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FLOW OF BLOOD IN EYE VESSELS WITH ALLOWANCE FOR AGGREGATION

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A nonlinear mathematical model of blood flow in a vessel has been constructed where blood is considered as a suspension with aggregating and deformable particles and vessel walls possess elasticity according to the Hooke law. The blood viscosity, which is dependent on the gradient of the rate of shear on the vessel wall, becomes a function of the time in the case of pulsatory motion. The cases of normal blood flow in eye vessels and of that in diabetes mellitus have been considered as examples. It has been shown that in the latter case the contribution of the aggregability of erythrocytes to the value of the viscosity of blood substantially increases.

The stability of the blood flow in eye vessels is a vital requirement for ensuring normal vision. The eye is characterized by a very intense metabolism, particularly, carbohydrate metabolism. The maximum rate of blood supply in the body is realized precisely in its vascular tract. This determines the extremely high sensitivity of the retina to a disorder in the blood supply — even within 40 to 60 min after the discontinuation of circulation it dies. In addition to ensuring a high metabolic rate, excessive blood flow in eye vessels is required for temperature stabilization of the organ of sight and protection against damages induced by intense light loads [1].

Mathematical modeling of the hemodynamics of the human vasculatory system is based on solution of the equations of motion of blood in the vessels [2, 3]. One usually disregards the non-Newtonian character of this flow. The mathematical description proposed in [4–6] for the rheology of blood and plasma allow a more complete pattern of blood flow in vessels. The rheological model reflects the dependence of the viscosity of blood on the hematocrit and the gradient of the rate of shear. Although there exists a certain characteristic value of the gradient of the rate of shear for each type of blood vessel, this quantity changes during each cycle of cardiac contraction. Furthermore, the gradient of the rate of shear on the surface of vascular epithelium also depends on the dilation of a vessel in transmission of a pulse wave. Because of this, it is of interest to calculate the change in the viscosity of blood inside the vessel as a function of the time. We make the following assumptions:

(1) the rheological behavior of the blood is described by the model [4] allowing for the aggregability and deformability of erythrocytes;

(2) the difference of the pressures at the inlet and outlet of the vessel is a harmonic function of time;

(3) vessel walls possess elasticity according to the Hooke law;

(4) the deformations of the vessel walls are sufficiently small for the motion to be considered to be one-dimensional.

In the one-dimensional approximation, the equation of motion of the blood in the vessel has the form

$$\frac{dq}{dt} = -\frac{8\eta q}{\pi r^2} - \frac{\pi r^2}{\rho}\frac{\Delta p}{l}. \qquad (1)$$

Equation (1) represents the balance of forces acting on the blood which flows in the vessel. The inertial force is on the left-hand side of the equation, while the force of viscous friction and the external driving force are on the right-hand side. Here we disregard gravitational forces and forces due to the change in the velocity profile along the vessel length.

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The stress σ in the vessel wall is related to the intravascular pressure p as follows:

$$\sigma = p \frac{r_0}{h} (1 - \nu^2) . \tag{2}$$

From the data of [7], $\nu = 0.43$ for the tissues of the vessel wall.

The increase in the vessel r is represented in this case by the Hooke law

$$\varepsilon = \frac{\sigma}{E} . \tag{3}$$

Then, introducing the notation $r = r_0(1 + \varepsilon)$, we represent the equation of motion in the form

$$\frac{\rho}{\pi r_0^2 (1+\varepsilon)^2} \frac{dq}{dt} + \frac{8\eta q}{\pi r_0^4 (1+\varepsilon)^4} = -\frac{\Delta p}{l} . \tag{4}$$

We substitute the expression obtained in [4] for viscosity into the equation of motion:

$$\eta = \eta_{pl} \left(1 + k_0 + k_1 \exp\left(-\frac{\gamma}{\gamma_a} \right) + k_2 \exp\left(-\frac{\gamma}{\gamma_d} \right) \right). \tag{5}$$

Expressing the gradient of the rate of shear γ by the volumetric flow rate q, under the assumption of the Poiseuille flow

$$\gamma = \frac{4q}{\pi r^3} \tag{6}$$

we obtain the nonlinear equation of motion in the following form:

$$\frac{dq}{dt} = -\frac{8q}{\rho r^2} \left[\eta_{pl} \left(1 + k_0 + k_1 \exp\left(-\frac{4q}{\pi r^3 \gamma_a} \right) + k_2 \exp\left(-\frac{4q}{\pi r^3 \gamma_d} \right) \right) \right] - \frac{\pi r^2}{\rho} \frac{\Delta p}{l} , \tag{7}$$

where the sought quantity, i.e., the volumetric rate of flow of the blood q, is involved in both the left-hand and right-hand sides of the equation.

