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INNOVATIONS IN THE MODELING OF THE RHEOLOGICAL PROPERTIES OF BLOOD

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A simple substantiation of the application of backward light scattering to diagnostics of the aggregation state of blood has been proposed. It has been shown that the kinetics of spontaneous and shear aggregation obeys the kinetics of second order (Smolukhowski kinetics) and that the Smolukhowski constant is a function of the shape of an erythrocyte and the concentration of a high-molecular-weight polymer and it linearly depends on the rate of shear. The form of the dependence of the average size of erythrocyte aggregates on the rate of shear has been established. An expression for the apparent viscosity of blood as a function of the average size of an erythrocyte has been obtained; this expression has the form of a logarithmic asymptotics which remains constant with variation of the macromolecular composition of the plasma, the action of plasmapheresis, and the change in the hematocrit and enables one to determine both the rate of shear at which the process of disaggregation begins and the rate of shear in total disaggregation of erythrocytes and accordingly the maximum and minimum values of the viscosity of the blood.

Introduction. Procedures studying the aggregation properties of blood have recently begun to prevail in hemorheological investigations. Most of these methods involve recording of the backward light scattering from the blood surface. However there is no theoretical substantiation and investigation of the relation between the parameters obtained and the viscosimetric characteristics of the curve of flow of the blood. We seek to propose our own interpretation of the method and to investigate the relations between the parameters of micro- and macrorheology at least as a first approximation.

The erythrocytes of human blood form linear aggregates in whole blood, which are called rouleaux. Rouleaux are destroyed under the action of the external force and are reconstructed again once its action ceases, i.e., they are reversible. The formation of rouleaux significantly affects the rheological behavior of blood in the flow. In this connection, a great deal of experimental and theoretical investigations of the processes of formation and destruction of erythrocyte aggregates have been described. The flow of erythrocyte aggregates has been observed microscopically in a modified "cone–plate" viscosimeter [1–3] and it has been shown that the size of the aggregates in human blood decreases with increase in the rate of shear. Shiga et al. have designed a device for determination of the rate of formation of rouleaux. In addition to the modeling of the kinetics of spontaneous aggregation throughout the range (from the stopping of the flow to the total aggregation of erythrocytes) by the sum of two exponents [5, 6], it has been proposed that the Smolukhowski kinetics be used [7]. A mathematical model of the process of aggregation of erythrocytes has been proposed in [8] in accordance with the Smolukhowski theory developed for description of the kinetics of agglomeration of colloidal particles. The equation obtained involved two parameters characterizing the aggregation: the average size of rouleaux in equilibrium and the aggregation rate. Here the influence of such factors as the temperature, dilution with plasma and dextran in different concentrations, and decrease in the osmolarity of a medium was evaluated.

In this work, we propose the simplest model of backward scattering of light in aggregation and disaggregation of erythrocytes within whose framework we discuss the range of applicability of the Smolukhowski theory to description of these processes and make comparisons to experimental data obtained by the methods of aggregometry (photometry of backward light scattering) of [6, 7, 9, 10].

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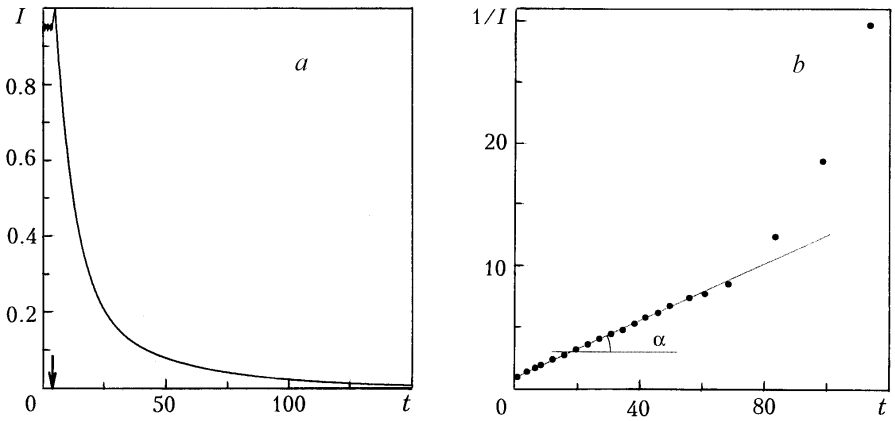

Fig. 1. Curve of spontaneous aggregation of erythrocytes as a function of the change in the intensity of backward scattering of light I (a); in the coordinates (t, $1/I$) (b). The arrow shows the instant of stopping of the flow. t, sec; I, conv. units.

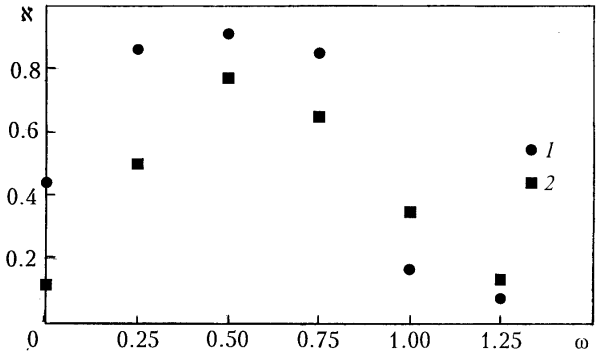

Fig. 2. Rate of the process of spontaneous aggregation א vs. concentration of high-molecular-weight dextran ω in two experiments on different samples of whole blood: 1) healthy male; 2) healthy female. ω, %; א, sec^{-1}.

