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STATE OF THE MICROCIRCULATION AFTER MASSIVE TRANSFUSION OF DOGS WITH HOMOLOGOUS DONORS' BLOOD

V. P. Matvienko

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Normovolemic exchange transfusion with homologous donors' blood causes moderate slowing of the blood flow in the microcirculation of the recipient dogs together with mild or moderately severe intravascular aggregation of erythrocytes. In 25% of cases acute phenomena of retention of blood in the mesenteric microvessels develop, accompanied by a fall in the level of perfusion in the microvessels of the bulbar conjunctiva. Acute disturbances of the microcirculation are transient in character.

KEY WORDS: blood transfusion; complications of blood transfusion; microcirculation.

Transfusion with massive doses of homologous donors' blood leads to the development of a series of disturbances in the recipient collectively described as the homologous blood syndrome [1, 8, 15-17]. Disturbances of the hemodynamics, gas exchange [12], hematopoiesis, the peripheral blood [4, 6], liver function, and the system of phagocytic monocytes [7] have been investigated experimentally in this condition. However, few histopathological investigations have been made of the microcirculatory disorders, which play an important role in the pathogenesis of this syndrome [1, 8].

This paper describes the results of a biomicroscopic study of the microcirculation in the mesentery and the bulbar conjunctiva of dogs during normovolemic exchange transfusion of homologous donors' blood using an arteriovenous shunt [16].

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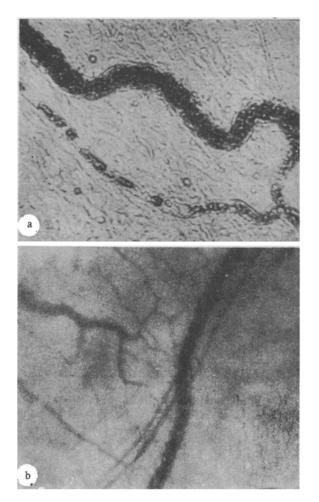


Fig. 1. Signs of granulation and fragmentation of blood flow in microvessels 1.5 h after exchange transfusion: a) microvessels of mesentery  $(180 \times)$ ; b) microvessels of bulbar conjunctiva  $(90 \times)$ .

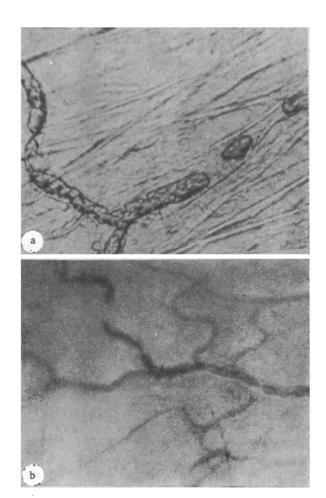


Fig. 2. Intravascular aggregation of erythrocytes during period of acute circulatory disorders: a) microvessels of mesentery (180 ×); b) microvessels of bulbar conjunctiva (112.5 ×).

TABLE 1. Blood Pressure in Dogs during Homologous Blood Transfusion (M ± m)

Group of animals	Initial blood pres- sure, mm Hg	Time after beginning of replacement transfusion, min							
		2	5	10	15	30	60	90	120
Control 1	143±4 139±4 145±7	143±4 137±4 107±8*	143±4 136±5 72±6†	142 <u>+</u> -4 133 <u>+</u> -6 90 <u>+</u> 5*	142 <u>+</u> 4 129 <u>+</u> 6 95 <u>+</u> 8*	141 <u>+</u> 4 123 <u>+</u> 5 106 <u>+</u> 8†	134 <u>+</u> 4 115 <u>+</u> 6* 119 <u>+</u> 6*	133 <u>+</u> 4 111 <u>+</u> 6* 116 <u>+</u> 6*	131±7 110±5* 118±5*

\*P < 0.05 compared with control.

+P < 0.01 compared with control.

## EXPERIMENTAL METHOD

Experiments were carried out on 24 mongrel dogs weighing 15-20 kg (16 experimental and 8 control). Donors' blood compatible with respect to erythrocyte group factors was heparinized 16-18 h before the experiments. Immediately before injection it was filtered through a nylon filter with pores 80-120 nm in diameter. The whole volume of donors' blood (110-120 ml/kg body weight of the recipient) was contained in a vessel connected to the femoral artery and vein. The exchange transfusion took place on account of the arteriovenous pressure gradient at a speed of 90-110 ml/min in the course of 30 min at a temperature of 32-37°C. In the control, autologous blood was passed through an arteriovenous shunt under identical con-

TABLE 2. Development of Aggregation of Erythrocytes in Mesentery and Bulbar Conjunctiva of Dogs during Homologous Blood Transfusion