We note that the plasma viscosity is involved in expression (7) as a constant quantity, but in accordance with [5] one can also represent it as a function of the gradient of the rate of shear.

The pressure difference between the inlet and outlet of the blood vessel is assumed to be harmonic with a cardiac rate ω:

$$\Delta p\,(t) = p_0 + B \sin(\omega t) . \tag{8}$$

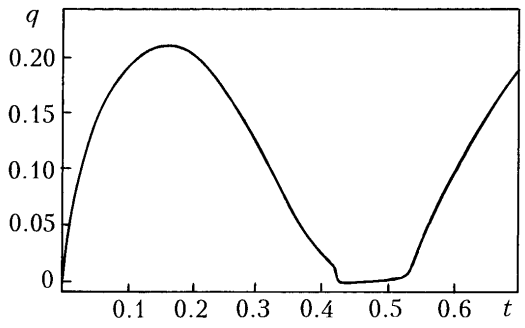
The conditions of circulation of blood in the eye and in other organs differ. The characteristic properties of the blood circulation in the eye cause the high load experienced by the walls of intraocular vessels.

The eyeball is supplied with blood from the ophthalmic artery (the diameter is about 2 mm), which is a large branch of the internal carotid artery. After the branching of the ophthalmic artery the diameter of the internal carotid artery decreases from 5.4 to 3.8 mm. Such a narrowing of the diameter of the main vessel keeps the pressure of blood in the ophthalmic artery at a high level and ensures an intense blood flow in this important branch.

According to their anatomic signs, blood vessels are subdivided into the vascular system of the retina, which is formed by the central retinal artery, and the vascular system of the uveal tract, which occurs due to the posterior (short and long) ciliary arteries [8, 9]. In the latter, there is concentrated the bulk of the intraocular blood vessels and its role is determined by the fact that the greatest amount of blood (no less than 80%) intended to nourish the eye formations carrying out the act of vision, i.e., the retina, the ciliary body, and the iris, is circulating in the vessels of

TABLE 1. Indices of the Hemodynamics of Orbital Vessels

Index	Ophthalmic artery	Central retinal artery	Central retinal vein	Posterior ciliary artery	
				short	long
Velocity of blood flow during the systole, cm/sec	32.7	10.6	4.36	14.7	16.8
Velocity of blood flow during the diastole, cm/sec	9.2	2.9	–	4.2	5.2
Average velocity, cm/sec	16.7	5.6	–	8.1	9.3
Peripheral-resistance index RI, %	72	73	–	67	69



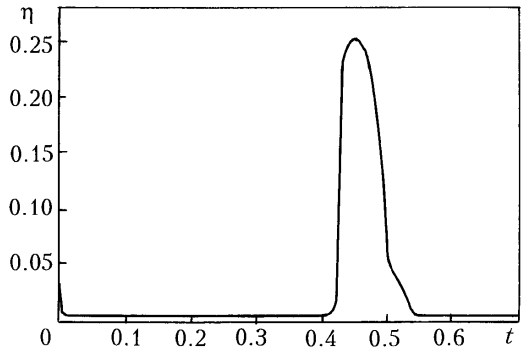


Fig. 1. Calculated value of the rate of flow of blood through the ophthalmic artery with harmonic change in the head during one cardiac cycle. *q*, ml/sec; *t*, sec.

Fig. 2. Change in the viscosity of blood in the ophthalmic artery. η, Pa·sec; *t*, sec.

the tract. In the uveal tract, aqueous humor is produced, which is of primary importance for the state of ophthalmotonus (intraocular pressure) and participates in the exchange of the nonvascular formations of the eyeball, the cornea, the crystalline lens, and the vitreous humor.

