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EFFECT OF TEMPERATURE ON THE RHEOLOGY OF BLOOD IN SURGICAL OPERATIONS ON THE HEART AND MAJOR VESSELS

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The effect of lowered temperatures (hypothermia) on blood rheology during surgical operations on the heart and major vessels is considered. The analysis is based on laboratory and clinical investigations under various temperature conditions of rheometry.

During the development of a major disease, cardiovascular patients acquire a rheological status that is most fravorable to perfusion of organs and tissues and thus contributes to the emergence of oxygenation [1]. The parameters of the blood flow, in turn, reflect and are governed by changes that have already taken effect in the blood, including its rheological parameters [2].

Bringing a patient into and out of the hypothermic state requires exact matching of the energy consumption requirements of tissues and meeting these requirements. However, the theory does not have clear concepts on reasons for the emergence of irreversible damage to vitally important cell organoids under conditions of shortage or absence of energy supply: whether this takes place as a result of primary disorders of vitally important structures or is induced by some indirect disorders, e.g., excess concentrations of calcium or other ions, etc. Nevertheless, it has long been established empirically that, under certain conditions, a low body temperature makes it possible to maintain the vitality of tissues, i.e., their functions can be maintained upon a sharp decrease in energy consumption.

Hypothermia has found most widespread application in cardiovascular surgery in operations carried out under conditions of extracorporal blood circulation. Thus, the temperature is decreased to 24–27°C during operations on the heart, and the minimum temperature reaches 11–13°C in aorta reconstruction operations accompanied by termination of blood circulation. In both cases, the energy consumption requirements of tissues must be decreased, provided that their vitality is maintained. Hypothermia exerts its protective action first of all on cells of the cerebrum, spinal cord, miocardium, kidneys, and liver parenchyma.

Another aspect of this clinical problem concerns the duration of bringing the patient out of the hypothermic state, when heating of tissues, especially the cerebrum, can surpass the possibilities of the systems of blood circulation and breathing to deliver the necessary amount of oxygen and readily oxidizable substrates.

The objective of the present work was to study the rheological properties of blood and the relationships between micro- and macrorheological parameters on a background of nonphysiological changes in the temperature of the patient's body during operations on the heart and major vessels under conditions of extracorporal blood circulation.

Experimental. The rheological properties of blood were studied in 56 patients who underwent operations on the heart and 18 patients who underwent aorta reconstruction operations with prolonged stoppage of blood circulation. Both types of patients are of interest, first of all, due to the fact that hypothermia is an essential component of surgical interventions of this type. However, cardiosurgical patients undergo a less prolonged and pronounced effect of temperature changes, and they usually have a lower of hemodilution degree.

The rheological state of blood and plasma was investigated by the viscosimetric method in the range of shear velocities of 10–300 sec^{-1} and at 200 sec^{-1}, respectively, on an AKR-2 rotation viscosimeter (Russia). The viscosity values obtained were modified by the condition

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$$\eta\ (\max) = 1\ ;\ \eta\ (j) = \eta\ (i)/\eta\ (\max)\quad (\text{arb. units}) \tag{1}$$

and then were processed using a model that we proposed earlier [2, 3] to characterize the dependence of the blood viscosity on the shear velocity:

$$\eta\ (j) = \eta\ (\max)\ (m + (1 - m) \exp\ [- b\ (\eta\ (i) - T)])\ , \tag{2}$$

where $\eta(\max)$ is the maximum value of the blood viscosity in a particular data set (mPa·sec), $\eta(i)$ is the blood viscosity corresponding to a particular shear velocity (mPa·sec), and $\eta(j)$ is the modified value of the blood viscosity, expressed in arbitrary units.

The following parameters were calculated on the basis of the data obtained [4]: 1) relative blood viscosity expressed as the ratio of the maximum blood viscosity in a particular data set to the plasma viscosity, 2) minimum disaggregating shear velocity (parameter T of the model), i.e., the shear velocity at which disaggregation of cell conglomerates in the flow begins (this parameter depends first of all on the state of the central hemodynamics at a particular instant and determines the fluidity of blood as a function of the force tension), 3) shear stress $\tau = \eta\gamma$, 10^{-1} N/m^3, where γ is the shear velocity in sec^{-1}.