•	•	_								
	Total number of animals	Number	Number of animals with signs of aggregation of erythrocytes and normal blood flow							
Group of animals		(	during transfusion				1.5 h after transfusion			
		no aggrega- tíon	mild degree of aggrega- tion	moderate degree of aggregation	severe degree of aggregation	no aggrega- tion	mild degree of aggrega- tion	moderate degree of aggregation	severe degree of aggrega- tion	
In microvessels of mesentery										
Control	8	6	2	0	0	5	3	0	0	
2	8 12 4	$\begin{array}{c c} & 6 \\ 4 \\ 0 \end{array}$	5 0	0 3 0	0 0 4	5 2 0	6 0	4 3	0	
In microvesesls of bulbar conjuctiva										
Control 1 2	8 12 4	6 8 0	2 3 0	0 1 3	0 0 1	5 3 0	3 5 1	0 4 2	0 0 1	

Legend. Absence of aggregation — uniform homogeneous blood flow; mild degree of aggregation — granular blood flow in capillaries and postcapillary venules; moderate degree of aggregation — granular blood flow in venules and arterioles, fragmented blood flow in capillaries and postcapillary venules; severe degree of aggregation — fragmented blood flow in arterioles, venules, and capillaries [13].

ditions. The animals were anesthetized with pentobarbital (30 mg/kg) and heparin was injected (4 mg/kg) before the experiments. The state of the microcirculation in the mesentery and in the bulbar conjunctiva was investigated and the systemic blood pressure determined in the femoral artery in the course of 2 h after the beginning of the exchange transfusion. The microhemodynamics in the mesentery of the small intestine was studied by means of an original apparatus designed on the basis of the principles of the method of horizontal biomicroscopy of the mesentery [16]. The apparatus was assembled with the MBR-1 microscope, a Zeiss (East Germany) eyepiece camera and an ON-28 illuminator. The preparation of mesentery was stabilized with buffered Ringer's solution, pH 7.4, 37°C, containing 1% gelatin [5, 9, 11, 19]. The microcirculation in the vessels of the bulbar conjunctiva was studied with an apparatus described in [10, 14].

## EXPERIMENTAL RESULTS AND DISCUSSION

The microcirculation in the mesentery small intestine of control animals during shunting of the blood flow and in the posttransfusion period was characterized by a steady and constant blood flow in all parts of the system. In the bulbar conjunctiva in most cases a rapid and structural blood flow continued in all types of microvessels. The blood pressure remained stable throughout the period of observation (Table 1).

Depending on the character of the disturbances the experimental animals could be divided into two groups. In most of them (12 dogs, group 1) no significant changes took place in the microcirculation and blood pressure during exchange transfusion. In the posttransfusion period the pressure fell gradually (Table 1) and moderate disturbances of the microcirculation developed (Table 2). The blood flow in the mesentery of the small intestine was slowed.

The blood flow in the capillaries and postcapillary venules became fragmented in type through separation into segments of free plasma (Fig. 1a). Features of granulation of the blood flow — a state of nonhomogeneity of the blood flow resulting from the appearance of single erythrocytes, aggregates of erythrocytes, and intervals of free plasma — were seen in the collecting venules 25-50 mm in diameter. In accordance with Björk's classification [13] these changes in the structure of the blood flow can be classed as phenomena of a mild or moderately severe degree of erythrocyte aggregation. Similar but rather less marked changes in the blood flow developed at this period in the microvessels of the bulbar conjunctiva (Fig. 1b). Some decrease also was observed in the number of functioning capillaries (from 8-12 to 6-8 per field of vision).

In a minority of animals (4 dogs, group 2) the disturbances of the hemodynamics developed 2-4 min after the beginning of exchange transfusion and were manifested as a fall of blood pressure (Table 1) and marked disturbances of the microcirculation. In the mesenteric microcirculation retention of blood took place. The blood flow was considerably slowed and the blood accumulated initially in the venules but later in the capillaries and arterioles. "Rouleaux" of erythrocytes formed and consolidated in the postcapillary venules, capillaries, and precapillary arterioles. Dense, steroidal aggregates formed in venules 25-50 nm in diameter (Fig. 2a). Compact stasis developed in individual microvessels.

Signs of hyperfusion of the microcirculatory system were observed in the bulbar conjunctiva during this period. The lumen of the arterioles 30-100 nm in diameter contracted by 30-60%. The number of functioning capillaries was reduced from 8-12 to 4-6 per field of vision  $(90 \times)$ . The blood flow was slowed. Signs of intravascular aggregation of erythrocytes appeared. Fragmentation of the blood flow spread from the capillaries and postcapillary venules to collecting venules 25-50 nm in diameter (Fig. 2b). However, the severity of the aggregation in these microvessels of the conjunctiva was less on the whole than in the vessels of the mesentery (Table 2).

Acute disorders of the hemodynamics in the dogs of group 2 were transient in character, and the blood flow and blood pressure gradually returned to normal after 5-10 min (Table 1). In the posttransfusion period only moderate disturbances of the blood flow still remained in these animals, similar to those in the dogs of subgroup 1 (Table 2). The acute disorders of the microcirculation evidently reflects the accumulation of blood in the portal system and hypovolemia in the remaining parts of the vascular system. Redistribution of the blood in this way, attributable probably to the local liberation of vasoactive substances and to spasm of the hepatic veins, has been found after transfusion with massive doses of homologous blood [15, 16] and after transfusions of blood incompatible with respect both to group [3] and species [2].

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