The ciliary body and the iris receive most of the blood from the posterior long ciliary arteries (PLCAs) and interior ciliary arteries; blood supply of the vascular tract is carried out mainly via the posterior short ciliary arteries (PSCAs) [9]. The posterior ciliary arteries (short and long) forming the vascular tract are straight branches of the ophthalmic artery, as is the central retinal artery. Therefore, the values of the blood pressure in the nourishing vessels of the retina and the vascular tract are of the same order [8].

The indices of the hemodynamics of the orbital vessels of the human eyes have been widely investigated in recent years [10, 11]. The blood flow in PLCAs and PSCAs has been measured in [11], which no one was able to do before. The average velocity of the blood during a cardiac cycle in the PSCAs was 8.1 ± 1.7 cm/sec and that in the PLCAs was 9.3 ± 1.4 cm/sec.

When the blood circulation in the ciliary body is impaired, the release of aqueous humor is disturbed, which leads to a change in the protein, lipid, enzymatic, and water exchange. Under metabolism conditions characteristic of diabetes mellitus, this leads to the development of diabetic cataract. The vascular pathology in diabetes mellitus is underlain by the process (specific for this disease) of infiltration of microvessel walls by glucoproteins and lipoproteins contained in the blood plasma.

Apart from the pathomorphologic changes in the microcirculatory channel, one observes, in diabetes mellitus, a disturbance of the microhemodynamics, changes in the rheological properties of the blood, and retardation of the blood flow up to stasis in severe cases (sharp retardation or stopping of the motion of the contents in vessels); one also detects an increase in the blood viscosity, the aggregation of erythrocytes and a decrease in their deformability, microthrombosis [12], and the development of microangiopathies [13].

Thus, investigation of the hemodynamics of the eye, particularly, of the ciliary arteries, is of great importance for studying the pathogenesis and clinical picture of many diseases.

TABLE 2. Velocity of Blood Flow in Ciliary Arteries [10]

Diagnosis	Velocity, cm/sec		Flow rate, ml/sec
	maximum	average	
Open-angle glaucoma of the 2nd stage with diabetes mellitus of the 2nd type	4.52	2.01	0.95
Open-angle glaucoma of the 2nd stage	10.30	6.51	2.01
Diabetes mellitus of the 2nd type	7.13	5.07	1.75
Normal condition	15.02	8.76	3.66

TABLE 3. Dimensions of the Branches of the Ophthalmic Artery [14]

Type of branch of the ophthalmic artery	d, mm			l, mm		
	d_{max}	d_{min}	$\langle d \rangle$	l_{max}	l_{min}	$\langle l \rangle$
Lateral PLCA	0.4	1.2	0.81 ± 0.11	22	41	36.25 ± 0.20
Medial PLCA	0.3	0.8	0.61 ± 0.14	16	28	23.74 ± 0.25
PSCA	0.1	0.3	–	8	19	14.12 ± 0.26

We consider as an example blood flow in the ophthalmic artery. For it there are data on both the average values of the blood flow and the pulsations during one cycle of cardiac contractions (Table 1 [11]). However, data indicating higher velocities of flow have also been obtained [13]; according to them, the normal maximum systolic velocity of blood in the ophthalmic artery (normally) attains 65 cm/sec, the maximum diastolic velocity of blood is 14 cm/sec, and the peripheral-resistance index attains 0.65–0.72. The peripheral-resistance index RI (Purselo index) is a characteristic of the vessel's resistance and it represents a relative change in the flow area of the vessel during the diastole in relation to the flow area during the systole.

Based on the mathematical model presented above we have composed a program of numerical calculation enabling us to investigate the hydrodynamics of blood flow in a vessel with elastic walls. Here it was used not only in the normal case but also for studying the distinctive features of blood flow in patients having diabetes mellitus. Figures 1 and 2 show results of the numerical solution of the nonlinear equation of motion for the case of a sine change in the pressure in the ophthalmic artery. By selecting the values of the systolic pressure p_0 and the pulse component of the pressure B we attained the required values of the maximum and average velocities of flow of the blood in the arteries (over the period of a cardiac cycle) (see Table 1).

