The best results of arterial reconstructions accompanied by the formation of an AVA were thus observed in the dogs of experimental group 3, in which the diameter of the AVA was 40-60% of the diameter of the graft, for the prostheses were patent throughout the period of postoperative observation and the volume of the blood flow reaching the distal arterial bed was an adequate blood supply for the limb. Consequently, for the prevention of early postoperative thrombosis when arterial reconstructions are performed and the state of the drainage channels is poor, it is advisable to perform an AVA in addition. In such cases the AVA with a diameter equal to 40-60% of the diameter of the graft is optimal.

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SEROTONIN TURNOVER IN PLATELETS AND MICROVASCULAR HEMOSTASIS IN SPONTANEOUS HYPERTENSION

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Elevation of the thrombogenic potential of blood vessels in hypertension is accompanied by changes in platelet function and by definite modification to the platelet–vessel wall system [1, 4]. Mechanism of interaction between platelets and the vessel wall during the formation of a platelet thrombus are connected with release of thromboxane A_2, serotonin (5-HT), and other substances from the dense granules and α-granules of the platelets [5]. According to data in the literature [10], 5-HT turnover characterizes the level of platelet function to a greater degree than metabolism of other release factors. Changes in the thromboresistance of the vessels can be studied in vivo by quantitative estimation of thrombus formation following strictly graded injury to blood vessels [4]. The aim of this investigation was to study 5-HT turnover in the platelets and the dynamics of thrombus formation in arterioles and venules of the small intestinal mesentery of spontaneously hypertensive rats (SHR).

EXPERIMENTAL METHOD

Experiments were carried out on 69 male albino rats weighing 380-400 g, of which 40 rats constituted a control group. Changes in 5-HT turnover in the platelets and the dynamics of thrombus formation in arterioles and venules of the mesentery were studied during a long period of raised blood pressure (BP) in 29 SHR. BP was measured by an acute method in the carotid artery, and in the hypertensive rats it was 180 ± 10 mm Hg. 5-HT turnover in the platelets was investigated by determination of its initial level, its rate of uptake through assimilation, and by the study of its transport and accumulation in the platelets and its release. The 5-HT concentration in platelets was determined by the method in [3]. To study

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TABLE 1. 5-HT Turnover in Platelets and Thrombus Formation in SHR

Parameter of 5-HT turnover and thrombus formation	Control (40)	SHR (29)
Initial 5-HT level in platelets, μg/mg	0.673±0.026	0.559±0.034*
5-HT uptake by platelets:		
5-HT concentration in platelet after additional absorption, μg/mg	1.015±0.045**	0.785±0.052*,**
absorption of 5-HT by platelets, %	50.8±7.8	40.5±10.9
rate of 5-HT absorption, μg/mg × min	0.068±0.0011	0.045±0.013**
Released reaction of 5-HT:		
5-HT concentration in platelet after incubation with ADP, μg/mg	0.479±0.035**	0.447±0.013**
5-HT release from platelets, %	28.8±6.6	20.1±8.2
Time of growth of thrombus until detachment of 1st embolus, sec:		
arteriole	13±1	24±3
venule	18±2	25±2
Time of final fixation of thrombus to vessel wall, sec:		
arteriole	62±14	55±3
venule	117±7	84±4*
Length of thrombus, μ:		
arteriole	45±6	72±4
venule	69±4	83±5
Area of cross section of thrombus, μ^2:		
arteriole	820±50	1880±60*
venule	1960±60	1990±90

Legend. Number of experiments given in parentheses. *$p < 0.05$ compared with control, **$P < 0.01$ compared with initial 5-HT level.

the ability of platelets to take up additional 5-HT, 1 ml of platelet-containing plasma was treated with 1 μ of exogenous 5-HT (Sigma, USA) in 0.1 ml of aqueous solution and incubated at 37°C for 5 min. The release reaction was induced by the addition of 10 μM disodium salts of ADP (Reanal, Hungary). The protein concentration in the platelets was determined by Lowry's method [6]. Injury to the arterioles and venules (40-50 μ) of the small intestinal mesentery of the rats was produced by measured exposure of the microvessels to radiation from an LGI-21 pulsed nitrogen molecular laser, focused in the plane of the object through the microscope objective. The conditions of irradiation were: wavelength 337 nm, pulse following frequency 50 Hz, diameter of the laser beam on the object 10 μ, exposure 0.5 sec, radiation energy $2 \cdot 10^{-2}$ J. The dynamics of thrombus formation in the mesenteric arterioles and venules was compared by the method described previously [2].

EXPERIMENTAL RESULTS

Concentrations of 5-HT, its accumulation in and release from the platelets in the control rats, and changes in these parameters in SHR are given in Table 1.

The initial 5-HT level in the platelets, as shown by the results of its determination in the control (0.673 ± 0.026 μg/ml), is in agreement with data in the literature [7]. On incubation of the platelets with 5-HT its concentration increased to 1.015 ± 0.045 μg/mg protein, which is 0.342 ± 0.052 μg/mg higher than the initial 5-HT level. The rate of transmembrane transport of 5-HT reached 0.068 ± 0.011 μg/(mg·min). The intensity of the 5-HT release reaction from the platelets, induced by ADP, was 28.8 ± 6.6% in the control. The 5-HT level in the platelets was reduced by 0.194 ± 0.044 μg/mg and reached 0.479 ± 0.035 μg/mg.