Materials and Methods. Blood was taken from the cubital vein and was stabilized with 0.3 ml of a 7% solution of ethylenediaminetetraacetic acid (EDTA) per 10 ml of blood. In all of the experiments, we used whole blood or a suspension of erythrocytes in autologous plasma with the required value of the hematocrit determined by standard centrifugation. Dextran-500 (D-500) was used to change the macromolecular composition of the plasma. The blood was stored using a glucose-citrate preservative at a temperature of $+4^{o}$C.

We investigated the aggregation and disaggregation of erythrocytes on a coaxially cylindrical aggregometer of our own design by recording a change in the intensity of the backward light scattering I from a 1-mm-thick layer of blood [6].

Results and Their Discussion. In spontaneous aggregation of erythrocytes, the curve of change of the backward light scattering is a monotonically decreasing function, and the entire process is completed during the first three minutes. The curve of spontaneous aggregation of diskocytes is straightened in the coordinates $1/I = f(t)$ with a correlation factor of more than 0.9 over $93 \pm 2\%$ of the overall amplitude of change of the light-scattering signal (Fig. 1). This suggests that the curve of change of the backward light scattering obeys the hyperbolic law with a rate constant of spontaneous aggregation א = tan α.

If we vary א by inducing the aggregation process by a high-molecular-weight dextran (D-500), we obtain the dependence of the rate of spontaneous aggregation א on the concentration of the aggregant (Fig. 2), which is consistent with the data in [8]. Thus, it may be assumed that the constant א is a function of the concentration of the high-molecular-weight aggregant in the plasma of the blood, i.e., א = f(ω).

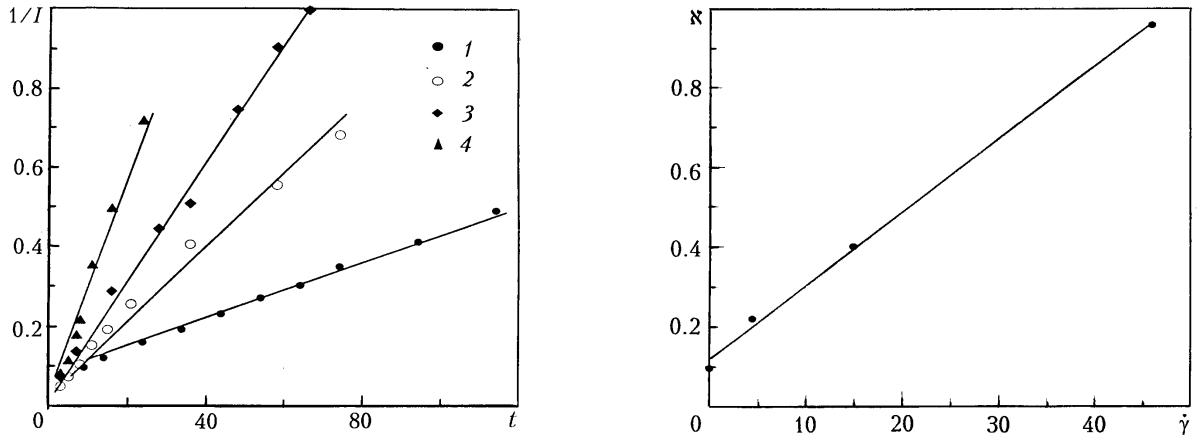

Fig. 3. Plots of the processes of shear aggregation of erythrocytes in the coordinates $1/I = f(t)$: 1) $\dot{\gamma} = 0$, 2) 4.5, 3) 15, and 4) 46 sec^{-1}. *t*, sec; *I*, conv. units.

Fig. 4. Rate constant of shear-induced aggregation ℵ vs. rate of shear. $\dot{\gamma}$, ℵ, sec^{-1}.

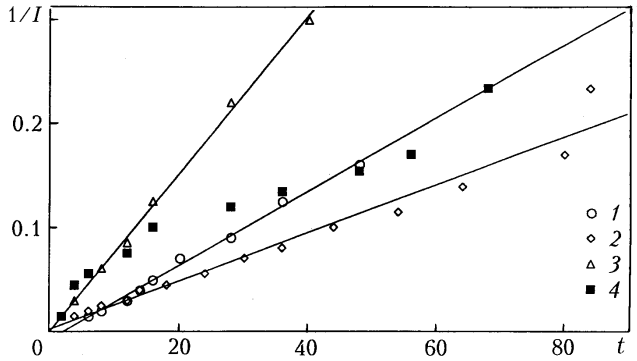

Fig. 5. Dynamics of the kinetics of spontaneous aggregation of erythrocytes $1/I$ with change in the shape of the cells as a result of the storage of the blood in a glucose-citrate stabilizer at a temperature of $+4^{o}$C: 1) issue; 2) 5 days of storage of the blood; 3) 15 days; 4) 25 days. *t*, sec; *I*, conv. units.

The possibility for the disclosed kinetics of aggregation to be preserved in the process of shear-induced approach of erythrocytes has been investigated in special experiments. After reaching the total disaggregation at 1000 sec^{-1} the rate of shear changed abruptly (in 1 sec) to one value: 0, 4.5, 15, or 46 sec^{-1}. From Fig. 3 it is clear that the kinetics of aggregation induced by the rate of shear corresponds to the linear dependence.

The constant of the process of formation of the aggregates ℵ also changes — it becomes a function of the rate of shear. Figure 4 shows that this dependence has the linear form

$$\aleph = \aleph_0 + B\dot{\gamma}\,.$$

The linear form of the kinetics of spontaneous aggregation of erythrocytes can be disturbed when the erythrocytes lose their diskoidal shape, which is caused by different actions but the most natural is the diskocyte becoming pin-like disks and then spherocytes and echinocytes when the blood is stored for longer than 20 days.

From Fig. 5 it is clear that the linear kinetics is preserved up to the storage limits (less than 20 days) and is transformed to an S-shaped curve with a total loss of shape.

