This mechanism minimizes blood pressure loss in capillaries and optimizes oxygen delivery to tissues. Hematocrit is one of the most important factors in blood rheology. Under normal conditions, hematocrit is around 40-45%. An increase in hematocrit to 60% (in polycythemia or dehydration) can increase blood viscosity by 2-3 times, which leads to a sharp increase in the load on the heart and myocardial ischemia. Conversely, a hematocrit below 25% (anemia) reduces blood viscosity, although it seriously reduces oxygen-carrying capacity. Therefore, the body tends to maintain hematocrit within a certain physiological range - this is the result of a compromise between optimal viscosity and optimal oxygen transport.

The rheological importance of plasma proteins should not be overlooked. High molecular weight proteins such as fibrinogen and alpha-2-macroglobulin form bridges between erythrocytes, enhancing their aggregation. Dysproteinemias (e.g., in myeloma) can dramatically increase blood viscosity, causing hyperviscosity syndrome. In this syndrome, blood flow decreases so much that the microcirculation of the brain, kidneys, and retina is severely impaired. Modern rheological research methods include viscometry (circular, capillary and vibrational Viscometers), measurement of erythrocyte deformation (micropipette method, laser diffraction – ectacitometry), aggregation assessment (photometric and microscopic methods), and magnetic rotation rheometry. These methods are becoming increasingly important in clinical practice for early detection of circulatory diseases, monitoring the effectiveness of treatment, and assessing prognosis.

Main part

Biophysical basis of rheological properties of blood

Blood rheology is formed as a result of complex interactions between its formed elements and plasma. The biophysical reason for blood to behave as a non-Newtonian fluid is the discrete nature of erythrocytes and their interactions with each other and with the surrounding fluid. Although the formed elements make up approximately 40–45% of the blood volume, their surface area and shape have a disproportionately large effect on the macroscopic viscosity of the

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blood. Erythrocyte morphology and deformability: The biconcave discoid shape of erythrocytes maximizes their surface area without changing their volume, which is favorable for gas exchange. But the most important mechanical advantage of this shape is the ability of the cell to undergo large deformations. The erythrocyte membrane has an elastic network consisting of spectrin, ankyrin, and other cytoskeletal proteins. This network allows the cell to change its shape from a cigar-shaped or tubular appearance when passing through a capillary with a diameter of 2-3 μm. A decrease in deformability is observed with membrane stiffening (e.g., as a result of glycation or oxidative stress) or cytoskeletal disruption (e.g., in spherocytosis).

Erythrocyte aggregation: At low shear rates, erythrocytes aggregate into a "coin stack" (rouleaux) form. This process is mainly mediated by fibrinogen and globulins in the plasma. These proteins neutralize the negative charge on the surface of red blood cells, reducing the repulsive force between cells. Under normal conditions, aggregation is reversible and physiological - it is weak enough to slow blood flow in venules, but aggregates break down at the entrance to capillaries. In pathological conditions (e.g., inflammation, diabetes, burn disease), aggregation increases, leading to microcirculation blockade and tissue hypoxia.

Dependence of blood viscosity on shear rate: The dynamic viscosity of blood decreases monotonically with increasing shear rate. At low slip rates (up to 1 $s^{-}1$), the viscosity can exceed 100 mPa•s, while at higher speeds (100 $s^{-}1$ and above) it drops to 3-4 MPA•s (close to plasma viscosity). This behavior is described by the Casson model: $\sqrt{\eta} = \sqrt{\eta}\ \eta + \sqrt{(\tau\ \tau/\gamma)}$, where η is the viscosity, η_0 is the viscosity at infinitely high displacement, τ.is the leakage limit, γ is the displacement rate. The leakage limit (yield stress) is usually in the range of 1-5 mPa, which is directly proportional to the level of aggregation.

