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THE MICROCIRCULATORY SYSTEM OF HAMSTERS UNDER STRESS AND AFTER PROPHYLACTIC INJECTION OF IONOL

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Disturbances of the terminal blood flow, of vascular permeability, and of the morphological and functional state of the mast cells were found in experiments on rats subjected to immobilization or to electrical stimulation [1, 2]. The degree of generalization of these disturbances and their organ specificity, however, remained unexplained, which necessitated the study of the state of the microcirculatory system in the mucosa of the retrobuccal pouch (MRP) of hamsters after exposure to stress. In consideration of data showing that stress-induced injuries can be effectively prevented by the antioxidant ionol [4-6, 9], and experimental study of prevention of disturbances to the microcirculation with the aid of this compound was carried out under conditions of stress.

EXPERIMENTAL METHOD

Experiments were carried out on 96 Syrian hamsters weighing 120-150 g. Immobilization of the animals for 1 and 24 h and graded whole-body electrical stimulation for 3 h were used as extraordinary stimuli.

For the biomicroscopic study of the microcirculation in the hamster MRP, an apparatus based on the "Docuval" microscope (Carl Zeiss, East Germany) was used.

Quantitative estimation of vascular permeability was carried out by luminescence contact biomicroscopy on an apparatus based on the Soviet LYUMAM KF-1 microscope, using bovine globulin, labeled with fluorescein isothiocyanate (FITC) as the marker. Ionol was injected intraperitoneally in a dose of 100 mg/kg three times in the course of three days. In the case of immobilization for 24 h, the 4th injection of ionol was given 8 h after the beginning of immobilization. The results were subjected to statistical analysis by Peters' method, using Moldenhauer's factor [7].

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TABLE 1. Effect of Stress and Ionol on Degranulation of Mast Cells in Hamster MRP

Experimental conditions	Percentage of degranulated mast cells	Significance of differences
1. Control	0,8±0,20	
2. Immobilization for 1 h	2,0±0,25	$P_{1-2} = 0,04$
3. Immobilization for 24 h	3,4±0,30	$P_{2-5} = 0,01$
4. Ionol	1,0±0,10	$P_{3-1} = 0,001$
5. Ionol + immobilization for 1 h	1,1±0,10	
6. Ionol + immobilization for 24 h	2,6±0,10	$P_{6-3} = 0,03$

Legend. Five animals in each group.

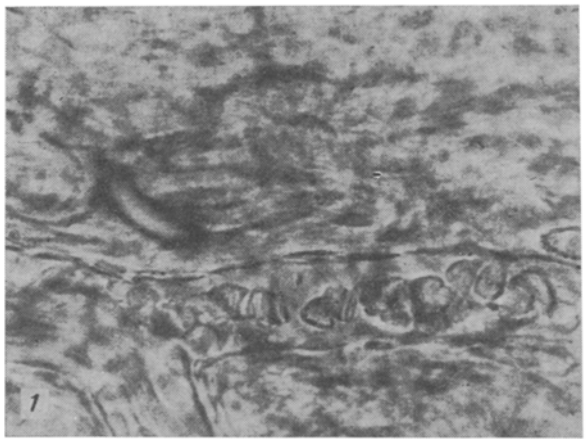

Fig. 1

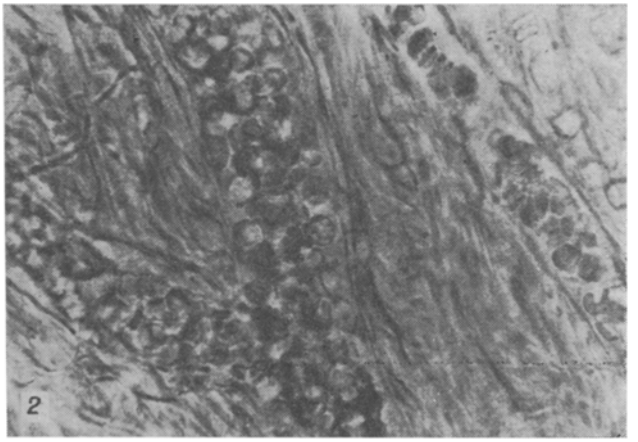

Fig. 2

Fig. 1. Aggregation of erthrocytes in MRP of a hamster after immobilization for 1 h. Here and in Fig. 2, biomicroscopy, 180x.

Fig. 2. Slowing of blood flow in venules and aggregation of erythrocytes in MRP after immobilization for 24 h.

EXPERIMENTAL RESULTS

The biomicroscopic study of MRP of hamsters immobilized for 1 h revealed disturbances of the microcirculation (Fig. 1): slowing of the blood flow in the venules and in the venular segments of the capillaries (70% of animals), the appearance of aggregation of erythrocytes in capillaries and venules 20-40μ in diameter (80%), and the development of stasis (40%).

