their content of unsaturated fatty acids, which are a substrate of LPO, and hence to restriction of LPO activation. Second, periodic repeated activation of LPO may induce synthesis of antioxidant enzymes (superoxide dismutase, glutathione peroxidase, catalase) and may thereby increase tissue resistance to the LPO inducer.

Considering the important role of increased resistance of the body to complex and essentially stress-inducing situations as a factor in the organism's successful adaptation to the external environment, these and other possible mechanisms of such adaptation, in the writers' view, deserve experimental study.

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HYPOTENSIVE ACTIVITY OF PLASMA PROTEINS DURING NORMOVOLEMIC EXCHANGE TRANSFUSION

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An important role in the mechanism of action of blood transfusion and, in particular, of massive blood transfusions, is ascribed to incompatibility between plasma proteins of donor and recipient [3]. After transfusion of allogenic blood an increase in the content of high-molecular-weight protein fractions is observed in animals' blood plasma, whereas after transfusion of autologous blood no such changes were found [5]. This reorganization of the protein system of the recipient's blood is accompanied by the appearance of abnormal fractions (protein complexes), which have unusual physicochemical properties and biological activity. This leads to a change in the absolute and relative levels of physiologically active substances, resulting in modified reactivity of the microvascular wall and the development of circulatory disturbances in the microvascular bed [2]. However, no data have been obtained on the role of regulator proteins in the genesis of these phenomena.

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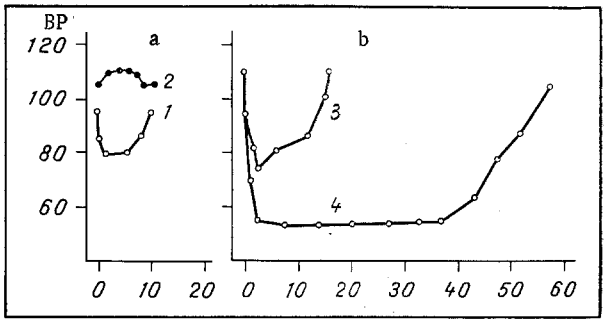

Fig. 1. Hypotensive activity of rabbit plasma (a) and of protein fractions isolated from it (b). Abscissa, time of observation (in min); ordinate, BP (in mm Hg). 1) Effect of plasma on BP after blood transfusion; 2) action of plasma before experiment; 3) effect of macromolecular fraction (M1); 4) effect of submolecular fraction (M2).

