of Ca^{++} from the myofibrils by mechanisms of ion transport located in the sarcoplasmic reticulum and sarcolemma [11-13]. Activation of lipid peroxidation in the myocardium [4, 8] and injury by products of this oxidation to the Ca^{++}-transporting mechanism of the sarcoplasmic reticulum [2] and mitochondrial membranes [1] and sarcolemma in the cardiomyocytes, and also a decrease in the glycogen concentration in the myocardium [6] have been found in EPS. This suggests that in the poststress period processes of Ca^{++} transport and the energy supply to the contractile mechanism are disturbed in the cardiomyocytes. As a result, the number of residual actomysin cross-linkages increases, the number of active centers on the protofibrils is reduced, and the reduction of extensibility of the atria and of the systolic tension capable of being developed by them, which was revealed by the present experiments, arises.

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In vivo HEMATOCRIT STUDY IN THE MICROCIRCULATORY SYSTEM BEFORE AND AFTER DEXTRAN INJECTION

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KEY WORDS: microcirculation; microvessels; hematocrit; dextran.

The rheologic properties of the blood and, in particular, its viscosity depend to a large extent on the hematocrit index. This index has hitherto been determined in mixed or venous blood by centrifugation in glass capillary tubes. Under these conditions the hematocrit index is usually overestimated because of changes in size of the erythrocytes, between which a layer of plasma always remains. Meanwhile, the hematocrit index is widely used to determine the circulating blood volume and during treatment with blood substitutes. Knowledge of the precise values of the hematocrit index is thus very important not only for practical medicine but also for the construction of a correct mathematical model of the circulation. Yet information on the level of the hematocrit index in different parts of the cardiovascular system is very limited in amount and contradictory in nature [4, 9, 11]. Investigations of the hematocrit index in microvessels have recently been published [5, 8-10].

The object of this investigation was to study the hematocrit index *in vivo* in microvessels before and after injection of polyglucin, a widely used Soviet dextran preparation.

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TABLE 1. Changes in Hematocrit Index in Microvessels of Rat Mesentery before and after Injection of Dextran (1 ml/100 g)

No.	Microvessels	Normal (M ± m)			Dextran (M ± m)			d/b
		n	diameter, μ	hematocrit index, %	n	diameter, μ	hematocrit index, %	
			a	b		c	d	
1	Arterioles	83	15—20	32,6±0,9	67	15—20	28,4±1,1 $P_{b-d}<0,01$	—23
2	Capillaries	17	8—10	11,2±1,2 $P_{1-2}<0,0001$	8	8—10	7,7±1,0 $P_{b-d}<0,05$ $P_{1-2}<0,0001$	—31
3	Venules	69	15—20	31,0±1,3 $P_{1-3}>0,1$ $P_{2-3}<0,0001$	78	18—23	26,1±0,9 $P_{b-d}<0,01$ $P_{1-3}>0,1$ $P_{2-3}<0,0001$	—16
4	Arteriolo-venular anastomoses	41	10—15	44,2±1,6 $P_{1-4}<0,0001$ $P_{2-4}<0,0001$ $P_{3-4}<0,0001$	22	13—18	28,5±3,1 $P_{b-d}<0,001$ $P_{1-4}>0,1$ $P_{2-4}<0,0001$ $P_{3-4}>0,1$	—36

Legend. n) Number of measurements, d/b) change in value of hematocrit index after injection of dextran (in % of normal).

EXPERIMENTAL METHOD

Experiments were carried out on 45 noninbred male albino rats weighing 160-280 g, anesthetized by intramuscular injection of urethane in a dose of 1.6 g/kg body weight. The hematocrit index was determined in microvessels of the rat mesentery by the method in [1]. The method consisted of biomicroscopy and photography of the microvessels by means of a ISFH-400 flash tube. Flash photography reproduced something similar to a frame stop effect, whereby a picture not of a continuous flow of blood, but of the separate cells constituting this flow of blood, could be obtained. In that way the shape and size of each erythrocyte and also their number could be determined. The hematocrit index in arterioles, capillaries, venules, and arteriolo-venular anastomoses was calculated by the equation given in a previous publication for determining the hematocrit index in a capillary [11]:

$$H = \frac{N \cdot V}{\left(\frac{D}{2}\right)^2 \cdot \pi \cdot L},$$

where H is the hematocrit index (in percent), N the number of erythrocytes in a given segment of the microvessel, V the volume of an erythrocyte, on average 80 μ^3, D the diameter of the microvessel (in μ), $\pi = 3.14$, and L is the length of the segment of the vessel (in μ). The numerator on the right hand side of the equation thus shows the volume of erythrocytes in the microvessel, the denominator the volume of the microvessel or of plasma filling it. Altogether 210 determinations of the hematocrit index were made in the microvessels before injection and 175 after injection of dextran. Dextran was injected into the femoral vein in a dose of 1 ml/100 g body weight. The hematocrit index was determined in the microvessels 30 min after injection of dextran. An "Olivetti" computer was used for mathematical analysis of the results.

EXPERIMENTAL RESULTS

In vivo determination of the hematocrit index in arterioles showed that, if measured at intervals of 10 min, it does not change significantly in the course of an hour. When determined repeatedly in the same region of the microvessel, values were obtained for the hematocrit index which differed by 5-10%. The greatest deviations (10%) from the mean were observed in capillaries, the smallest (5%) in arterioles. The causes of this scatter of measurements could be both the natural error of the method and also the vasomotor response of proximal segments of the afferent arterioles.

