the formation predominantly of antiaggregant substances in the vessel, whereas low initial activity is determined by the formation of very small quantities of antiaggregants but by a high content of agents with the opposite effect on platelets.

It can thus be concluded from these results that antiaggregating activity of blood vessels cannot be justifiably reduced simply to the effect of PGI_2 synthesized in them. More probably a whole range of agents, differing in their effects on platelets and their stability in plasma, is released from the vessels into the blood stream. Under ordinary conditions the effect of antiaggregants predominates in secretion from the vascular wall, but the possibility naturally cannot be ruled out that the vascular wall may be in a state in which proaggregants will be predominant in the combination of substances secreted by it. This view is confirmed by the cases of initial proaggregating activity of segements from the middle cerebral artery, removed from the zone of a brain infarct, described previously [2]. The complex nature of antiaggregating activity of the vascular wall, which can be more accurately defined as the platelet-active properties of the vessels, must evidently be taken into account both during interpretation of experimental results and during analysis of the importance of this phenomenon in regulation of the circulation and development of its disorders.

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TIME COURSE OF RECOVERY OF THE MICROCIRCULATION AFTER STRESS

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The writer showed previously that immobilization and generalized electrical stimulation induce changes in the terminal blood flow and vascular permeability in the rat mesentery [1, 2]. However, the time course of recovery of the microcirculation and of the state of the microvascular wall and mast cells (MC) after stress has not been studied. The investigation described below was devoted to the study of these problems.

EXPERIMENTAL METHOD

Experiments were carried out on 185 male Wistar rats weighing 200-250 g. Immobilization for 24 h or electrical stimulation for 6 h were used as extremal stimuli. An apparatus based on the Docuval (Carl Zeiss, East Germany) microscope was used for biomicroscopic study of the mesenteric microcirculation. Vascular permeability in the mesentery was studied by luminescence contact biomicroscopy followed by quantitative photometry on a LYUMAM KF-1 microscope. Fluorescein isothiocyanate-labeled globulin was used as indicator of disturbances of vascular permeability. The morphological and functional state of the MC was assessed by biomicroscopy and also by examination of mesenteric preparations. The latter were obtained after intravital fixation of the mesentery by intraperitoneal injection of 15 ml of Carnoy's fixing solution.

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TABLE 1. Disturbances of Microcirculation in Rat Mesentery after Immobilization for 24 h

Experimental conditions	No. of rats	Severity of microcirculatory disturbances, % of number of animals in series							
		slowing of blood flow		erythrocytic aggregation		plasmatic vessels	stasis	pavementing of leukocytes	degranulation of MC
		venules	arterioles	capillaries	venules				
Immobilization (24 h)	13	100	69	100	100	92	100	40	100
After immobilization									
1 day	5	100	60	100	100	80	80	40	20
2 days	5	80	20	60	40	60	40	20	20
3 days	5	60	—	60	40	40	40	20	—
4 days	5	60	—	60	20	20	40	—	—
5 days	5	60	—	60	20	20	20	—	—
6 days	5	40	—	40	20	—	20	—	—
14 days	13	23	—	7	7	—	—	—	—
Control	10	20	—	—	10	—	—	10	—

TABLE 2. Disturbances of Microcirculation in Rat Mesentery after Electrical Stimulation for 6 h

Experimental conditions	No. of rats	Severity of microcirculatory disturbances, % of number of animals in series							
		slowing of blood flow		erythrocytic aggregation		plasmatic vessels	stasis	pavementing of leukocytes	degranulation of MC
		venules	arterioles	capillaries	venules				
Electrical stimulation (6 h)	10	50	—	70	90	60	70	100	100
After electrical stimulation:									
17 h	6	50	—	50	50	66	50	50	33
24 h	6	16	—	16	16	—	—	6	—
Control	10	20	—	—	10	—	—	10	—

TABLE 3. Number of MC in Mesentery and Degree of Their Degranulation after Stress (M ± m)

Experimental conditions	Mean number of MC per field of vision (135×)	% of degranulated MC
Immobilization (24 h)	20,8±0,6*	0,70±0,04*
After immobilization:		
1 day	21,1±0,6*	0,22±0,01
2 days	22,1±0,7	0,10±0,07
3 days	23,9±0,5	0,11±0,01
Electrical stimulation (6 h)	13,2±0,6*	1,40±0,40*
After electrical stimulation:		
6 h	17,2±0,4*	0,18±0,03
17 h	20,4±0,5*	0,11±0,01
24 h	24,4±0,3	0,10±0,01
Control	25,2±1,6	0,09±0,06

Legend. *P < 0.05.

In the course of the experiments the animals' general state and their body weight was determined. After the end of the experiments the adrenals were weighed and the presence of erosions and ulcers in the stomach was noted. The results were subjected to statistical analysis with calculation of the error of the means by Peters' method, using Moldenhauer's factor [5].

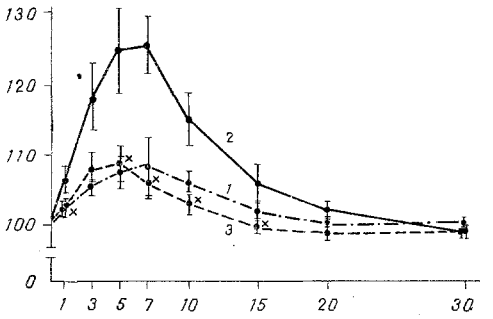

Fig. 1. Permeability of mesenteric microvessels in rats after immobilization for 24 h. Abscissa, time after injection of serum (in min); ordinate, increase in intensity of fluorescence (in %). 1) Intensity of fluorescence in intact rats, 2) immediately after immobilization, 3) 1 day after immobilization. *P < 0.05 compared with series II and III.