The change in the flow rate q with time is nearly sinusoidal (Fig. 1) but it is subjected to significant nonlinear distortions in the regions corresponding to low flow rates. For the calculated variant the cardiac rate is equal to 100 beats per minute (1.667 Hz), the artery radius is 0.7 mm, the thickness of the artery wall is 0.2 mm, the value of the elastic modulus of the vessel walls is taken to be $8 \cdot 10^5$ Pa (as in [3]), the pressure difference along the artery length is 0 to 7.5 mm Hg, the velocity of flow of the blood within one cardiac contraction is 0. to 65 cm/sec, and the gradient of the rate of shear is 4.3 to 3670 sec^{-1}. Maxima corresponding to low values of the gradients of the rate of shear, appear on the resulting viscosity changes of the blood in the vessel (Fig. 2). At these instants of time, the blood viscosity increases more than 60 times — from 4 to 253 mPa·sec.

From the data published in the literature on the velocity of blood flow in ciliary arteries in the normal case (Table 2) and in the cases of diabetes mellitus and open-angle glaucoma [10], we have calculated viscosity changes of the blood in the ciliary arteries during one cardiac cycle.

For the computations we needed the diameters and lengths of the arteries under study. We used the data of [14] presented in Table 3. The lateral and medial branches of PLCAs were taken for the calculations.

The values of the blood viscosity for patients having diabetes mellitus were estimated in accordance with [15], where it has been obtained that the viscosity of the blood in them is increased 2.5 times as compared to the healthy patients.

Figures 3–5 give results of the calculations of the blood flow in ciliary arteries, performed using the constructed model, in the case of different pathologies.

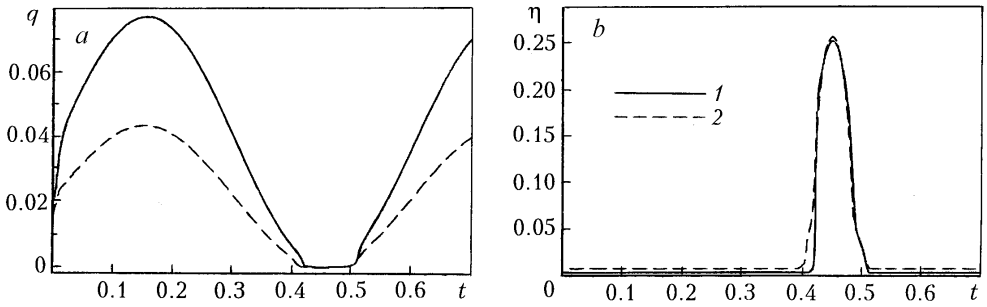


Fig. 3. Flow rate (a) and viscosity (b) of blood in the lateral branch of PLCAs vs. time: 1) healthy patients; 2) patients having a severe case of diabetes mellitus. q, ml/sec; η, Pa·sec.

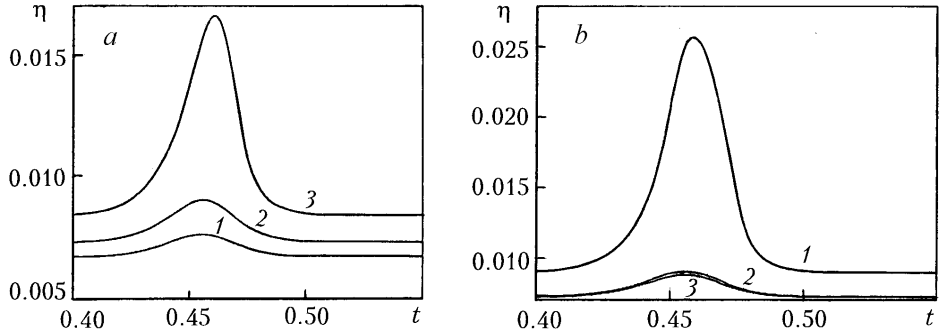


Fig. 4. Viscosity of blood vs. time for different cases of diabetes mellitus (a) [1) easy case, 2) moderate case, and 3) severe case] and for different durations of the disease (b) [1) more than 10, 2) 5 to 10, and 3) up to 5 years]. η, Pa·sec; t, sec.

