Hydrodynamics of whole and diluted blood in a microchannel with stenosis

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The flow of whole and diluted blood with erythrocyte concentrations of 1, 5 and 10% was studied in a microchannel with a stenosis made by soft photolithography. Differences in flow rates and structure before and after constriction were found. Erythrocyte rates on the axis of symmetry in whole blood after constriction are slightly lower than before it, while in diluted blood, on the contrary, they are significantly higher. The orientation of erythrocytes perpendicular to the flow lines, after the whole blood passes the stenosis, suggests that the process of thrombus formation is more likely not before, but after the constriction.

Keywords: microfluidic device, stenosis, blood, erythrocyte.

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Vessels of the vascular system of the human body branch and become narrower with distance from the heart. An increase in the number of vessels is accompanied by a significant increase in their total cross section and a reduction in blood flow velocity, while the shear strain rate changes only several fold [1]. Stenosis (constriction) of blood vessels disrupts the natural conditions of blood flow: the blood flow velocity in a narrow vessel section increases instead of decreasing (as in vessels of a healthy organism); consequently, the shear strain rate also increases significantly, which is abnormal with respect to the hemodynamics of a healthy organism [1]. Stenosis has various causes (muscle spasm or atherosclerotic plaque buildup) and may be either instantaneous (spasm) or protracted (lipid deposition under the endothelial layer of a blood vessel). It was demonstrated that the shear stress and hydraulic resistance for blood increase as stenosis grows, while the flow velocity in a blood vessel decreases [2]. This increased shear stress may, in turn, induce profound changes in permeability of the vessel wall for procoagulants, initiating intravascular blood coagulation [3]. This is the reason why the blood flow behavior during stenosis needs to be understood in order to find ways to counteract thrombus formation. The geometry of a stenotic artery, the length and depth of stenosis, and the power law exponent (non-Newtonian behavior) are important factors that affect blood flow [4]. The use of numerical methods based on mesoscale modeling of blood flow provided an opportunity to characterize the motion of identical or different blood cells in shear and microcapillary flows with simulation of hematological diseases and disorders [5]; however, in addition to examining the motion of individual erythrocytes, one also needs to factor in the asymmetry of the blood flow structure. The aim of the present study is to investigate experimentally the flow of whole and diluted blood before and behind a constriction at erythrocyte concentrations of 1, 5, and 10%.

A transparent microfluidic device (MFD) with a stepped constriction (1/20 of the cross section of the main microchannel) was designed and fabricated by soft photolithography for the purpose of examining the features of blood flow during the development of stenosis. Since a high-resolution high-speed camera with a short-focus lens is needed to distinguish the motion of individual erythrocytes, experiments were carried out in planar channels. Our standard MFD has depth $2h = 50\,\mu$m, a length of approximately 10 mm (two channels with length $l_1 = 5$ mm and a constriction between them), and width $b = 1$ mm with a constriction $l_0 = 100\,\mu$m in length and $a = 50\,\mu$m in width. These dimensions could vary slightly due to manufacturing errors; saline flow was used for calibration. The cross-sectional area of the wide channel with a depth of $50\,\mu$m and a width of 1 mm corresponds to that of a cylindrical vessel $250\,\mu$m in diameter. The microchannel dimensions were chosen so that the cross-sectional area was close to that of arterioles (with the corresponding shear strain rate of approximately $100\,\mathrm{s}^{-1}$). The volumetric blood flow rate through a parallelepiped-shaped microchannel is given by the updated Poiseuille formula [1]:

$$Q = 2h^2 b \frac{n}{2n+1}\left(\frac{\Delta p h}{k l}\right)^{1/n}, \qquad (1)$$

where h is the half-depth, b is the width, Δp is the pressure difference, k is the consistency, and n is the non-Newtonian behavior index (from the Ostwald–de Waele model; see [1]).

Using (1), one may calculate the ratio of pressure differences in wide and narrow parts of the microchannel:

$$\frac{\Delta p_1}{\Delta p_0} = \left(\frac{l_1}{l_0}\right)\left(\frac{a}{b}\right)^n, \qquad (2)$$

