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HEMORHEOLOGICAL DISORDERS IN HEMOPHILIACS

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Rheological properties of blood (blood and plasma viscosity, deformability and aggregation erythrocytes) in hemophiliacs are studied. The blood viscosity is found to be increased at both high and low shear rates. The plasma viscosity is higher and aggregation of erythrocytes is enhanced in hemophiliacs in the stage of exacerbation of chronic arthropathy.

At present, hemorheological disturbances that usually bring about microcirculatory disorders are considered very important in the pathogenesis of many diseases. The microvessel bed serves for performing trophic, regulatory, integrative, and protective functions of blood. It is at the microcirculatory level that oxygen is supplied to tissues and utilized by them, transcapillary exchange is carried out, and tissue homeostatis that is necessary for vital activity is created. Disorders of microcirculatory hemodynamics and associated disturbances of regional blood circulation have an adverse effect on functions of all organs and systems, which aggravates prior disease.

It is known that blood is a non-Newtonian viscoelastic liquid that consists of formed elements suspended in plasma, which is a colloid solution. Since the total volume of erythrocytes is 50 times those of leucocytes and thrombocytes, the concentration and mechanical properties of erythrocytes are of primary importance for characterization of blood fluidity. The main factor that determines the blood viscosity is the volume concentration of erythrocytes (their content and average volume), determined by hematocrit. Plasma is an important rheological parameter. It is a Newtonian liquid, whose viscosity is determined by the content of fibrinogen, globulins, and (insignificantly) albumins in it. An increase in the blood viscosity at low shear rates can be explained by formation of monetary columns of erythrocytes, i.e., by their physiological aggregation. The question of the aggregation mechanism has not been answered yet. The theory of a bridge mechanism suggested by Chien is a most popular one. In accordance with this theory, bridges of fibrinogen or other large-molecule proteins that facilitate aggregation of erythrocytes at decreased shear rates are adsorbed on the surface of erythrocytes. The net aggregation force is the difference between the adhesion force in the bridges, the electrostatic repulsive force of negatively charged erythrocytes in the bridges, and the shear force, which induces disaggregation [1]. It is known that erythrocyte aggregation is most sensitive to various disturbances of the protein balance.

Deformability of erythrocytes is also an important hemorheological factor. It is a set of physical and geometric properties that allow a cell that has a diameter of $7-8\ \mu$m to flow in microcirculation capillaries that have a diameter of $2-5\ \mu$m.

At present, changes in microrheological properties of blood (aggregation and deformability of erythrocytes) are considered to be of special importance. They play an important role in the flow of blood in microvessels and influence the development of many clinical syndromes that can be observed in cardiovascular insufficiency, various forms of shock, hypertensive disease, renal and hepatic failure, diabetes, thromboembolic disease, etc.

In evaluating blood rheology, the effect of hemostatic indices on the blood fluidity should not be neglected. Performing their functions in a common vascular bed, affecting each other, and enhancing their mutual effect, rheology and hemocirculation compose a single system that provides the ability of blood to flow at all the levels of branching of the vascular bed. The development of many clinical syndromes that can be observed in hypertensive

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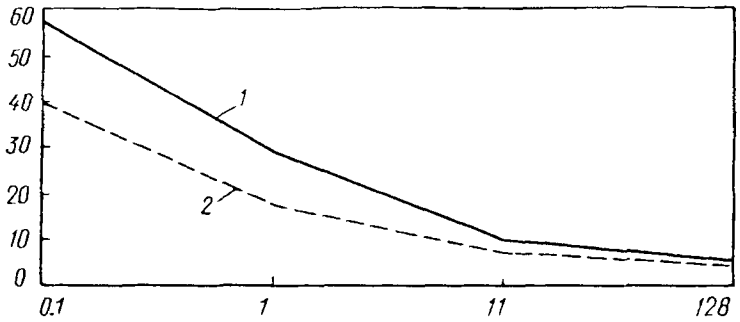


Fig. 1. Plot of blood viscosity versus shear rate in hemophiliacs (horizontal axis, shear rate, sec^{-1}; vertical axis, blood viscosity, mPa·sec): 1) patients, 2) donors.

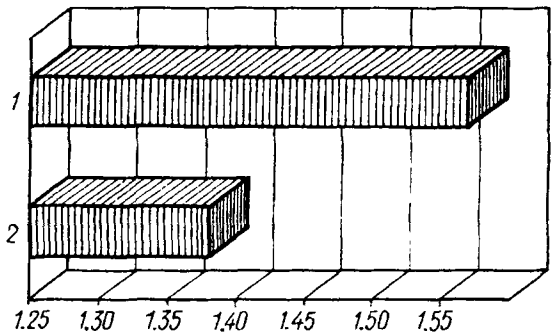


Fig. 2. Plasma viscosity in hemophiliacs (horizontal axis, plasma viscosity, mPa·sec): 1) patients, 2) donors.