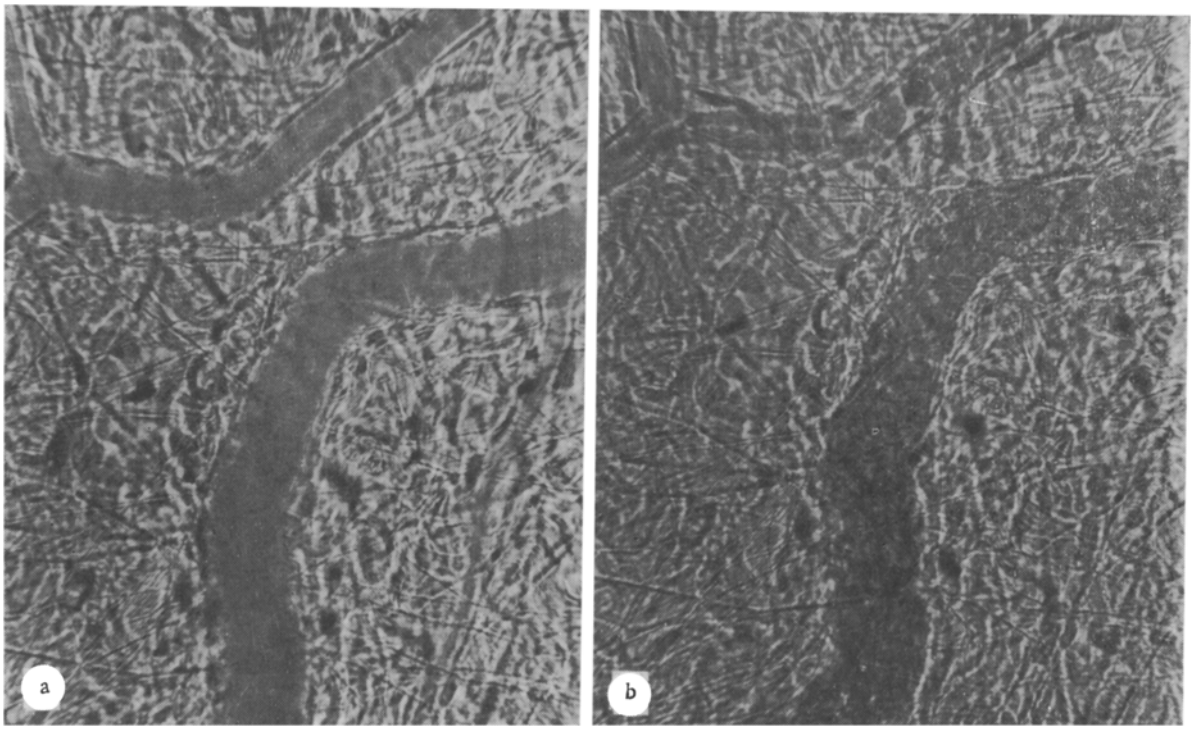

Fig. 2. Region of microvascular bed of rat mesentery: a) initial state of blood flow: homogeneous blood flow, cells in axial channel; b) same region after injection of submolecular M2 fraction: velocity of blood flow reduced in vein and arteriole, blood cells clearly visible.

The aim of this investigation was to study the effect of protein fractions obtained from the recipient's plasma after blood transfusion on arterial pressure, the microcirculation, and physiologically active substances in model experiments on healthy animals.

EXPERIMENTAL METHOD

A model of normovolemic exchange transfusion with allogeneic blood was used. Experiments were carried out on 39 Chinchilla rabbits weighing 2-3 kg and on Wistar rats weighing 200-250 g. On the day of the experiment, donors' blood was taken from two or three rabbits. The animals were bled from the carotid artery after preliminary injection of pentobarbital (50 mg/kg) and heparin (500 U/kg). Blood from the different donors was mixed in equal volumes, after which a volume equal to the circulating blood volume (65 ml/kg) was transferred to a thermostatically controlled vessel, which was connected by catheters to the carotid artery and subclavian vein. Exchange transfusion was carried out by opening the arteriovenous shunt and monitoring pressure in the carotid artery for 30 min. Before the normovolemic exchange transfusion, a blood sample taken from the experimental animals to obtain the recipient's original plasma (TP) was obtained, and fractionated by the method described previously [3]. For biotesting, besides the OP and TP samples, fractionation products of TP also were tested — the total macroprotein fraction M1 (mol. wt. over 2×10^2 daltons) and the M2 subfraction (mol. wt. 4×10^6 daltons) isolated from it. Protein was estimated spectrophotometrically $\left(E\frac{0,1\%}{278}=1\right)$ and by Lowry's method. The effect of plasma and its protein fractions on the arterial blood pressure (BP) and microcirculation was studied in experiments on rats. Each sample was tested in five or six experiments. The preparations were injected intravenously into the rats in a dose of 0.25 mg protein/100 g body weight; the volume of solution injected was always standard (1 ml/100 g body weight). BP was measured in the carotid artery and recorded for 35-40 min on a Barovar instrument (from Alvar Electronic). Activity of the samples was expressed in conventional units of hypotensive effect (HE): 1 HE unit was taken to be a reduction of BP by 10 mm Hg in the course of 1 min. The microcirculation of the same rats was studied simultaneously by intravital biomicroscopy of the mesenteric vascular bed. Ringer's solution at constant temperature (37°C, pH 7.4), containing 1% gelatinol, was used as the irrigating solution. Qualitative characteristics of the circulation in the microvascular bed were studied in the initial state and for 1 h after injection of the test preparation, with simultaneous photomicrography of the object. Physiologically active substances were studied in experiments *in vitro*. A cell test system consisting of leukocytes and platelets from healthy rabbits was used as the experimental model to study serotonin-releasing activity of the plasma proteins. The test fractions were incubated for 30 min with the leukocyte-platelet suspension, after which the serotonin concentration was determined in the incubation medium and cell mass by the method described previously [1, 4]. The level of serotonin-releasing activity was expressed as a percentage of the total serotonin concentration in the leukocyte-platelet suspension.