The suspension stability of blood was estimated from its viscosity in the absence of cell reactions (parameter m of the model), i.e., as a parameter depending only on the composition of the suspension medium and the volume of the suspended phase. The rate of erythrocyte sedimentation was also used in the investigations.

Aggregation and deformability of erythrocytes were characterized by the corresponding erythrocyte aggregation and deformation indices (EAI and EDI, respectively) expressed as

$$\text{EAI} = \eta\ (\max)/\eta\ \ (\text{at}\ \ \gamma = 100\ \text{sec}^{-1})\ ;\ \ \text{EDI} = \eta\ \ (\text{at}\ \ \gamma = 100\ \text{sec}^{-1})/\eta\ \ (\text{at}\ \ \gamma = 300\ \text{sec}^{-1})\ .$$

Clinical data were processed using the expert software Blood Aggregation State (version 2.1), Prognosis (version 1.0), and Cardiorespiratory Disease Diagnostics (version 5.05) developed in 1990-1995 by our laboratory in collaboration with the Cardioreanimation Department of the Scientific Center for Surgery [5].

Statistical data analysis was carried out using methods that made it possible to take into account and minimize the effects of surgical interventions such as infusion and medicinal therapy, anesthetic measures, the special features of the extracorporal blood circulation, etc.

Results and Discussion. At the beginning of the narcosis period, an increase in the blood viscosity at all shear velocities on the background of a simultaneous decrease in the blood flow rate was observed (Fig. 1). Despite the hemodilution, an increase in the blood velocity by a factor of 2–2.5 compared to the beginning of the operation was observed at all shear velocities on the background of the cooling of the patient. However, the plasma viscosity virtually did not change upon cooling to 28–27°C. At lower temperatures, it increased linearly but by not more than a factor of 1.4–1.5. In our opinion, the circumstance that the rate of the blood viscosity increase exceeded the rate of the plasma viscosity increase upon cooling is of particular importance.

The difference between the values of the arterial and central vein pressures determines the perfusion pressure in peripheral and, mainly, microcirculatory vessels. Its value became stable already at the beginning of the extracorporal blood circulation, and therefore, one could expect a linear temperature dependence of the shear stress and the minimum deaggregating shear rate. However, an analysis of these "force" parameters has shown that the shear stress grows exponentially with a decrease in temperature to 28–27°C and then becomes almost constant. A similar dynamics has also been established for the minimum disaggregating shear rate, but the dependence reached a plateau earlier, already at temperatures of 32–31°C.

The data obtained substantiated the well-known postulates of a linear relationship between the inverse temperature and the natural logarithm of the ratio of the blood and plasma viscosities. It is known from the theory that an increase in the apparent asymptotic viscosity takes place that is connected with molecular-kinetic processes in blood. It is assumed that the temperature dependence is determined by plasma properties, and not by erythrocyte bonding. Therefore, hemodilution, e.g., decreasing the hematocrit value, is an imperative condition for preserving perfusion of tissues and preventing blood stasis on the background of a simultaneous drop in the blood flow rate

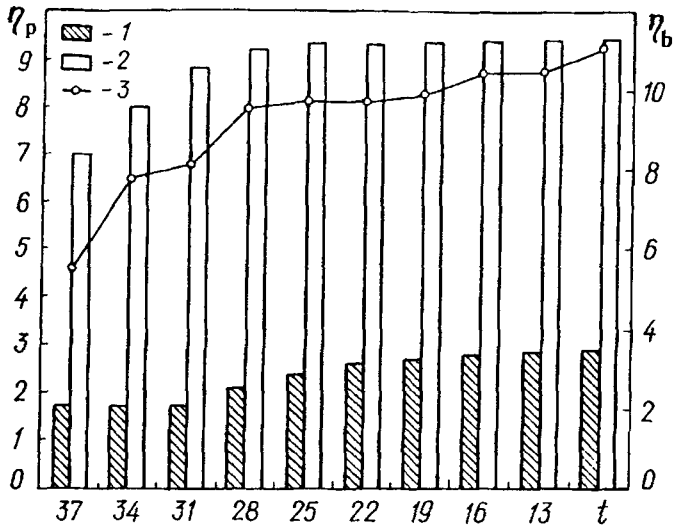

Fig. 1. Dynamics of macrorheological parameters on the background of cooling: 1) η_p; 2) MDSV, sec^{-1}; 3) η_b at a shear velocity equal to MDSV, mPa·sec.

