REACTIVITY OF THE MESENTERIC MICROCIRCULATORY BED IN RATS WITH EXPERIMENTAL DEHYDRATION

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Maintenance of the fluid balance of the body is one of the bases of homeostasis in man and animals [3, 7, 9, 10]. The two extreme forms of changes in the fluid balance, namely edema and dehydration, essentially unite the leading mechanisms of general pathological disturbances in various diseases [1, 11]. The behavior of the microcirculatory system, which is responsible for regulation of the fluid exchange in the body during edema, has been sufficiently well investigated. However, the role of microcirculatory mechanisms in adaptive responses to dehydration has received little study.

This paper gives the results of an intravital investigation of the microcirculatory bed at the stages of alimentary dehydration.

EXPERIMENTAL METHOD

Experiments were carried out on 24 male albino rats weighing 200 g, allowed free access to dry food but completely deprived of water for 3, 6, and 12 days. The microcirculatory bed was studied in the mesentery by the intravital transillumination method [5, 15]. The animals were anesthetized with 0.6% pentobarbital solution in a dose of 5 mg of the dry substance/100 g body weight. The MBI-6 microscope was used for biomicroscopy. Negatives taken in the course of the experiments on a Mikrofot camera, further enlarged by 12 times, were used for morphometry of the diameters of all the microvessels [6]. The results of morphometry were subjected to statistical analysis by Student's test.

EXPERIMENTAL RESULTS

An interconnected role in the mechanisms regulating microcirculatory homeostasis in the mesentery at the stages of dehydration is played by vascular, intravascular, and extravascular changes. Their intensity depends on the duration of water deprivation of the animals.

The response of the arterioles and precapillaries of the mesentery to dehydration took the form of changes in the diameters of these vessels. Both a decrease in the mean values of the diameters and regions of spastic contraction of their walls were observed (Fig. 1a, b). After 3 days of dehydration a significant decrease in the diameters of the arterioles by 6% and a tendency for the diameters of the precapillaries to decrease were observed (Table 1). The coefficient of transverse deformation of the arterioles, reflectingthe degree of theirlocal spastic contractions, did not exceed 10%. After 6 days of dehydration the diameters of the arterioles and precapillaries were significantly reduced by 12 and 15% respectively (Table 1). The coefficient of transverse deformation of the arterioles rose to 17%. On the 12th day of dehydration the decrease in the diameters of the arterioles and precapillaries amounted to 19 and 23% of the control respectively. The coefficient of transverse deformation of the arterioles was increased to 37%, and the arterioles and precapillaries were more tortuous.

Changes in the exchange sections of the microcirculatory bed of the mesentery took the form of a decrease in the number of perfused capillaries in the central zones of the vascular