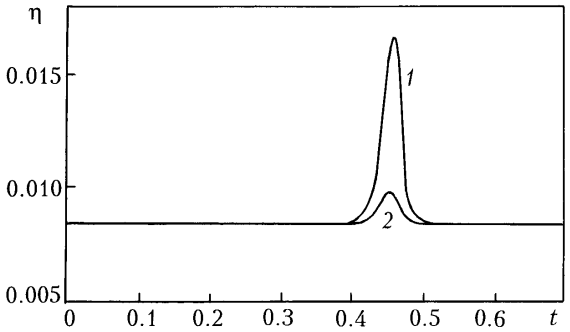


Fig. 5. Viscosity of blood vs. time for different branches of PLCAs: 1) lateral branch; 2) medial branch. η, Pa·sec; t, sec.

Figure 3a is the time dependence of the flow rate of blood in PLCAs. For curve 1 the average and maximum velocities of the blood flow in the artery correspond to the values given in [10] (in the absence of pathology). Curve 2 represents the reaction of the rate of flow of the blood through the lateral branch of the PLCA for patients having a severe case of diabetes mellitus at the viscosities indicated in [15]. Figure 3b is the calculated time dependence of the viscosity of blood for the same two cases — healthy patients and those having a severe case of diabetes mellitus. The presence of a pronounced viscosity peak is explained by the nonlinear relationship (5) between the blood viscosity and the gradient of the rate of shear.

The change in the viscosity of blood in the vessel with time as a function of the degree of seriousness of the case of diabetes mellitus is shown in Fig. 4a. Here the viscosity maxima are more pronounced, which is attributed to the substantial contribution of the aggregability of erythrocytes to the rheological properties of blood for this group of patients, which in turn can produce more serious pathological effects.

Figure 4b gives the values of the blood viscosity for patients having diabetes mellitus with allowance for the duration of the disease. All other things being equal, the largest growth in the viscosity of the blood is observed in the patients with a long period of existence of the disease. The maximum value of the viscosity in this case increases approximately three times, and for durations of the disease of 5 and 10 years these changes virtually do not differ.

Figure 5 is the time dependence of the viscosity of blood for different branches of PLCAs. The blood viscosity for the lateral branch of the arteries in question has a more pronounced maximum than that for the medial branch of the same arteries. The branches of the ciliary arteries under study differ in size.

The presence of the maxima on the given calculated curves has the following physical nature: as the flow velocity and consequently the velocity gradient on the surface of vascular epithelium decrease, the contribution of the processes of aggregation of erythrocytes to the total value of the viscosity increases. The aggregation of erythrocytes is in turn closely related to the formation of thrombi, since the formation of a thrombus represents irreversible aggregation of erythrocytes. Further investigations in the field of mathematical modeling of the blood flow in vessels will contribute to the prediction of the possibilities of thrombosis.

Continuation of the investigations in this direction is tied to the necessity of allowing not only for the elastic properties of vessel walls but also for the viscous properties, including the relaxation of stresses and the deformation lag.

Also, to more correctly predict the behavior of the viscosity of blood in vessels we need data on the viscosity and composition of the plasma so as to separate the plasma-related effects and the influence of erythrocyte aggregation.

The numerical results obtained show the possibility of a sharp increase in the contribution of the aggregability to the total value of the viscosity of blood at certain instants of time. Since the influence of the aggregability is substantial only at low rates of shear (at high rates of shear, the aggregates are destroyed [4]), the aggregation of erythrocytes takes on particularly great significance under the conditions of ischemia. This effect invites further investigation, since in pathological states this process can become irreversible.

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NOTATION

r, radius of the vessel, mm; q, volumetric flow rate of blood, ml/sec; Δp, pressure difference between the inlet and outlet of the vessel, mm Hg; p_0, value of the pressure difference during the diastole, mm Hg; B, harmonic component of the pressure difference, mm Hg; ρ, density of blood, kg/m^3; t, time, sec; h, thickness of the vessel wall, mm; ν, Poisson coefficient; ε, relative radial deformation, equal to the change in the vessel radius under stress σ; E, elastic modulus of the vessel wall, Pa; γ, gradient of the rate of shear, sec^{-1}; d and l, diameter and length of the branches of the ophthalmic artery, mm; $\langle ... \rangle$, average value; η, viscosity of blood, Pa·sec; ω, cardiac rate, Hz; k_0, k_1, k_2, γ_a, and γ_d, parameters of the rheological model of blood. Subscripts: 0, initial value; pl, plasma; a, aggregability; d, deformability; max, maximum; min, minimum.

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