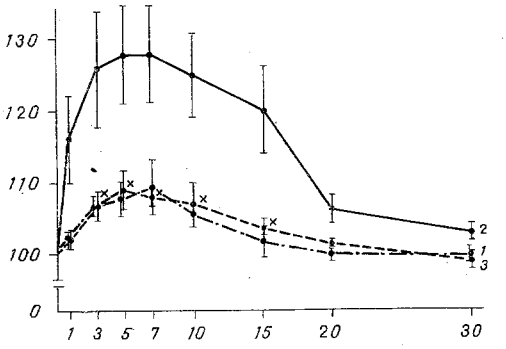

Fig. 2. Permeability of mesenteric microvessels in rats after electrical stimulation for 6 h. 1) Intensity of fluorescence in intact rats, 2) immediately after electrical stimulation, 3) 6 h after electrical stimulation. Remainder of legend as to Fig. 1.

EXPERIMENTAL RESULTS

When examined 24 h after immobilization for 24 h or electrical stimulation for 6 h the rats moved freely about the cage, they were active, and ate well. Immobilization for 24 h caused a decrease in body weight of the rats on average by 9%, and electrical stimulation for 6 h caused a decrease of 6%. Six days after immobilization 50% of the experimental rats began to gain weight on average by 2%. After 14 days the gain in weight was 12%. One day after electrical stimulation 50% of the rats gained in weight by 2%. The weight of the adrenals in the rats 6 days after immobilization and 1 day after electrical stimulation was increased. After immobilization 40% of rats developed gastric ulcers, and 1 day later still, ulcers were found in 60% of animals. Six days after immobilization neither ulcers nor erosions could be found in the stomach of the experimental rats. Single erosions were observed after electrical stimulation in only one (8%) of 13 rats. No erosions were found in the stomach of the rats 24 h after electrical stimulation.

Biomicroscopic study of the state of the microcirculation in the rat mesentery 1-6 and 14 days after immobilization showed that after 1 day the terminal blood flow was disturbed to the same extent as immediately after immobilization. All animals showed slowing of the blood flow in the venules, and in more than half of the rats, in the arterioles also. Erythrocytic aggregates in the form of "rouleaux" and large conglomerates of erythrocytes were found in all animals. In 80% of cases "plasmatic" vessels and stasis were found. On the 2nd-3rd day after immobilization all disturbances of the microcirculation were preserved. On the 4th-5th day slowing of the blood flow continued in the venules, with erythrocytic aggregation in the capillaries, although these phenomena were less marked. Stasis and "plasmatic" vessels were still present in 20% of cases. On the whole, it can be said that at this stage the blood flow was restored in 50% of the animals. Normalization of the microcirculation was found 14 days after immobilization in all the experimental animals (Table 1).

Biomicroscopy of the rat mesentery 17 h after electrical stimulation showed that the terminal blood flow remained disturbed. It was slowed in the venules, and erythrocytic aggregation, plasmatization of the vessels, and stasis were present. However, 24 h after stimulation appreciable normalization of the microcirculation was observed (Table 2).

Estimation of the state of vascular permeability showed that in rats 1 day after immobilization it was significantly reduced, and the same as in the control (Fig. 1). In animals exposed to electrical stimulation for 6 h normalization of vascular permeability had taken place 6 h after the end of stimulation (Fig. 2).

Since MC play an important role in regulation of the microcirculation, a special series of experiments was carried out to determine the state of these cells at different times after the action of stressors. The results of these experiments were as follows. The number of MC in the mesentery 24 h after immobilization was reduced, although the degree of their degranulation was indistinguishable from that in the control, as also was the degree of degranulation of these cells.

Six hours after electrical stimulation the degree of degranulation of MC in the mesentery was not increased, although their number was reduced. It still remained low 17 h after stimulation, and was not restored until after 24 h. The intensity of degranulation of MC was the same as in the control (Table 3).

Disturbances of the microcirculation thus correlated to some degree with changes in the animals' general state and the intensity of the stress reaction. Immobilization for 24 h caused more profound and prolonged disturbances in the microcirculatory system than electrical stimulation for 6 h. Normalization of vascular permeability correlated with the morphological and functional state of MC. These cells evidently played an important role in the pathogenesis of disturbances of vascular permeability. As target cells for a number of biologically active substances (catecholamines [6, 9], acetylcholine [7, 11], prostaglandins [8, 12], and polypeptide "P" [10, 13]) MC can change vascular permeability on account of the histamine, serotonin, and heparin contained in their granules. The writers' previous experiments showed that short-living biologically active substances such as histamine, serotonin, bradykinin, prostaglandins, polypeptide P, and so on, participate in the mechanism of the disturbances of vascular permeability associated with stress [1, 3, 4], and it is this which gives these disturbances their phasic and transient character. Changes in the microcirculation, on the other hand, may depend to a greater degree on disturbances of the central hemodynamics and rheologic disorders, and they may therefore be more enduring in character.

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