One basic property of the constant ℵ is the dependence of the process of aggregation on the concentration of aggregating erythrocytes. Results of the experiments on five samples of blood in a wide range of the hematocrit of 0.1 to 0.8 are shown in Fig. 6. The correlation coefficient was 0.72, i.e., ℵ is a linear function of the hematocrit.

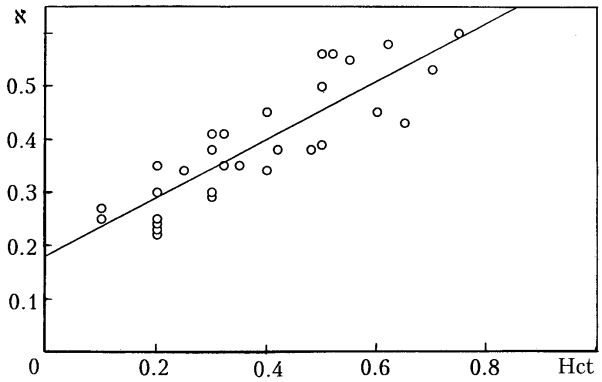

Fig. 6. Linear correlation of the dependence of the rate of spontaneous aggregation of erythrocytes on the volume concentration of erythrocytes (hematocrit). Hct, rel. units; $\aleph$, $\sec^{-1}$.

The above examples show that the kinetics of spontaneous and induced aggregation of erythrocytes belongs to the kinetics of second order and it is described by the Smolukhowski equation as applied to the aggregation of erythrocytes in the form

$$\frac{1}{n} - \frac{1}{N_0} = \aleph t \,. \tag{1}$$

From (1) we obtain

$$\frac{\langle N \rangle}{N_0} - \frac{1}{N_0} = \aleph^* t \tag{2}$$

or

$$\langle N \rangle - 1 = \aleph^* N_0 t \,. \tag{3}$$

Thus, the quantity $1/I$ is in proportion to the average size of erythrocyte aggregates $\langle N \rangle$ determined by the number of erythrocytes in the aggregates.

Let us consider in the most general form the formation of the time-varying component of backward-scattered light in aggregation of erythrocytes. The constant component of backward-scattered light is related to the scattering on the plasma and the internal structure of an erythrocyte, which are unaffected by the process of formation of erythrocyte aggregates. Therefore, the change in the light scattering in aggregation is a result of the different number of refractions in transmission by the layer of blood, since only the plasma–erythrocyte membrane interface changes in the process of aggregation for the relative refraction index $n_r = 1.07$. Indeed, in erection of rouleaux, the interface of one rouleaux changes as

$$S(t) = S_0 + S_1 \langle N(t) \rangle \,, \tag{4}$$

whence, summing over the number of aggregates in unit volume $n = N_0 \langle N(t) \rangle$, we obtain

$$S_{\text{tot}}(t) = \sum_i^n S_i(t) = S(t)\, n = S_0 n + S_1 \langle N(t) \rangle\, n \,,$$

$$S_{\text{tot}}(t) = \frac{S_0 N_0}{\langle N(t) \rangle} + S_1 N_0 \,. \tag{5}$$

Since the total interface is in proportion to the intensity of backward light scattering, varied in the process of aggregation, i.e., $S_{tot}(t) \sim I(t)$, then $1/I(t) \sim \langle N(t) \rangle$

$$I(t) = N_0 \left(\frac{S_0}{\langle N(t) \rangle} + S_1 \right) \tag{5'}$$

or

$$\langle N(t) \rangle = \frac{S_0 N_0}{S_{tot}(t) - S_1 N_0}. \tag{6}$$

Then the Smolukhowski equation will have the form

$$\frac{S_0 N_0}{I(t) - S_1 N_0} - 1 = \aleph^* N_0 t. \tag{7}$$

The obtained coefficient $\aleph = \aleph^* N_0$ must possess the properties of the rate constant of aggregation of second order and be controlled by the diffusion of erythrocytes.

First of all, this constant must be a function related to the diffusion coefficient of erythrocytes [11]:

$$D = f(\text{Hct})\, \alpha\dot{\gamma}.$$

This dependence has been confirmed experimentally, which is shown in Figs. 3, 4, and 6.

Acceleration of the spontaneous aggregation of erythrocytes upon the introduction of high-molecular-weight polymers (dextran, fibrinogen, immunoglobulins, etc.) depends not only on the rate of formation of macromolecular bridges but also on the rate of approach of the erythrocytes and the aggregates. The latter can be referred to neither Brownian motion nor sedimentation. It is common knowledge that one can disregard the Brownian mobility of erythrocytes [12]. Sedimentation is effective only in the vertical direction, whereas visual observation of the aggregation shows not only the vertical motion but also the horizontal motion of the aggregating erythrocytes and rouleaux, especially in plane blood layers with a thickness of tens of μm (for example, the Goryaev chamber) and in sufficiently diluted suspensions with a hematocrit of 0.2–0.1. In accordance with different theories, the diffusion coefficient of particles is in inverse proportion to the viscosity of a medium [13]. As the concentration of the high-molecular-weight components of the plasma increases, its viscosity $\eta_{pl} = \eta_0(1 - k\omega)^{-1}$ grows [14]; therefore, the acceleration of aggregation is inconsistent with the available theories that could describe the process of approach of erythrocytes and rouleaux. A statistical analysis of voluminous clinical material has shown a high positive correlation between the constant $\aleph$ and the viscosity of the plasma of blood. Thus, the Spearman coefficient of rank correlation was ± 0.54 ($p < 0.05$) while the coefficient of linear correlation was $+0.50$ ($p < 0.01$). These data confirm the fact that the existing theories are unable to explain the process of approach in spontaneous aggregation. The hypotheses for the structuring of the plasma and the possibility of long-range interaction between erythrocytes have already been expressed in the literature [15, 16]. The mechanisms of approach and the viscous mechanisms counteracting the approach are competing. This is precisely the reason for the two-phase nature of a $\aleph$ change (see Fig. 2). With an increase of more than 0.5% in the concentration of dextran viscous effects begin to prevail, which keep the erythrocytes from approaching each other. The experiments show that $\aleph$ possesses all the properties of the Smolukhowski constant and hence the quantity $1/I$ is indeed in proportion to the average size of erythrocyte aggregates $\langle N \rangle$. Application of the Smolukhowski theory to description of the spontaneous aggregation of erythrocytes leads to certain discrepancies. The diffusion-controlled kinetics of second order [17] assumes a rather free movement of the reacting components, i.e., the distance between the erythrocytes must be larger than their size. However, when the hematocrit is 0.4, the average distance between the cells is only 1.5 μm, which is much smaller than the erythrocyte size. Not only does such a concentration exclude translational motion but it also restricts the rotational mobility of the cells [18]. It is probable that only cluster construction of erythrocytes, related to the restricted free rotation of them, in stopping the blood can facilitate the diffusion erection of rouleaux from individual erythrocytes within the cluster. In this case the kinetics of aggregation is