[6]. In other words, hemodilution seemingly bufferizes an increase in the blood viscosity. It is believed that, taking into account the above-mentioned circumstance, the blood viscosity at 37°C is virtually the same as at 25°C. Most likely, this can be shown to be true if blood viscosity values are corrected only with respect to the hematocrit value. However, a temperature decrease both affects the blood plasma structure and changes substantially the process of erythrocyte aggregation and their deformability. These facts form the basis for the counteropinion that, despite hemodilution, an increase in blood viscosity actually takes place in response to a temperature decrease. It should be noted that our observations agree with this concept.

Dynamics of microrheological parameters are presented in Fig. 2. As is evident, a pronounced increase in erythrocyte deformability and a decrease in the suspension stability of blood were detected on the background of cooling of the patient to 32–31°C. Taking into account that an increase in shear tension was detected simultaneously, we can assume that the microrheological changes in this temperature range have a compensatory character directed toward maintainance of tissue perfusion on the background of the hypothermia.

A monotonic almost linear change in the microrheological parameters, namely, the erythrocyte sedimentation rate and their aggregation and deformability indices, was observed within the temperature range from 32 to 28–27°C. With a further decrease in the temperature, a sharp decrease in the aggregation and sedimentation rate of erythrocytes and, which is essential, their deformability is observed. However, a paradoxical increase in the aggregation ability of erythrocytes, followed with a small delay by their sedimentation rate, was observed in the temperature range from 18–17 to 13–11°C. On the other hand, the erythrocyte deformability continued to decrease, which was substantiated by results of a "packing test." Desprite an increase in the plasma viscosity, a pronounced decrease in the suspension stability of blood was simultaneously detected upon cooling the patient in the same range from 28–27 to 18–17°C. A further temperature decrease no longer affected this parameter substantially.

An analysis of the data has shown that the relationship between the temperature and the microrheological parameters is not described by a unique function but can be successfully represented by a piecewise linear approximation. Most likely, the nonlinearity of the temperature dependence of the viscosity of blood is determined by the changes in the microrheological properties on the background of hypothermia.

The following circumstance draws attention. The increase in the blood viscosity with a decrease in the temperature takes place in a rather smooth manner. By contrast, the microrheological parameters change rather sharply and the direction of their changes is different in different temperature ranges. In this connection, it is important that the growth of the blood viscosity exceeded the rate of increase of the plasma viscosity upon decrease

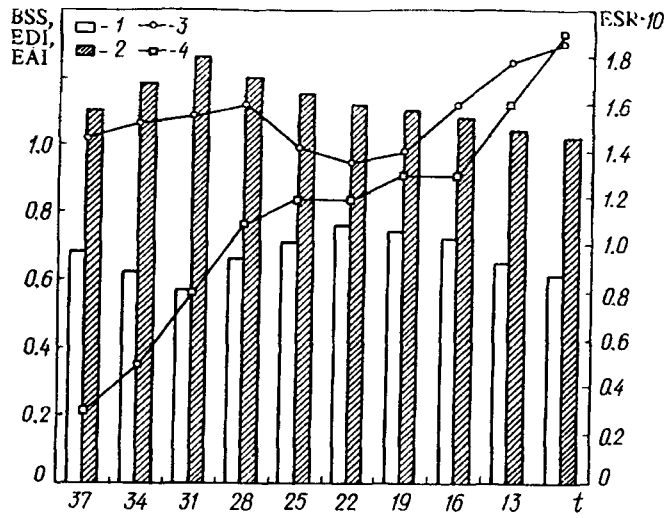

Fig. 2. Dynamics of microrheological parameters on the background of cooling:
1) BSS, 2) EDI, 3) EAI, 4) ESR.

of the temperature. Therefore, it is the suspension medium, i.e., the plasma, that resists the general effect of the blood viscosity increase.

Our explanation is as follows: the life-compatible changes in the quantities of the components of plasma are rather large, which determines its role as a conservative, most stable element in blood as a suspension system. In other words, plasma comprises a buffer resisting pathological changes in blood viscosity and, as a consequence, a decrease in its fluidity. However, these buffer possibilities are limited, and at a certain instant, the modifying effect of the temperature starts to influence the viscosity properties of plasma itself. This is the instant when the increase in the blood viscosity acquires a decompensated character under conditions of hypothermia.