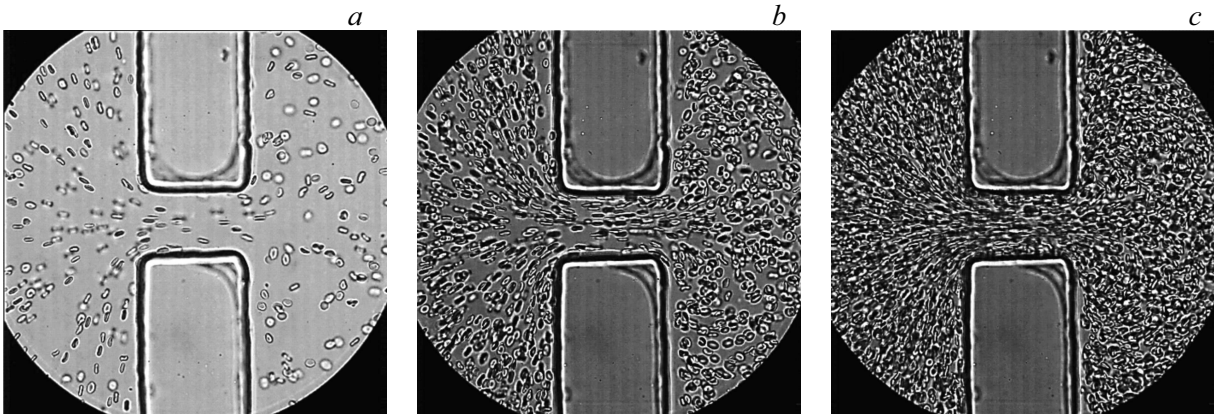

Figure 1. Blood flow with an erythrocyte concentration of 1 (*a*), 5 (*b*), and 10% (*c*). Microfluidic device (length × width × depth): 10 mm × 1 mm × 55 μm; constriction: 90 × 60 × 55 μm.

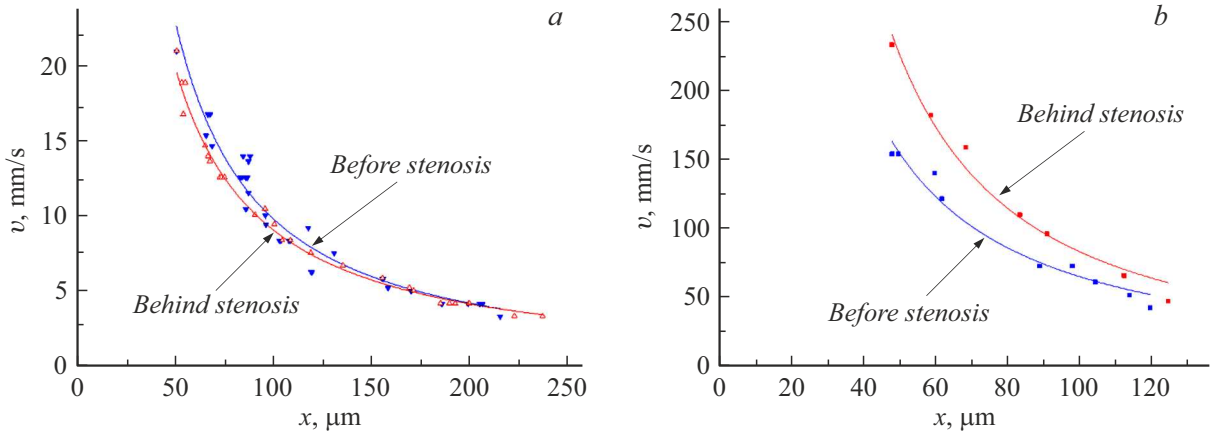

Figure 2. Dependence of the erythrocyte flow velocity on distance before and behind stenosis for whole (*a*) and diluted blood with 1% of erythrocytes (*b*) at a pressure difference of 500 Pa.

where a and b are the widths and l_0 and l_1 are the lengths of the constriction and the wide part, respectively.

It follows from (2) that the ratio of pressure differences in the wide and narrow parts of our MFD for a Newtonian fluid ($n = 1$) is 2.5. The ratio for blood with index $n = 0.8$ is 4.55. The size of the constriction was chosen in such a way that ratio 1/20 of widths of the planar channel yielded a ratio of pressure differences corresponding to a radii ratio of the constriction and the wide part of approximately 1/2 for a cylindrical vessel:

$$\frac{\Delta p_1}{\Delta p_0} = \left(\frac{l_1}{l_0}\right)\left(\frac{r}{R}\right)^{3n+1}, \qquad (3)$$

where r and R are the radii of the constriction and the wide part, respectively.