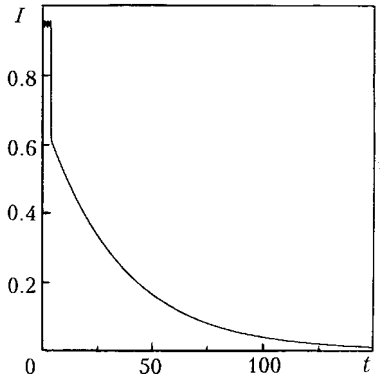

Fig. 7. Change in the intensity of backward light scattering I in the case of hereditary hypercholesteremia. t, sec; I, conv. units.

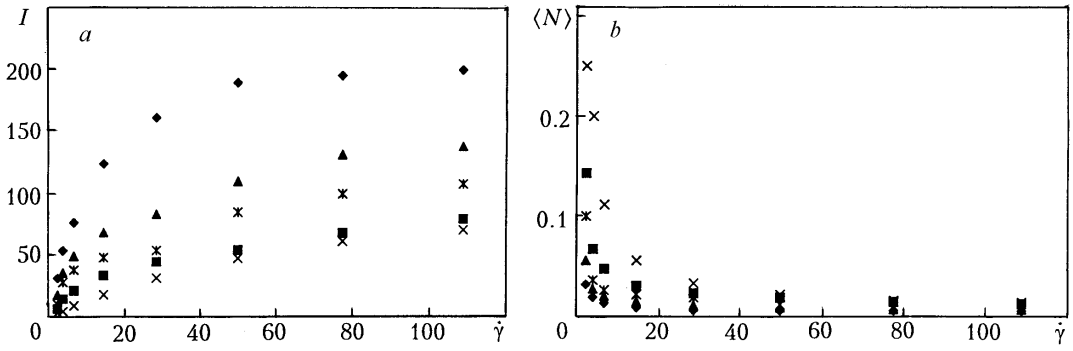

Fig. 8. Intensity of backward light scattering I (a) and average size of the aggregates $\langle N \rangle$ (b) vs. rate of shear $\dot{\gamma}$. The points belong to different blood samples differing in aggregate strength that cannot be evaluated quantitatively in this presentation of the results. $\dot{\gamma}$, $\sec^{-1}$; I, conv. units; $\langle N \rangle$, rel. units.

controlled by the rotational diffusion of the erythrocytes. The formation of paired aggregates is due to the rotation of the erythrocytes, which in turn disturbs the orientation of neighboring cells. Thus, the rotational motions in the volume will be stochastic. This process ends in the "collapse" of the cluster into one aggregate followed by the coalescence of the structures formed. As we believe, the motive force of the aggregation is the rate of formation of intererythrocyte "bridges" and the length of the erythrocyte's "atmosphere" [15] consisting of structurized macromolecules.

Normally and in most of the pathologic states, we have a wide distribution of the erythrocytes in aggregation properties to the extent that individual cells do not participate in the aggregation process at all and they remain excluded from the rouleaux. Therefore, the curve of change of the intensity of backward light scattering is usually monotonically decreasing. If we have a synchronous formation of paired aggregates, the intensity of backward light scattering must change nearly twofold in accordance with (5′). Such a kinetics of spontaneous aggregation of erythrocytes very seldomly occurs; we have recorded it [19, 20] only in hereditary hypercholesteremia as a reflection of the monoclonality of the aggregation properties of erythrocytes (Fig. 7).

At the present time, the kinetic approach prevails in modeling the aggregation and disaggregation of erythrocytes in shear flows of blood [21–23] and generalized kinetic equations have been derived with allowance for the sticking together and breaking of aggregates. According to these models [21–23], large aggregates are broken, upon a stepwise increase in the rate of shear, and the length-distribution function of the aggregates in the system changes in the direction of smaller lengths. The stationary distribution is formed via the transient process of breaking of large aggregates and sticking together of small ones with the formation of a certain average size. The assumption substantiated experimentally and theoretically that the quantity $1/I$ is in proportion to the average size of erythrocyte aggregates $\langle N \rangle$ can be employed for analysis of the process of disaggregation of erythrocytes in the shear flow of blood. Disaggregation was carried out by increasing stepwise and successively the rate of shear from the instant of equilibrium total aggregation at $\dot{\gamma} = 0$ [20]. The aggregation state of whole blood was determined by continuous measurement of