Therefore, it is evident that, on the background of cooling of the organism, the aggregation activity and deformability of erythrocytes are leading factors controlling the conditions of blood flow, especially, in peripheral vessels. In other words, under conditions of hypothermia and with constant force characteristics, the dynamics of the rheological properties of blood is governed mainly by the functional state of the erythrocytes. In our opinion, certain discrepancies between this conclusion and the concept of the leading role of plasma in this process originate from the conditions of the investigations: results of *in vitro* experiments by no means necessarily coincide with clinical data.

The problem of the reversibility of the above-mentioned hemorheological changes is of paramount importance for clinical practice. It should be noted that the current context assumes that the reversibility does not consist in the recovery of the original values of the rheological parameters. Surgical modification of the coronary or major alveus instantaneously affects the blood rheology. The new conditions of blood flow determine the formation of a rheological state adequate for the new level of blood supply to tissues and organs. Therefore, we evaluate the reversibility from the extent to which the new values of the rheological parameters correspond to the required level of tissue blood flow. In other words, the observed changes in the rheological parameters on the background of a particular state of the central hemodynamics either enhance or inhibit the vital activity and energy production of tissues. The frequency of organ disorders and the risk levels of thrombohemorrhagic and hypoxic complications play the role of criteria.

As is evident from Fig. 3, the dynamics of the microrheological parameters during heating of the patient is basically different from that observed on the background of cooling. First of all, the parameters virtually did not change until the patient's temperature reached 27–28°C. Then, an increase in the suspension stability of the blood, improvement in the erythrocyte deformability, and some decrease in their aggregation activity took place. Simultaneously, a decrease in the minimum disaggregating shear velocity and the shear stress was observed.

It is crucial that the fastest response to a temperature increase was demonstrated by the plasma viscosity, whose decrease was reliably detected already at 20–21°C. The jump in its values at 32–33°C was not directly

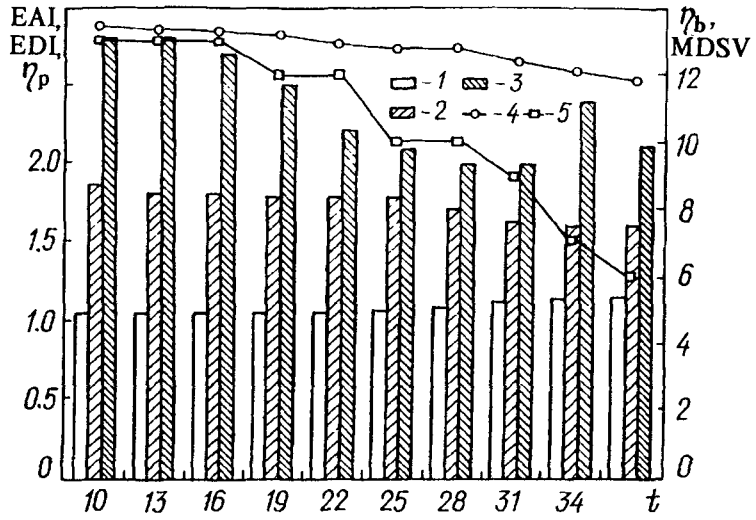

Fig. 3. Dynamics of rheologiocal parameters on the background of heating: 1) EDI, 2) EAI, 3) η_p, 4) η_b, 5) MDSV, sec^{-1}

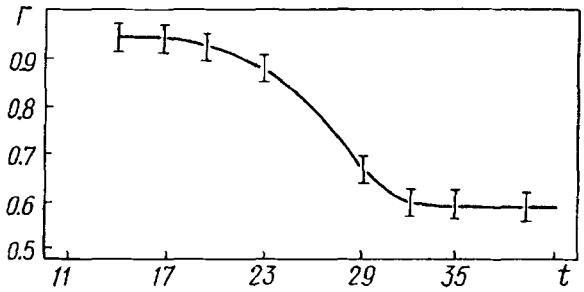

Fig. 4. Effect of hypothermia duration and temperature on the degree of risk of hypoxic damage to organs and tissues. $\Gamma = f(\eta_{max}$, Hct, EAI, EDI, $t)$.

caused by a temperature effect: this was a consequence of the emergence of a large amount of metabolites and products of tissue activity from the "opening" peripheral alveus.