During immobilization of the hamsters for 24 h the state of the microcirculation in MRP worsened. In all the animals the blood flow in the venules was slowed (Fig. 2). Erythrocytic aggregates in the form of rouleaux or of conglomerates of these cells, which were irregular in shape and of considerable size, were found in the capillaries and venules of 90% of the animals. Stasis and plasmatization of the microvessels were more marked. During electrical stimulation for 3 h even more severe disturbances of the microcirculation than after immobilization for 24 h were found. Slowing of the blood flow could be detected not only in the venular, but also in the arteriolar microvessels, and marked aggregation of erythrocytes was present in all the animals.

After comparison of these results with those of experiments conducted previously on rats it was concluded that, despite the difference in character and duration of action of the stressors, similar disturbances of the terminal blood flow were found in the rat mesentery and the hamster retrobuccal pouch. In particular, the appearance of aggregation of erythrocytes should be noted in hamsters, in which sedimentation of the erythrocytes takes place under normal conditions ten times more slowly than in rats [3]. These data are evidence of the specificity of erythrocytic aggregation for the microcirculatory disorders associated with

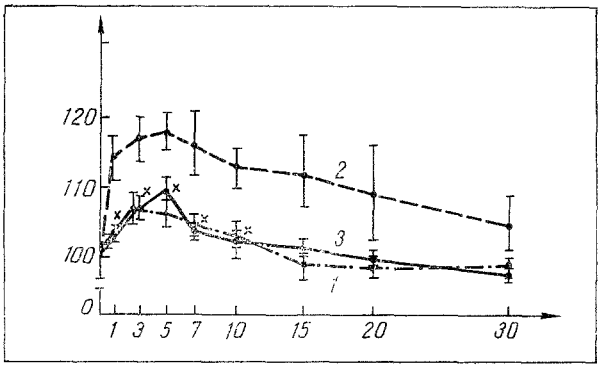

Fig. 3. Permeability of venular microvessels of hamster MRP for FITC-labeled globulin after immobilization of animals for 24 h and administration of ionol. Abscissa, time of injection of serum (in min); ordinate, increase in intensity of fluorescence (in per cent of initial background, taken as 100); a) control, b) immobilization for 24 h, c) immobilization for 24 h + injection of ionol. ×) Statistically significant difference between experimental groups (b, c).

stress. The presence of a similar kind of microcirculatory disturbances in animals of different species, as well as data in the literature with correlate with our own and which indicate similar changes in the microcirculatory system as a result of exposure to external factors [8, 10, 11], are evidence of the generalized character of microcirculatory disturbances in stress.

Besides the common features of the microcirculatory disorders, organ-specific features also were found. For instance, the extraordinarily well developed vascular network in the hamster retrobuccal pouch and the presence of many arteriolo-ateriolar and venulo-venular shunts functioning under normal conditions helped to preserve the blood flow unchanged over a wide area of the organ.

Quantitative analysis of vascular permeability showed that in intact hamsters, just as in intact rats, an outflow of FITC-labeled globulin is observed through the wall of the venules, although in the latter this process is more marked. Immobilization of the animals for 24 h led to a significant increase in vascular permeability for globulin in the venular portion of the microvascular bed (Fig. 3). An increase in the outflow of globulin through the wall of venules 20-40μ in diameter also occurred after electrical stimulation of the hamsters for 3 h.

The results correlated with data obtained on the mesentery of rats exposed to the action of these same stressors [1].

The mast cells in the hamster MRP, like those in the rat mesentery, increased their secretion of physiologically active substances by degranulation (Table 1), but this process took place in the earlier period of immobilization (1 h) in hamsters, whereas in rats a significant increase in degranulation was observed after 6 h of immobilization. An increase in degranulation of the mast cells, accompanied by increased outflow of histamine, serotonin, kallikrein, and proteases from them, may be one cause of the increase in vascular permeability.

Exposure to stress thus causes injury to membranes of erythrocytes, endotheliocytes, and mast cells. One cause of injury to these membrane structures could be activation of lipid peroxidation during stress [4]. Accordingly, attempts to prevent stress-induced disturbances of the microcirculatory system by the antioxidant ionol were undertaken. Injection of ionol did not affect the state of the terminal blood flow, of vascular permeability, or of the mast cells. Biomicroscopic investigation conducted on the retrobuccal pouch of hamsters immobilized for 1 and 24 h revealed no difference in the state of the microcirculation in animals receiving and not receiving ionol. However, prophylactic administration of ionol significantly reduced the increased vascular permeability found after immobilization for 24 h (Fig. 3) and also reduced degranulation of the mast cells (Table 1).

Prophylactic administation of ionol thus diminished the damaging action of stress on the microcirculatory system.

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