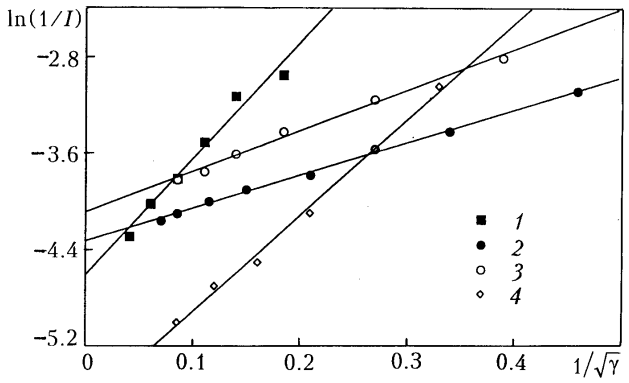

Fig. 9. Quantity $1/I$ proportional to the average aggregate size $\langle N \rangle$ vs. rate of shear in the coordinates $(1/\sqrt{\dot\gamma}, \ln(1/I))$. The points correspond to the blood samples with different strength of the aggregates: 1 and 4 denote the blood samples with lower strength of the aggregates than 2 and 3 (the aggregate strength is determined from the slope of the plot). $\dot\gamma$, $\sec^{-1}$. I, conv. units.

the intensity of backward light scattering $I(\dot\gamma)$. The flow curve $\eta_a = \eta_a(\dot\gamma)$ of the same sample of blood was obtained on a viscosimeter with a floating measuring beaker within the rates of shear from 1 to 200 $\sec^{-1}$. Figure 8a shows the dependence of I on $\dot\gamma$ that can be approximated by the function of the form

$$I(\dot\gamma) = I\left[1 - \exp\left(-\frac{\dot\gamma}{\beta}\right)\right], \tag{8}$$

which was the empirical reason to take it as a basis for the system being currently used for evaluation of the aggregate strength [9].

Figure 8b shows that the dependence $1/I(\dot\gamma) \sim \langle N(\dot\gamma)\rangle$ on the change in the rate of shear appears as a rapidly decreasing function which is straightened in the coordinates $(1/\sqrt{\dot\gamma}, \ln(1/I))$. Figure 9 gives four experimental curves of the blood samples differing in the strength of the aggregates (different slopes of the curves: the larger the slope, the slower the change in the aggregate size).

The function $\ln\langle N\rangle = f(1/\sqrt{\dot\gamma})$ is in conformity with the general principles formulated in [24], where Scott-Blair has proposed the following equation describing the breaking of bonds on change in the rate of shear:

$$\frac{dJ}{d\dot\gamma} = \frac{J(\dot\gamma)}{\dot\gamma}. \tag{9}$$

Since the number of bonds corresponds to the average number of erythrocytes in an aggregate $\langle N\rangle$ and $\dot\gamma$ can be represented as the power function $\dot\gamma^m$, we obtain

$$\frac{d\langle N\rangle}{d\dot\gamma} = A\frac{\langle N\rangle}{\dot\gamma^m}. \tag{10}$$

When $m = 3/2$, we have

$$\ln\langle N\rangle = \frac{C_1}{\dot\gamma^{1/2}} + C_2. \tag{11}$$

Satisfying the boundary conditions $\langle N\rangle\big|_{\dot\gamma=\dot\gamma_2} = 1$, and $\langle N\rangle\big|_{\dot\gamma=\dot\gamma_1} = N_0$, we obtain

$$C_2 = -\frac{C_1}{\dot\gamma_2^{1/2}},$$

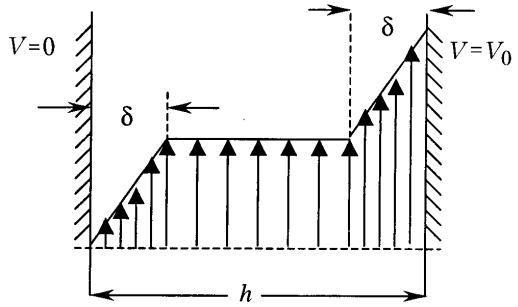

Fig. 10. Profile of the velocities of laminar blood flow between the cylinders of the aggregometer at a low rate of shear corresponding to the core flow.

$$\ln \langle N_0 \rangle = C_1 \left(\frac{1}{\dot{\gamma}_1^{1/2}} - \frac{1}{\dot{\gamma}_2^{1/2}} \right).$$

Then (11) has the form

$$\ln \langle N \rangle = \frac{\ln \langle N_0 \rangle}{\left(\frac{1}{\dot{\gamma}_1^{1/2}} - \frac{1}{\dot{\gamma}_2^{1/2}} \right)} \left(\frac{1}{\dot{\gamma}^{1/2}} - \frac{1}{\dot{\gamma}_2^{1/2}} \right). \tag{12}$$

Such a semiempirical approach is quite in the tradition of the rheology of concentrated disperse systems [25].

A relation similar to (12) is given in [26] for the average size of rouleaux L:

$$\frac{L}{L_0} = \frac{k_0}{k_0 + k_1 \dot{\gamma}^m} = \frac{1}{1 + k_1 \dot{\gamma}^m}, \tag{13}$$

where $L = L_0$ at $\dot{\gamma} = 0$.

A more complex theoretical equation for the average aggregate size has been proposed in [22]:

$$\langle N \rangle = \frac{1}{2} (1 + \sqrt{1 + 2\lambda}), \tag{14}$$

where

$$\lambda = \frac{2}{k_{cd}} \left\{ 1 + \frac{k_{12}}{\dot{\gamma}/\dot{\gamma}_s} \right\} \text{ at } \frac{\dot{\gamma}}{\dot{\gamma}_s} \le 1; \quad \lambda = \frac{2}{k_{cd}} \left\{ \frac{1}{\dot{\gamma}/\dot{\gamma}_s} + \frac{k_{12}}{(\dot{\gamma}/\dot{\gamma}_s)^2} \right\} \text{ at } \frac{\dot{\gamma}}{\dot{\gamma}_s} \ge 1,$$

and $\dot{\gamma}_s$ is the rate of shear at whose lower value the process of shear aggregation dominates over disaggregation.