Nevertheless, as during the cooling, the dynamics of the viscosity values of whole blood was more smooth. However, even on the background of physiological temperatures of 35–36°C, the viscosity of whole blood at all shear velocities remained higher than normal.

The results of the work suggest that the following are the leading factors affecting the reversibility of the rheological properties of blood: 1) the duration of the stay at the minimum temperature; 2) naturally, the value of the minimum temperature reached during the surgical intervention.

Taking into account that irreversible disorders in the blood rheology are directly related to the degree of thrombohemorrhagic complications during the postperfusion period, we considered the problem of the effect of the duration of the hypothermic period on the rheological properties of blood. As was expected, the longer the hypothermic period, the more pronounced the thrombohemorrhagic syndrom and, correspondingly, the less reversible the changes in the rheological parameters.

However, an analysis of the data has revealed that the possibility of forming a rheological state in which satisfactory blood flow is provided (first of all in the peripheral alveus) is only 38–40% determined by the duration of the hypothermic period (Fig. 4). The main share of the variability of the level of risk of thrombohemorrhagic complications (60–62%) is determined by the minimum temperature reached during the surgical intervention [7].

We have managed to approximate the risk level of hypoxic complications by a model in which the plasma viscosity, hematocrit, erythrocyte deformability index, minimum disaggregating shear velocity, and temperature are used as parameters.

According to this model, the probability of hypoxic complications decreases rapidly with change in the temperature from 21–22 to 31–32°C. At lower and higher temperatures, this dependence virtually approaches a

plateau, i.e., the risk of hypoxia is attributable to other causes not of a rheological nature. On the other hand, reversal of hypothermic changes in the rheological parameters of blood is most intense within the temperature interval from 21 to 32°C. In our opinion, the level of risk of thrombohemorrhagic and hypoxic complications and the frequency of organ disorders can be used in this case as reversibility criteria for hemorheological changes on the background of hypothermia [8].

In clinical practice, it is of course important to know where the boundary between the normal and pathological states is located and, therefore, what prognostic value the observed changes in the rheological parameters on the background of hypothermia have for the entire organism. No definite answer han been given to these questions so far, and we also cannot give an answer today. Nevertheless, we are certain that the answer cannot be found if blood rheology is considered as an isolated entity: data on the state of other systems of the organism must be included. In our opinion, today this is the most promising approach to the solution of the problem of diagnostics and prevention of homeostasis disorders in patients operated upon under conditions of extracorporal blood circulation.

CONCLUSIONS

1. Cooling of the patient is accompanied by a persistent increase in the plasma velocity. On the background of cooling of the organism, the erythrocyte aggregation activity and deformability are leading factors controlling the conditions of blood flow, especially in the peripheral alveus. The general increase in the blood viscosity observed as a result of the action of all factors is induced, first of all, by changes in the microrheological parameters of the blood.

2. The dynamics of the rheological parameters during heating of the patient is governed mainly by the plasma viscosity, whose value is determined by changes in the biochemical composition of the plasma on the background of reperfusion.

3. None of the rheological parameters recover their original value after major operations on the heart and vessels. However, this circumstance bears witness not to pathological but to compensatory changes in the rheological properties of blood taking shape under the new conditions of blood flow and tissue supply.

4. In blood as a suspension system, plasma plays the role of a conservative and most stable component preventing pathological changes in the blood viscosity and, as a consequence, a decrease in its fluidity upon nonphysiological temperature changes. On the other hand, the reversibility of changes in the rheological parameters depends on the duration of the hypothermic period and the minimum temperature reached during the surgical operation.

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NOTATION

MDSV, minimum disaggregating shear velocity, sec^{-1}; BSS, blood suspension stability, arb.units; EAI, erythrocyte aggregation index, arb.units; EDI, erythrocyte deformation index, arb.units; ESR, erythrocyte sedimentation rate, mm/h; Γ, probability of hypoxic complications, arb.uunits; Hct, hematocrit, %; t, temperature, °C; η_p, η_b, plasma and blood viscosity, mPa·sec.

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