Let us find the flow rates for Newtonian and non-Newtonian fluids in our MFD with pressure difference $\Delta p = 500$ Pa. The flow rate for a Newtonian fluid calculated by formula (1) ($n = 1$, dynamic viscosity $\mu = 5$ mPa · s is used instead of k, and the entire length $l = 10$ mm is factored in) is 0.104 μl/s without stenosis and 0.087 μl/s with stenosis. In order to perform calculations for the channel with stenosis, the pressure distribution within the narrow and wide parts was determined from the obtained ratio of pressure differences, and the flow rate was calculated using formula (1). The flow rate determined using formula (1) for blood with $n = 0.8$ and $k = 0.013$ without stenosis is 0.116 μl/s; with stenosis factored in, the ratio of pressure differences is 4.55, and the flow rate is 0.102 μl/s. Let us calculate the flow velocity ($v = Q/S$) and the shear strain rate ($\dot{\gamma} = v/h$) based on the flow rate (Q) and the cross-sectional area (S). With pressure difference $\Delta p = 500$ Pa, the flow velocity is $v_0 = 40.8$ mm/s at a shear strain rate of 1632 s^{-1} in the narrow part. The corresponding values in the wide channel are 20 times lower: 2 mm/s and 80 s^{-1}.

Let us compare the flow of whole blood of a healthy patient (with the EDTA K3 anticoagulant) and diluted blood (fluid with anisotropic elements: erythrocytes with their volume concentration in a saline solution being 1, 5, and 10%). The process was recorded with a high-speed camera at a framing rate of 10 000 fps through an inverted OLYMPUS IX71 microscope (observation from below) at

room temperature with a constant pressure difference of 500 Pa that was monitored by a pressure sensor. At a concentration of 1%, the majority of erythrocytes are oriented parallel to the vertical plane in the inlet region and parallel to the horizontal plane in the outlet region (Fig. 1, *a*). A parabolic distribution of carrier phase velocities in the MFD gap induces the rotation of vertically oriented erythrocytes, which undergo sedimentation in the wide part in the laminar flow as they move. Almost all of them end up in the lower part of the channel. When the concentration increases to 5 and 10% (Figs. 1, *b*, *c*), the percentage of vertically oriented erythrocytes in the inlet region decreases; vertical orientation is found predominantly in the lower layer of cells moving at a lower velocity. In the outlet region, the number of erythrocytes oriented perpendicular to the flow lines increases with an increase in the erythrocyte concentration. The coordinate shift of erythrocytes (the *x* axis) positioned on the axis of symmetry in successive frames (Fig. 2) was compared to find the velocities. With the same pressure difference, the erythrocyte flow velocity in diluted blood with 1% of erythrocytes is an order of magnitude higher than the corresponding velocity in whole blood. Erythrocytes accelerate before the constriction and within it. The erythrocyte flow velocities on the axis of symmetry of the model in whole blood are reduced somewhat behind the constriction; in diluted blood, they, on the contrary, become significantly higher. Discocytes in the flow of native blood are also oriented along the flow lines in the area before stenosis and within it. Behind stenosis, they rearrange perpendicular to the flow lines and parallel to each other, inducing an increase in viscosity and slowing down the flow.

Thus, differences in the velocity and structure of flow of whole and diluted blood were revealed. The erythrocyte flow velocities on the axis of symmetry of the model in whole blood are reduced somewhat behind the constriction; in diluted blood, they, on the contrary, become significantly higher. The accumulation of erythrocytes oriented parallel to each other and perpendicular to the flow lines in whole blood behind stenosis suggests that thrombi are more likely to form in a blood vessel not before a constriction, but behind it. These data on the features of flow in microchannels with stenosis will help lay the foundation for the development of a new method for diagnosis and treatment of vascular diseases.

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Conflict of interest

The authors declare that they have no conflict of interest.

References

[1] A.T. Akhmetov, A.A. Valiev, A.A. Rakhimov, S.P. Sametov, R.R. Khabibullina, Proceedings of the Mavlyutov Institute of Mechanics, **11** (2), 210 (2016) (in Russian). DOI: 10.21662/uim2016.2.031

[2] O. Prakash, O.D. Makinde, S.P. Singh, N. Jain, D. Kumar, Int. J. Biomath., **8** (1), 1550010 (2015). DOI: 10.1142/S1793524515500102

[3] O.S. Rukhlenko, O.A. Dudchenko, K.E. Zlobina, G.Th. Guria, PloS One, **10** (7), e0134028 (2015). DOI: 10.1371/journal.pone.0134028

[4] S. Sriyab, Cardiovasc. Hematol. Disord. Drug Targets, **20** (1), 16 (2020). DOI: 10.2174/1871529X19666190509111336

[5] D.A. Fedosov, H. Noguchi, G. Gompper, Biomech. Model. Mechanobiol., **13** (2), 239 (2014). DOI: 10.1007/s10237-013-0497-9

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