Relations (13) and (14) have not been checked experimentally, and we are unable to attain their accurate quantitative agreement with our experimental data since they have been derived from the concept of the erection and destruction of rouleaux in the shear flow without restricting the mobility of cells. When the hematocrit is 0.4, the impossibility for the erythrocytes to freely move makes probable just end interaction in the case of random orientation of the cells. To preserve the rouleau approach to aggregation we must recognize the cluster composition of the stopped erythrocyte flow that ensures the rouleau structure at low rates of shear, and the process of destruction of the aggregates with growth in the rate of shear is effected by splitting of asymmetric formations consisting of rouleaux. This process of destruction covers the boundary wall layer with a gradual decrease in the dimensions of the core flow and increase in the thickness of the wall layer whose viscosity grows with the concentration of the rouleaux in it (Fig. 10).

Thus, the average size of erythrocyte aggregates is a conventional quantity reflecting mainly the processes in evolution of the wall layer. From Fig. 10 it is clear that with such a flow the rate of shear specified by the viscosime-

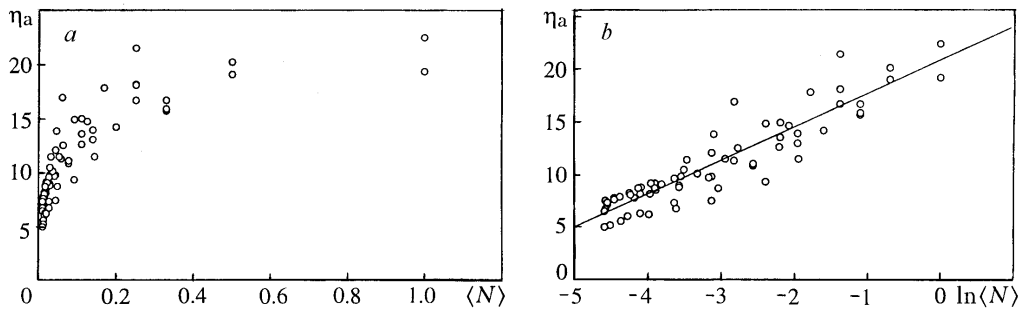

Fig. 11. Apparent viscosity of blood vs. average size of erythrocyte aggregates (a); in a semilogarithmic coordinate system (b) (r = 0.92, $p < 0.05$). $\langle N \rangle$, rel. units; η_a, mPa·sec.

ter is the value averaged over the gap thickness h and it can differ by an order of magnitude from the true value in the boundary layers [27]. Therefore, the relation between the apparent viscosity η_a and the average size of the aggregates $\langle N \rangle$ can be just phenomenological, which is shown in Fig. 11a. The viscosity of each blood sample was determined on a rotational viscosimeter, and the aggregometry was determined by the method of backward light scattering. The vessel part of both devices corresponded to geometrical similarity. The dependence obtained is nearly logarithmic, which is consistent with none of the theories published earlier.

The dependence in Fig. 11a is straightened in the coordinates (ln (1/I), η_a) (with a coefficient of linear correlation of r = 0.92), as is shown in Fig. 11b.

To confirm the fact that such straightening occurs in the case of a change in the volume concentration of erythrocytes we conducted experiments for hematocrits of 0.2 and 0.6. The linear dependence of the viscosity of blood on the average size of the cell aggregates on a semilogarithmic scale holds as the volume concentration of the cells changes.

One cannot obtain such a dependence by employing only the hydrodynamic disturbance of the flow in concentrated suspensions. Even cellular hydrodynamic models can describe the behavior of only not aggregating particles, and allowance for the axial ratio yields a function of rapid increase. However we can rely on the opinion of Happel and Brennev [28] that friction due to the contact of particles can be of crucial importance at high concentrations. In this case, the shearing resistance is much higher than that predicted only from hydrodynamic considerations and it will strongly depend on the distance between particles. Therefore, the viscosity of blood as of a concentrated suspension can, as a first approximation, be a function of the free volume of the aggregate, i.e., the quantity (1 – Hct)/n. Thus, we may write that the rapidity of change of the viscosity η_a as the aggregate size $\langle N \rangle$ changes is a function inversely proportional to the free volume of the plasma per aggregate:

$$\frac{d\eta_a}{d\langle N \rangle} = \frac{B}{\dfrac{1 - \text{Hct}}{n}} = B \frac{N_0}{(1 - \text{Hct})\langle N \rangle}. \tag{15}$$

Since $N_0 \sim$ Hct

$$\frac{d\eta_a}{d\langle N \rangle} = \text{const} \frac{\text{Hct}}{1 - \text{Hct}} \frac{1}{\langle N \rangle}, \tag{16}$$

whence

$$\eta_a = C_1^* \frac{\text{Hct}}{1 - \text{Hct}} \ln \langle N \rangle + C_2^*. \tag{17}$$

When $\langle N \rangle$ = 1, the apparent viscosity is equal to the asymptotic viscosity ($\eta_a = \eta_\infty$), i.e.,