EXPERIMENTAL RESULTS

All 19 samples of plasma tested had a definite effect on BP (Fig. 1). In response to injection of the TP preparation BP fell by 10-15 mm Hg compared with its initial level (110 mm Hg). However, 5-6 min later BP was restored to its original level. The value of HE in rats of this group was 9.0±3.4 units. After injection of the M1 fraction into the rats there was a greater decrease in BP below its initial level. The value of HE in this case was 40± 3.5 units. Injection of the M2 subfraction caused the greatest and most prolonged fall of BP (on average to 50 mm Hg), and it remained at this level for 30-35 min, after which this parameter was spontaneously restored. The greatest HE (800±22.7 units) was found in rats of this group. By contrast the effect of the recipient's OP on BP of the rats was negligible, with none of the characteristic features of hypotension. As reflected in the value of HE, activity of OP and physiological saline was approximately equal (6±1.2 and 6±0.6 units respectively).

Investigation of the microcirculation revealed significant changes only after injection of the M2 fraction, which led to gradual slowing of the blood flow — initially in venules of small diameter, later in capillaries and arterioles (Fig. 2). At the same time the axial blood flow was narrowed, and this was accompanied by granulation and centralization of the blood cells. Changes in the blood flow in the microvascular bed were observed for 35-40 min and corresponded exactly to the period of the visible hypotensive effect of the M2 fraction.

A parallel trend of these phenomena also was clearly observed in the second phase: with restoration of the rat's BP the velocity of the blood flow increased and its structure in the microvessels was restored to normal.

Investigation of physiologically active substances showed that the total macromolecular fraction had higher serotonin-releasing activity than the plasma from which the preparation was obtained. Addition of 4 mg of the M1 fraction to the leukocyte-platelet suspension led to release of three times more serotonin (27.2±2.36 μg/ml) than samples of the original plasma (7.92±0.68). However, the protein fraction obtained from plasma of intact animals possessed the same activity, and no difference could be found between the experimental and control samples with respect to this feature. Significant differences between the groups were found when subfractions of macromolecular proteins were tested. For instance, addition of 4 mg of high-molecular-weight fraction M2 obtained from TP to the leukocyte-platelet suspension led to more intensive serotonin release (26.5±1.3) than in the control (the analogous plasma fraction from intact rabbits) (20.8±3.0). Investigation of the serotonin-releasing activity of all protein fractions revealed an important general feature distinguishing the development of the serotonin-releasing reaction under these conditions: all protein fractions caused serotonin release but only in the presence of autologous plasma of the rabbit from whose blood the leukocyte-platelet suspension was obtained. Incubation of the suspension with the recipient rabbit's own plasma (from which the protein fractions were obtained) did not cause serotonin release.

After normovolemic exchange transfusion with allogenic blood obtained from several donors, the plasma of the recipient rabbits thus acquired hypotensive activity. In the course of isolation and purification of the macromolecular proteins of the transfusion plasma, the level of its hypotensive activity rose and was many times higher than the hypotensive activity of the original plasma. The macroprotein subfraction of the recipient's plasma acquired marked hypotensive activity, which was directly linked with disturbance of the blood flow in the microvessels. Dependence of the state of the blood flow in the microvascular bed on BP, which was discovered under these experimental conditions, is evidence that the reaction of the physiologically active substances is primary, and disturbance of the microcirculation is secondary.

The response of the recipients to transfusion of homologous blood from several donors is thus formed with the participation of the protein system of the blood and of physiologically active substances. Interaction between proteins can evidently be regarded as an important stage in the genesis of post-transfusion complications.

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