The mean momentary value of the hematocrit index in microvessels 8-28 μ in diameter before and after injection of dextran is given in Table 1. This shows that the hematocrit index in arterioles 15-20 μ in diameter was 32.6% compared with 11.2% in capillaries. In venules 15-20 μ in diameter the hematocrit index reached 31%, whereas in arteriolo-venular anastomoses the hematocrit index reached it highest value: 44.2%.

These observations showed that the hematocrit index depends on the diameter of the microvessel and on the angle at which it branches off. These experiments confirmed observations of Mchedlishvili and Gelin on the role of the angle of branching in the distribution of blood in the microvessels [2, 3, 7]. The hematocrit index also is affected by separation of the plasma and erythrocytes, which takes place due to branching of the vessels [7].

The hematocrit index also depends on the velocity of the blood flow which, in turn, is determined by the arterial pressure gradient.

The hematocrit index in microvessels thus decreases from arterioles to capillaries and increases again with a change to venules. Arteriolo-venular anastomoses, which have the highest value of the hematocrit index, are an exception to this rule. Kanzow et al. [8] found microvessels in which the hematocrit index was greater than can be predicted by the Fahraeus—Lindquist effect [6]. The authors cited suggest that these vessels may be functional shunts. This suggestion also is confirmed by the results of the present experiments showing a high value of the hematocrit index in arteriolo-venular anastomoses which are shunts of this type.

Intravenous injection of dextran caused a brief increase in the velocity of the blood flow, dilatation of the venules and arteriolo-venular anastomoses, a decrease in the hematocrit index, swelling of the walls of the microvessels and nuclei of the endothelial cells of the microvessels, an increase in pavementing of the leukocytes in the venules, and degranulation of mast cells. The greatest changes in the microcirculation were observed during the first 30 min after injection of dextran. Later the original pattern of the microcirculation was gradually restored. Values of the hematocrit index obtained 30 min after injection of dextran are given in Table 1.

The results are evidence that the greatest decrease in the value of the hematocrit index occurred in the arteriolo-venular anastomoses (by 36%) and capillaries (by 31%), the smallest (by 16%) in the venules. In the arterioles the hematocrit index was reduced by 23% compared with its value obtained before injection of dextran (the value of the hematocrit index obtained before injection of dextran was taken as 100%). It follows from Table 1 that the hematocrit index in arteriolo-venular anastomoses, arterioles, and venules was equalized by the action of dextran. This fact may be indirect evidence of equalization of the pressure in the arterioles and arteriolo-venular anastomoses. A very important factor is the considerable (by 31%) fall in the value of the hematocrit index in the capillaries, and this may be reflected substantially in the process of exchange of materials through their wall and may lead to the development, in particular, of tissue hypoxia.

Since no significant aggregation of erythrocytes was observed in the mesenteric microvessels before injection of dextran, the deaggregating effect of dextran could not be estimated.

It can be concluded from these results that the hematocrit index, even in arterioles 15-20 μ in diameter, is commensurate in value with that obtained under clinical and laboratory conditions by centrifugation of blood in glass capillary tubes. The hematocrit index falls sharply in the capillaries but rises again in the venules. The value of the hematocrit index in the capillaries is very dynamic, but in arterioles it is more stable.

Depending on the presence of functional rest or loading in the capillaries, the number of erythrocytes may be greater or less, and this substantially alters the hematocrit index. There is reason to suppose that under pathological conditions, when perfusion of the capillaries is sharply reduced and they become "plasmatic," the hematocrit index in them may fall as low as tenths of 1 per cent.

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CHANGES IN ERYTHROCYTES AFTER INJECTION OF EXCESSIVE DOSES OF RETINOIDS

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Evidence that removal of damaged and old erythrocytes from the blood stream is effected by means of lymphocytes and macrophages has been published [1]. Vitamin A and retinoids have the property of stimulating immune defense nonspecifically [18]. Bearing in mind the detergent properties of compounds of this group [18] it can be tentatively suggested that injury to the erythrocyte membrane may be one stage in the mechanism of the adjuvant action of retinoids, similar to what is found during autohemotherapy.

Now that it is possible to use synthetic analogs of vitamin A (retinoids [15]) clinically, the investigator is faced with the problem of devising methods of detecting signs of overdosage of the compounds of this group. The most convenient tests for practical purposes could be those determining blood parameters, for the blood cells are among the first to be exposed to the action of retinoids. The plasma concentrations of vitamin A and retinoids also reflects to a definite extent the degree of saturation of the body with these substances.

Natural forms of vitamin A in large doses have been shown to have a damaging action on erythrocytes [19], although no methods have yet been devised for the study of erythrocytes as a test object for determination of the degree of hypervitaminosis A. As regards changes in the erythrocytes after administration of excessive doses of retinoids and the role of these changes in the mechanism of the adjuvant action of these compounds, these topics have not been discussed in the literature.

The aim of this investigation was to analyze morphological and functional changes in the erythrocytes of mice receiving large doses of retinoids.

TABLE 1. Effect of Retinoids on Number of Erythrocytes in 1 mm^3, Hemoglobin Concentration, and Osmotic Resistance of Erythrocytes in C57BL/6 Mice on the 40th Day of the Experiment (M ± m, n = 8)

Procedure	Erythrocytes, millions	Hemoglobin, g%	Osmotic resistance of erythrocytes, %	
			limit of minimal resistance	limit of maximal resistance
Oily solution (control)	8,47±0,19	15,0±0,2	0,65±0,01	0,48±0,01
MR	5,42±0,17*	13,3±0,1*	0,70±0,01*	0,51±0,01
13-CMR	4,97±0,18*	12,8±0,1*	0,69±0,02	0,52±0,01*
RC_{15}	5,93±0,16*	14,8±0,1	0,67±0,01	0,49±0,01

Legend. Here and in Table 3, *P < 0.05 compared with the control.

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