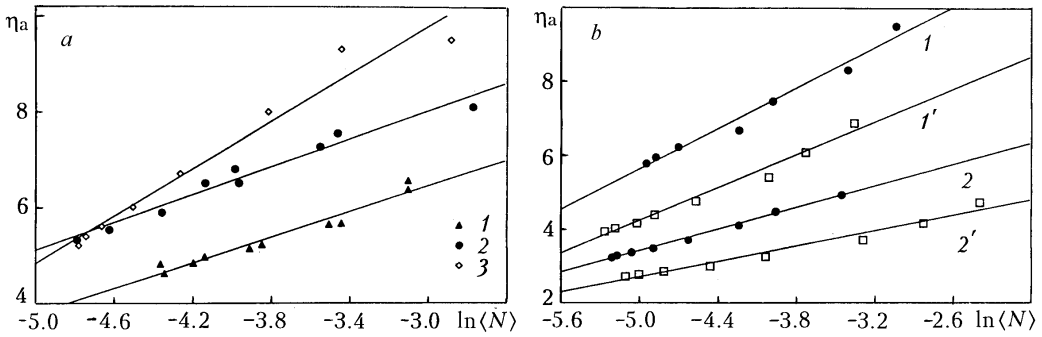

Fig. 12. Viscosity of blood vs. average size of erythrocyte aggregates: a) with change in the concentration of dextran D-500 in the blood [1) 0.5, 2) 0.25, and 3) 0]; b) before the procedure of plasmapheresis and after it [1 and 2) blood of two patients before the plasmapheresis; 1′ and 2′) blood of the same patients after the plasmapheresis]. $\langle N \rangle$, rel. units; η_a, mPa·sec.

$$\eta_a - \eta_\infty = C_1^* \frac{\mathrm{Hct}}{1 - \mathrm{Hct}} \ln \langle N \rangle , \tag{18}$$

where the constant C_1^* corresponds to the plasma viscosity.

The obtained function (17) has not been defined at Hct = 1, which is of no practical importance since such a value of the hematocrit is unattainable because of the effect of the captured plasma.

Dependence (17) has the same form as the aggregation state of the blood changes upon the introduction of high-molecular-weight dextran D-500 (Fig. 12a) and after the procedure of plasmapheresis (Fig. 12b), which points to the preservation of the established regularities with cardinal change in the macromolecular composition of the blood.

The obtained dependence of the viscosity of plasma on the hematocrit Hct and the free plasma volume (1 – Hct) is inconsistent with the universally adopted dependence $\eta_a \cong \dfrac{\eta_{pl}}{(1 - kT\,\mathrm{Hct})^m}$ [29, 30].

To check the dependence of the viscosity on the hematocrit and the aggregation state of the suspension in greater detail we have measured the viscosity of erythrocyte suspensions in the plasma of four healthy donors, as the hematocrit changed in the actually observed range 0.25–0.55. The measurements were carried out at rates of shear of 9 and 150 sec^{-1} on a Haake viscometer. We had $\ln \langle N \rangle$ = const in the first case and $\ln \langle N \rangle = 0$ in the second case since, when $\dot{\gamma}$ = 150 sec^{-1}, the total disaggregation normally sets in and $\langle N \rangle = 1$. The data obtained are presented in Fig. 13. The coefficient of correlation between η_a and the function Hct/(1 – Hct) is less than 0.9 for $p < 0.05$, but measurements at a rate of shear of 9 sec^{-1} have a systematic error of ≅ 1.7 mPa·sec, which is characteristic of Haake viscosimeters at low rates of shear. Extrapolation of the plot at $\dot{\gamma}$ = 150 sec^{-1} to the region Hct = 0.05 leads to suspension viscosities similar to the plasma viscosities (1.4 mPa·sec).

From the plots obtained, the rheological law (18) takes on the form

$$\frac{\eta_a}{\eta_{pl}} = 1 + C_1^* \frac{\mathrm{Hct}}{1 - \mathrm{Hct}} + C_2^* \frac{\mathrm{Hct}}{1 - \mathrm{Hct}} \ln \langle N \rangle , \tag{19}$$

where

$$\eta_\infty = \eta_{pl} \left(1 + C_1^* \frac{\mathrm{Hct}}{1 - \mathrm{Hct}} \right).$$

The constant C_1^* involves the deformability of erythrocytes, while the constant C_2^* involves the cohesive interaction of erythrocytes.

The logarithmic asymptotics not occurring earlier is quite obvious, since a possible increase in the viscosity with growth in the aggregate size is compensated for with the increase in the plasma volume around the aggregate,

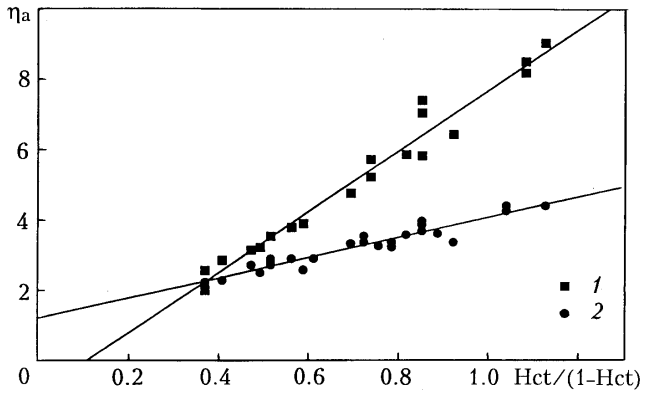

Fig. 13. Plots of the viscosity of an erythrocyte suspension as a function of Hct/(1 – Hct): 1) $\dot{\gamma}$ = 9 and 2) 150 sec^{-1}. Hct, rel. units; η_a, mPa·sec.

which leads to an increase in the thickness of the plasma layer between aggregates and a decrease in the probability of their direct interaction.