Correlation of hemodynamic processes and blood rheology

Hemodynamics studies the movement of blood in the cardiovascular system, and its main parameters – blood pressure, flow rate, peripheral resistance, wall tension, and turbulence – are directly related to the rheological properties of blood. According to Poiseuille's law (for laminar flow), the volumetric flow rate of a fluid flowing through a tube is inversely proportional to its viscosity: $Q = (\pi \cdot \Delta P \cdot r^4) / (8 \cdot \eta \cdot L)$. Although this law is not fully fulfilled in the vascular system, increased viscosity, especially in small arterioles and capillaries, forces an increase in the pressure gradient. Peripheral resistance (PVR) depends on blood viscosity and vessel length and diameter: $PVR = (8 \cdot \eta \cdot L) / (\pi \cdot r^4)$. A doubling of viscosity also doubles peripheral resistance, dramatically increasing the work the heart must do to pump blood. This condition can lead to myocardial hypertrophy and heart failure in the long term. Conversely, a decrease in viscosity reduces resistance, but there is a risk of a sharp drop in blood pressure (hypotension).

Rheological load on the heart: When the heart pumps blood into the vessels, it must overcome not only inertia and elastic resistance, but also the viscous resistance of the blood. As blood viscosity increases, the systolic work of the heart increases, and the oxygen demand of the myocardium increases. If there are atherosclerotic plaques in the coronary arteries, this condition can lead to angina pectoris and myocardial infarction. Therefore, rheological parameters are considered as a prognostic factor in cardiovascular diseases. Special features of blood flow in microcirculation: Capillaries have a diameter of about 4-8 μm, through which erythrocytes pass sequentially, one after another. Here, the viscosity of the blood decreases due to the Fåhraeus–Lindqvist effect. That is, as the vessel diameter approaches the diameter of the erythrocytes, erythrocytes move in the central axis, and a layer of plasma forms near the wall. This layer reduces the effective viscosity of the blood. However, if the hematocrit exceeds 60%, this mechanism fails and erythrocytes become trapped in the capillaries.

The effect of biophysical factors on blood rheology

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Blood rheology is influenced by a number of endogenous and exogenous factors. It is important to analyze them systematically. Temperature: Blood viscosity is very sensitive to temperature. When the temperature drops from 37°C to 25°C, blood viscosity increases by about 30-40%. This can lead to microcirculation disorders and tissue ischemia in conditions of hypothermia (for example, during surgical operations or exposure to cold). The fluidity of the erythrocyte membrane also depends on temperature - in the cold, the membrane permeability decreases, it becomes more rigid.

pH and gases: Changes in blood pH within the physiological range of 7.35 to 7.45 have little effect on erythrocyte deformability. However, acidosis (pH < 7.3) – for example, in diabetic acidosis or hypoxia – causes stiffening of the erythrocyte cytoskeleton, as the ionization of spectrin and other proteins changes. Hypoxia, on the other hand, increases the concentration of 2,3-bisphosphoglycerate in erythrocytes, which reduces the oxygen affinity of hemoglobin, but indirectly affects cell deformability.

Ionic strength and osmolarity: When the osmolarity of blood plasma changes (e.g., in dehydration or renal failure), erythrocytes swell (in a hypotonic environment) or shrink (in a hypertonic environment). Hypotonic swelling transforms erythrocytes into spherocytes and dramatically reduces their ability to deform. This condition leads to blockages and microcirculation disorders, especially in capillaries. Hormonal and metabolic factors: Stress hormones such as cortisol, adrenaline, and norepinephrine increase blood viscosity and erythrocyte aggregation. Insulin, on the other hand, reduces viscosity. In diabetes, long-term hyperglycemia leads to glycation of the erythrocyte membrane, that is, the covalent attachment of glucose molecules to membrane proteins, which reduces membrane elasticity and increases blood viscosity.