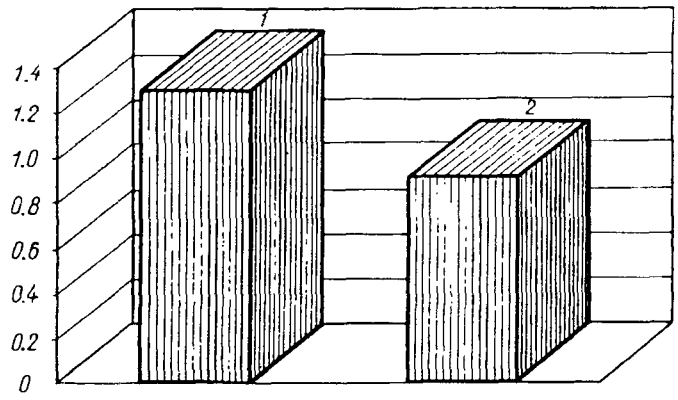
and thromboembolic diseases, myocardial infarction, and some other diseases is caused by disturbances of microrheological properties of blood that correlate with hypercoagulation, which, taken together, worsen the blood flow in the system of fine vessels and, eventually, lead to microcirculatory disorders. There is almost no information about rheological properties of blood in the case of decreased coagulability, which results in hemorrhages, in particular, in hemophilia.

In the present work we report results of a study of rheological properties of blood in hemophiliacs in the stage of exacerbation of chronic arthropathy. In this study asymptotic viscosity, the dependence of blood viscosity on the shear rate in the range 0.1–98 sec^{-1}, and plasma viscosity were investigated with a Low Shear 30 rotary rheometer (Contraves, Switzerland). The measurements were conducted at 37°C. Deformability of erythrocytes was determined by a filtration method in which erythrocytes pass through filters with 3-μm pores and a thickness of 10–15 μm using an IDA-1 device developed at the Hematological Scientific Center of the Russian Academy of Medical Sciences. The rigidity index, which is inversely proportional to the deformability of erythrocytes, was used as a characteristic of deformability. Aggregation of erythrocytes was measured photometrically in a Goryaev chamber [2].

At all the measured shear rates the blood viscosity in hemophiliacs was higher than that of normal donors (Fig. 1). It should be noted that in the patients the hematocrit was higher than the physiological norm.

In the patients, the plasma viscosity was significantly higher than this index in normal donors (Fig. 2). Aggregation of erythrocytes was enhanced substantially (Fig. 3), which correlated with a more pronounced increase in the blood viscosity at low shear rates. In hemophiliacs hemorrhages are accompanied by an inflammatory process, which often becomes chronic. Metabolic changes appear, and peroxidation starts, which plays an important role in development of the inflammation. Here antibodies are produced and immune complexes are formed [3]. The increased plasma viscosity and enhanced aggregation of erythrocytes observed in hemophiliacs can be explained by an increased content of immune complexes.

In these patients deformability of erythrocytes was almost the same as the physiological norm (Fig. 4). Meanwhile, a study of some properties of erythrocytes, in particular their acid resistance, showed that this index



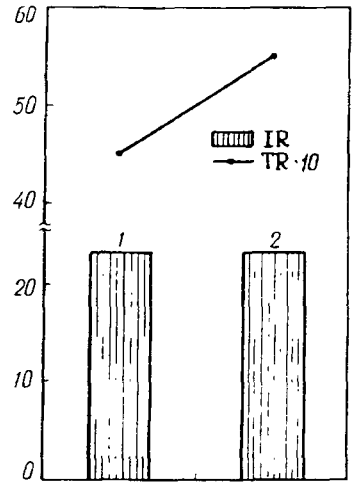


Fig. 3. Aggregation of erythrocytes in hemophiliacs (vertical axis, erythrocyte aggregation factor, arbitrary units): 1) patients, 2) donors.

Fig. 4. Deformability and acid resistance of erythrocytes in hemophiliacs (vertical axis, erythrocyte rigidity index, arbitrary units): 1) patients, 2) donors.

is lower than in normal donors, which indicates that in hemophiliacs' peripheral blood there are erythrocytes with lower stability and there are a higher number of "old populations."

Conclusion. Hemorheological disorders are found in hemophiliacs. Enhanced aggregation of erythrocytes and increased plasma viscosity typical of these patients indicate that microrheological properties of blood are changed and these changes are likely to be caused by disturbances of the plasma protein composition. The enhanced aggregation of erythrocytes is certainly not beneficial for microcirculation. On the other hand, it can be suggested that enhancement of aggregation of erythrocytes is a compensatory reaction in patients with lower blood coagulability since there is information that enhancement of aggregation of erythrocytes facilitates potentiation of blood coagulation [4, 5].

The present data can be taken into consideration in administration of hemostatic therapy specific for such patients, especially when plasma medications are given, which frequently results in additional microcirculatory disorders.

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