The rheological equation (19) well explains the appearance of a constant viscosity η_{max} and $\eta_{min} = \eta_\infty$. In the case of the total aggregation ($\langle N \rangle = \langle N_0 \rangle$) we attain

$$\eta_{max} = \eta_{pl} + \eta_{pl} C_1^* \frac{Hct}{1 - Hct} + \eta_{pl} C_2^* \frac{Hct}{1 - Hct} \ln \langle N_0 \rangle \tag{20}$$

and, as the rate of shear decreases further, the viscosity remains constant since all the erythrocytes are totally incorporated in the single aggregate sliding over the plasma layer. In total disaggregation ($\langle N \rangle = 1$ and $\ln \langle N \rangle = 0$), we attain the minimum (asymptotic) viscosity η_∞:

$$\eta_{min} = \eta_\infty = \eta_{pl} + \eta_{pl} C_1^* \frac{Hct}{1 - Hct}. \tag{21}$$

To reduce (19) to the final form we must take into account the dependence obtained earlier of the aggregate size on the rate of shear (12). Then we have

$$\frac{\eta_a}{\eta_{pl}} = \eta_{rel} = 1 + C_1^* \frac{Hct}{1 - Hct} + C_2^* \frac{Hct}{1 - Hct} \frac{\ln \langle N_0 \rangle}{\left(\frac{1}{\dot{\gamma}_1^{1/2}} - \frac{1}{\dot{\gamma}_2^{1/2}} \right)} \left(\frac{1}{\dot{\gamma}^{1/2}} - \frac{1}{\dot{\gamma}_2^{1/2}} \right). \tag{22}$$

A bound on the hyperbola, when $\dot{\gamma} \to 0$, is set by displacing the origin of coordinates by $\dot{\gamma}_1$, i.e.,

$$\frac{\eta_a}{\eta_{pl}} = \eta_{rel} = 1 + C_1^* \frac{Hct}{1 - Hct} + C_2^* \frac{Hct}{1 - Hct} \frac{\ln \langle N_0 \rangle}{\left(\frac{1}{\dot{\gamma}_1^{1/2}} - \frac{1}{\dot{\gamma}_2^{1/2}} \right)} \left(\frac{1}{(\dot{\gamma} + \dot{\gamma}_1)^{1/2}} - \frac{1}{(\dot{\gamma}_2 + \dot{\gamma}_1)^{1/2}} \right), \quad \dot{\gamma}_1 << \dot{\gamma}_2 . \tag{23}$$

On condition $\dot{\gamma}$ = 0 we can obtain from (23) the constant $\dot{\gamma}_1$ and accordingly the true value of the yield stress τ_0, which has the form

$$\tau_0 = \eta(\dot{\gamma}_1)\, \dot{\gamma}_1 , \tag{24}$$

where $\eta(\dot{\gamma}_1)$ is the viscosity of blood at $\dot{\gamma} = \gamma_1$.

CONCLUSIONS

The investigation carried out allows consideration of the process of spontaneous aggregation of erythrocytes as the kinetics of second order (Smolukhowski kinetics). We may assume that the variable component of the intensity of backward light scattering I in aggregation of the erythrocytes is in proportion as a first approximation to the total erythrocyte–plasma interface of the aggregates formed, and the quantity $1/I$ is in proportion to the average size of erythrocyte aggregates. Also, we have been able to establish that the relationship between the viscosity of the blood and the average size of the aggregates is linear in a semilogarithmic coordinate system, which enabled us to obtain a new curve of flow and to compose the rheological equation.

NOTATION

A and B, dimensionless coefficients; C_1, C_2, C_1^*, and C_2^*, integration constants; D, diffusion coefficient of erythrocytes, m^2/sec; Hct, hematocrit, rel. units; h, aggregometer-gap thickness; I, intensity of backward light scattering, conv. units; $J(\dot{\gamma})$, number of bonds between aggregating particles at a given rate of shear; k, numerical coefficient according to the theory of [14]; kT, Taylor coefficient; k_{cd} and k_{12}, constants consisting of a combination of three constants according to the theory of [22]; k_0 and k_1, constants according to the theory of [26]; L, linear dimension of rouleaux; L_0, linear dimension of rouleaux at $\dot{\gamma} = 0$; m, exponent; N_0 = const, number of erythrocytes in unit volume; $\langle N \rangle$ and $\langle N(t) \rangle$, average size of an aggregate, measured by the number of erythrocytes in one aggregate, and its variation with time; $n = N_0/\langle N \rangle$, number of aggregates in unit volume; n_r, relative refractive index; p, significance level; r, correlation coefficients; S_0 and S_1, end and side surfaces of one erythrocyte; $S(t)$, variation of the interface of one rouleau with time; S_{tot}, total interface in a unit volume of blood; t, time, sec; α, constant entering into the coefficient of diffusion of erythrocytes; β, hydrodynamic strength of erythrocyte aggregates, sec^{-1}; $\aleph$, Smolukhowski constant (rate of spontaneous aggregation), sec^{-1}; $\aleph^* = \aleph/N_0$; δ, wall-layer thickness; $\dot{\gamma}$, rate of shear, sec^{-1}; V and V_0, velocities on the interior and exterior walls of the aggregometer; $\dot{\gamma}_1$ and $\dot{\gamma}_2$, rates of shear in total aggregation and total disaggregation of erythrocytes, sec^{-1}; η_0, viscosity of the weighting medium, Pa·sec; η_a, apparent viscosity, Pa·sec; η_{pl}, viscosity of plasma, Pa·sec; η_{rel}, relative viscosity, Pa·sec; η_{max} and η_{min}, maximum and minimum viscosities independent of $\dot{\gamma}$, Pa·sec; η_∞, asymptotic viscosity, Pa·sec, τ_0, yield stress, Pa; ω, concentration of the high-molecular-weight aggregate in the plasma of blood, %. Subscripts: a, apparent; pl, plasma; rel, relative; max, maximum; min, minimum; 0, fixed value of the quantity; tot, total; r, refraction.

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