Hemodynamics is a science that studies the movement of blood throughout the body, its physical factors and biological control mechanisms, with the heart (pump), blood (fluid) and vessels (groove and resistive elements) as its main components. Blood flow is based on a pressure gradient: from high pressure to low pressure. The pulse generated by the heart (systolic pressure) and the elastic properties of the vessel walls determine arterial pressure, while peripheral resistance controls the volume of blood delivered to organs and tissues. The dynamic equations of blood flow are understood in terms of simple ideas: flow (Q) = pressure difference (ΔP) / resistance (R). This is the basic relationship used to measure and interpret the changes in these variables.The cardiac cycle and the pumping properties of the heart are the result of the synchronous activity of the heart chambers. During systole, blood is ejected from the opposing relaxed chambers; during diastole, the heart relaxes and fills. The volume of the heart per minute — the volume of blood per minute (cardiac output) - is expressed as the product of the volume of ejection per stroke with the number of beats of the heart, and changes rapidly depending on metabolic demand, nervous system activity and hormonal status. The concepts of preload (the initial stretch of blood entering the heart) and afterload (the peripheral pressure/resistance against which the heart must work) are central to understanding the heart's pumping capacity. According to the Frank-Starling law, the return of blood from the tissues increases the contractile support of myocardial fibers when they are stretched as a result of the event, but excessive stretching reduces the contractile effect.From the perspective of the structure and function of the vascular system, the arterial segment functions to pump blood at high pressure and distribute it to the periphery, while arterioles are the main source of vascular resistance. The tone of arterioles is dynamically regulated by endothelial signals, sympathetic innervation, and local metabolic factors. Capillaries are the site of substance exchange, where blood flow slows down, allowing for the exchange of gases, substances, and water. The venous segment, on the other hand, acts as

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a large volume of blood reservoir; venous valves, skeletal muscle pump, and intrathoracal pressure changes provide venous return.The Rheology of blood is an important factor for hemodynamics. The viscosity (viscosity) of the blood and the deformability of erythrocytes determine the flow resistance,aggregation of leukocytes and platelets can disrupt perfusion at the capillary level. From a hemodynamic standpoint, an increase in hematocrit increases viscosity, increasing peripheral resistance and cardiac load, while also affecting oxygen transport capacity.

Rheological changes in pathological conditions

In many diseases, impaired blood rheology becomes one of the central links in pathogenesis. The most important pathological conditions are listed below. Atherosclerosis and coronary heart disease: Blood flow in vessels with atherosclerotic plaques is turbulent, which increases the aggregation of erythrocytes. Platelet adhesion and aggregation begin on the surface of the plaques, and local rheological conditions deteriorate. As blood viscosity increases, the tangential stress on the plaque decreases, increasing the likelihood of plaque rupture, which is a direct cause of myocardial infarction and stroke.

Hypertension: in long-term arterial hypertension, the vessel walls thicken and their diameter decreases. This reduces the local slip rate. Low shear rates increase erythrocyte aggregation, which further increases viscosity - thus, a "circular" pathomechanism occurs: hypertension → increased viscosity → increased peripheral resistance → increased hypertension.Diabetes: In diabetes, long-term hyperglycemia leads to glycation of erythrocytes, their stiffening, and increased susceptibility to aggregation. Together with thickening of the capillary basement membrane, these changes are the basis for the development of diabetic retinopathy, nephropathy, and neuropathy. Glucose itself in the blood directly increases erythrocyte aggregation. Polycythemia and hemoconcentration: In polycythemia (pathological increase in the number of red blood cells) or hemoconcentration due to dehydration, the hematocrit increases to 55-60%. In this case, blood viscosity increases by 3-4 times, leading to clinical symptoms such as headache, tinnitus, visual impairment, and even thrombosis. The "hematocrit–viscosity–oxygen transport" curve shows that the optimal hematocrit is around 40-45%, above which oxygen transport decreases. Sepsis and systemic inflammation: in sepsis, under the influence of inflammatory cytokines (TNF-α, IL-1, IL-6), erythrocyte deformity sharply decreases, leukocytes are activated, cling to the vascular endothelium and block capillaries. Blood viscosity may initially decrease (due to vasodilation and hemodilution), and then increase sharply (due to capillary escape syndrome and hemoconcentration). Rheological disorders play an important role in the development of septic shock.

Methods for clinical assessment of rheological parameters

Today, there are a number of instrumental methods for assessing blood rheology. Each of them specializes in measuring a specific rheological property.