The intensity of the 5-HT turnover in the platelets was found to be reduced in SHR, as shown by a decrease both in its initial level to 0.559 ± 0.034 μg/mg compared with the control ($p < 0.05$) and it its uptake (0.226 ± 0.062 μg/mg, 40.5 ± 10.9% of the initial level) during incubation of the platelets with 5-Ht.

Inhibition of 5-HT transport to the platelet membrane may arise as a result of interaction between inhibitors and the submembranous contractile protein system, a change in transmembrane regulatory mechanisms, and inhibition of the adenylate cyclase system [8]. Some workers associate the decrease in the 5-HT concentration in the platelets of SHR with the appearance of a pool of platelets with functional changes in their membranes during the formation of hypertension. In SHR, because of disturbance of active 5-HT transport through the platelet cell membrane, a reduction of 33.8% was observed in the rate of its absorption (0.045 ± 0.013 μg/(mg·min) compared with the control (0.068 ± 0.011 μg/(mg·min). More marked inhibition of active 5-HT transport in SHR and a decrease of 40% in the rate of its accumulation were found previously [9]. These results it must be noted, were obtained in the presence of a higher BP, up to 200 mm Hg.

Spontaneous hypertension is accompanied by inhibition of 5-HT release. During ADP-induced release the loss of 5-HT from the platelets amounted to 0.112 ± 0.045 μg/mg, compared with 0.194 ± 0.044 μg/mg in the control.

The study of the dynamics of thrombus formation in the mesenteric microvascular bed of the small intestine, using a model of laser-induced thrombosis, showed (Table 1) higher values of the basic parameters of thrombus formation in the venules of the control rats than in the arterioles. For instance, the time of growth of the thrombus until detachment of the first embolus was 1.39 times longer in the venules (18 ± 2 sec) than in the arterioles (13 ± 1 sec), whereas the time of final fixation of the thrombus to the wall was 1.89 times greater in the venules (117 ± 7 sec) than in the arterioles (62 ± 4 sec). The length of the thrombus along the blood flow was 1.29 times greater in the venules of the control rats (69 ± 4 μ) than in the arterioles (45 ± 6 μ), and the area of cross section of the thrombus was 2.39 times greater (1960 ± 60 μ^2 in the venules, 820 ± 50 μ^2 in the arterioles).

In SHR (Table 1) the time of growth of the thrombus was longer than in the control, especially in the arterioles. The time of final fixation of the thrombus to the vessel wall was shorter in the venules of SHR than in the control, but in the arterioles it was virtually unchanged. The area of cross section of the thrombus in the venules was the same as in the control. A significant increase in size of the thrombus was found in the arterioles up to the time of detachment of the first embolus in SHR compared with the control. The length of the thrombus also was greater in both types of vessels, evidence of lowering of the resistance of the vessel wall to thrombosis.

Thus 5-HT turnover in the platelets constitutes a single system, embracing its uptake, transport, accumulation, and release. Changes in 5-HT turnover in the platelets in SHR are characterized by a decrease in the concentration of 5-HT and inhibition of its absorption and release, evidence of depression of platelet function relative to 5-HT. A slower growth of the laser-induced thrombus was observed in both types of vessels of SHR, with a significant increase in size of the thrombi in the arterioles compared with the control. Although 5-HT causes contraction of blood vessels, it has a minimal effect on platelets in the initial period of microvascular hemostasis [5], and for that reason the dynamics of thrombus formation is unconnected with the features of 5-HT turnover revealed by this experimental model.

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EFFECT OF ACUTE ANOXIA ON SERUM RENIN AND ERYTHROPOIETIN ACTIVITY IN RATS

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The kidneys have not only an excretory function, but they also play the role of an endocrine organ, producing biologically active substances and hormones such as renin, kinins, prostaglandins, and erythropoietin. The stimulus for renin secretion is a change in the blood supply to the kidneys and, in particular, reduction of the blood flow through the renal arteries, with a fall of the perfusion pressure [3]. However, changes in the hemodynamics of the kidney also affect the biogenesis of erythropoietin, a hormone which regulates erythropoiesis [7]. Thus a fall in the blood flow in the renal tissue may lead to simultaneous stimulation of these two biologically active substances.

This paper describes a comparative study of the serum renin and erythropoietin concentrations in rats with an "endocrine" kidney and changes in the activity of each of these compounds after exposure to a specific erythropoietic stimulus, namely anoxia.

EXPERIMENTAL METHOD

Inbred rats weighing 100-120 g and (CBA × C57Bl)F_1 mice were used. There were three main series of experiments: I) normal animals; II) rats on the 7th day of occlusion of the abdominal aorta; III) animals undergoing mock operations at the same time. The animals in each series were additionally exposed to anoxia for 4 h. The experimental model of an "endocrine" kidney was obtained by the method in [14]. The aorta of the anesthetized rats was ligated with Kapron on a stylet 0.34 mm in diameter, thus constricting it to the same size as the stylet. Adequacy of the model was verified by ligation of a ureter in some of the rats, followed by observing the presence or absence of hydronephrosis. The second control test was a histologic investigation during which the state of the parenchyma of the renal cortex and medulla was studied. On the basis of these two tests a technique for producing the "endocrine" kidney was developed. If a contralateral "intact" kidney was present, the rats did not develop renal failure. In some rats the right "intact" kidney was removed on the 7th day of occlusion of the aorta through a dorsal incision. During the next 4 h these animals were kept either under ordinary atmospheric conditions or in a hypobaric chamber. To exclude any effect of operative stress, a mock operation was performed on some of the animals, resembling the operation to obtain an "endocrine" kidney but without ligation of the aorta. Hypobaric anoxia, induced by exposure of the animals in a hypobaric chamber to

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