Viscometry: Rotational viscometers (e.g., Coaxial Cylinder Viscometer) measure the dynamic viscosity of blood at different shear rates. They determine viscosity due to aggregation at low speeds (0.1-10 s^{-1}) and minimal viscosity due to the orientation and deformation of erythrocytes at high speeds (100-1000 s^{-1}). Capillary viscometers measure the apparent viscosity of blood in a uniform flow. Ektacytometry (laser diffraction): This method assesses the deformability of erythrocytes. When a certain shear stress is applied to a blood suspension, the erythrocytes are stretched and an elliptical shape is formed as a result of the diffraction of the laser beam. The eccentricity of the ellipse gives the deformation index (EI). A decrease in EI indicates increased rigidity of the erythrocytes. Aggregation assessment: In the photometric method, the optical density of the blood suspension is measured over time. When aggregation begins, light transmission increases (as cells aggregate and the scattering surface decreases).

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Microscopic methods, on the other hand, allow direct observation of the morphology of aggregates (size, density, shape). Magnetic rotational rheometry: A new and non-invasive method in which paramagnetic hemoglobin inside erythrocytes is oriented by a magnetic field and provides information about the cell's deformation and aggregation based on its rotational ability. Clinical norms of blood viscosity: at 37°C, with a sliding rate of 200 s^{-1}, the viscosity of the blood of a healthy person is 3.5-5.5 mPa•s (slightly higher in men), and plasma viscosity is 1.1-1.3 mPa•s. At 1 s^{-1}, blood viscosity can increase to 10-20 mPa•S.

Pharmacological and physical correction of rheological disorders

Improving blood rheology is widely used for therapeutic purposes. The main areas are listed below. Hemodilution: Diluting the blood with saline, dextran, hydroxyethyl starch, or albumin reduces the hematocrit and reduces blood viscosity. This method is used in cases of stroke, myocardial infarction, and critical ischemic conditions. The optimal level of hemodilution is a reduction in hematocrit to 30-35%. Below this level, oxygen transport deteriorates. Antiaggregants: Aspirin, clopidogrel, dipyridamole block platelet aggregation. Their indirect effect on blood rheology is the prevention of microthrombus formation and improvement of microcirculation. Drugs that improve erythrocyte deformability: Pentoxifylline (trental) increases erythrocyte membrane flexibility, reduces fibrinogen concentration, and reduces blood viscosity. This drug is used in peripheral arterial disease, diabetic angiopathy, and chronic venous insufficiency. Kinins and prostaglandins (e.g., alprostadil) also improve erythrocyte deformability. Fibrinogen-lowering agents: Anabolic steroids, fibrates, statins, and angiotensin-converting enzyme inhibitors reduce blood viscosity by lowering fibrinogen levels. Plasmapheresis – removal of blood plasma and reinfusion of cells – dramatically reduces fibrinogen and other high-molecular-weight proteins and is effective in hyperviscosity syndrome. Physical methods: There is evidence that magnetic and laser therapy have a positive effect on blood rheology. Autotransfusion of blood with ultraviolet light (AUFOK) improves erythrocyte deformability and reduces aggregation. Long-term (remote) ischemic preconditioning can also improve microcirculation and blood rheology.

CONCLUSION

In conclusion, the rheological properties of blood are one of its important biophysical factors in ensuring vital processes in the body. Blood is not a simple liquid, but a biological environment with a complex structure, exhibiting non-Newtonian properties. Its viscosity, the ability of red blood cells to deform and aggregate, directly affects the movement of blood through the vessels.

The rheological properties of blood in hemodynamic processes ensure the effective functioning of the cardiovascular system. An increase or decrease in blood viscosity can affect the flow rate, pressure, and total resistance in the vessels, leading to the development of various pathological conditions. Especially at the level of microcirculation, the elasticity of erythrocytes and the fluidity of blood play a crucial role in oxygen supply to tissues.

Thus, the study of the rheological properties of blood is not only an important area of biophysics, but also of great importance in practical medicine for understanding, diagnosing, and preventing cardiovascular diseases.

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