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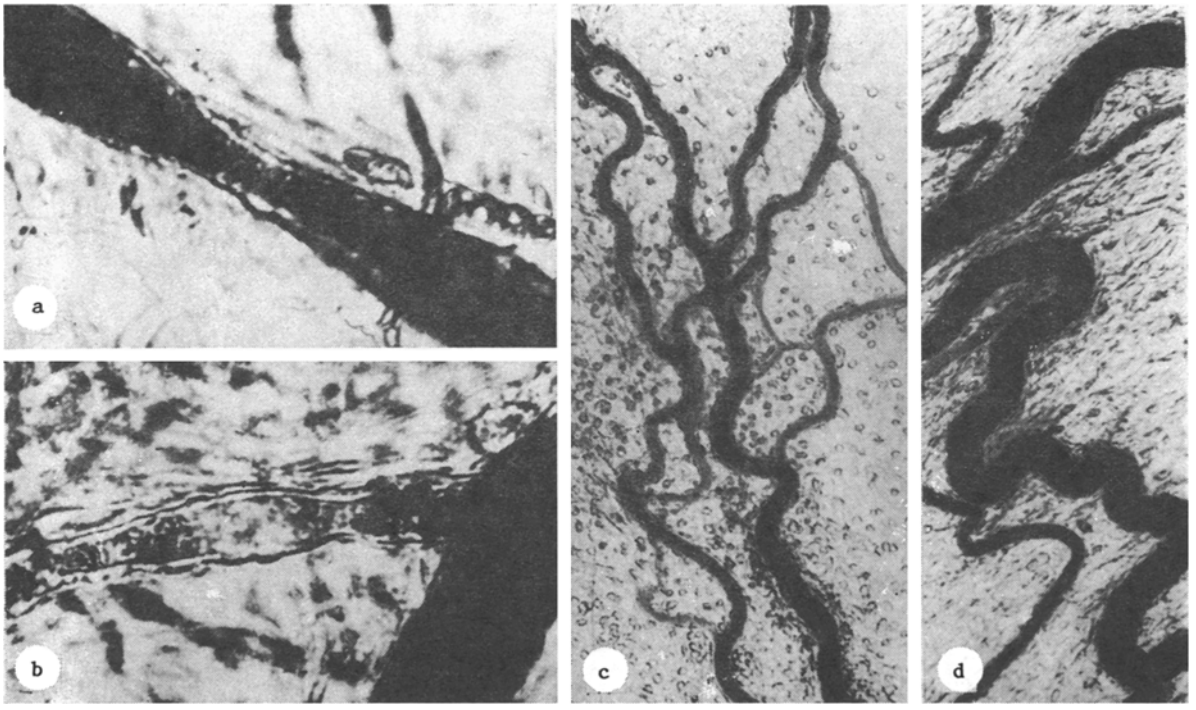

Fig. 1. Changes in the microcirculatory bed of the rat mesentery: a) region of spastic contraction of arteriolar wall (12th day of dehydration); b) region of spastic contraction of precapillary wall (12th day); c) ansiform capillary complexes (6th day of dehydration); d) tortuosity of postcapillaries and venules (6th day). Magnification: a, b) 140 ×; c, d) 63 ×.

TABLE 1. Changes in Diameters of Vascular Components of the Mesenteric Microcirculatory Bed of Albino Rats at Different Times of Alimentary Dehydration (M ± m)

Component of microcirculatory bed	Period of dehydration, days			
	control	3	6	12
Arterioles	17,7 ± 0,2	16,7 ± 0,3*	15,2 ± 0,2*	14,5 ± 0,2*
Precapillaries	10,6 ± 0,2	10,2 ± 0,2	9,0 ± 0,2*	8,2 ± 0,1*
Capillaries	7 ± 0,1	6,6 ± 0,1*	5,4 ± 0,1*	4,4 ± 0,1*
Postcapillaries	12,2 ± 0,2	11,7 ± 0,2	10,0 ± 0,1*	9,2 ± 0,1*
Venules	20,8 ± 0,3	20,6 ± 0,2	17,9 ± 0,1*	16,9 ± 0,1*

Legend. *p < 0.05 compared with control.

nodules. Disturbance of communication between the capillary components of adjacent arteriolo-venular complexes with reduction of the structural networks and with the formation of relatively isolated ansiform functional shunts were noteworthy features (Fig. 1c). The number of deformed and tortuous capillaries was increased. After the 3rd day of dehydration a significant decrease in the diameter of the capillaries by 6% was observed, after 6 days the decrease was 23%, and after 12 days of dehydration the decrease compared with the control was 34% (Table 1).

In the course of dehydration increased tortuosity of the postcapillaries and venules was identified (Fig. 1d). From the 6th day of dehydration there was a significant decrease in the diameters of the postcapillaries and venules by 18 and 14% respectively of the control. On the 12th day of the experiment the diameters of these vessels were reduced by 25 and 24% respectively (Table 1).

A particular feature of the functional microangioarchitectonics of the mesentery in the early and intermediate stages of dehydration was the discovery of many arteriolo-venular

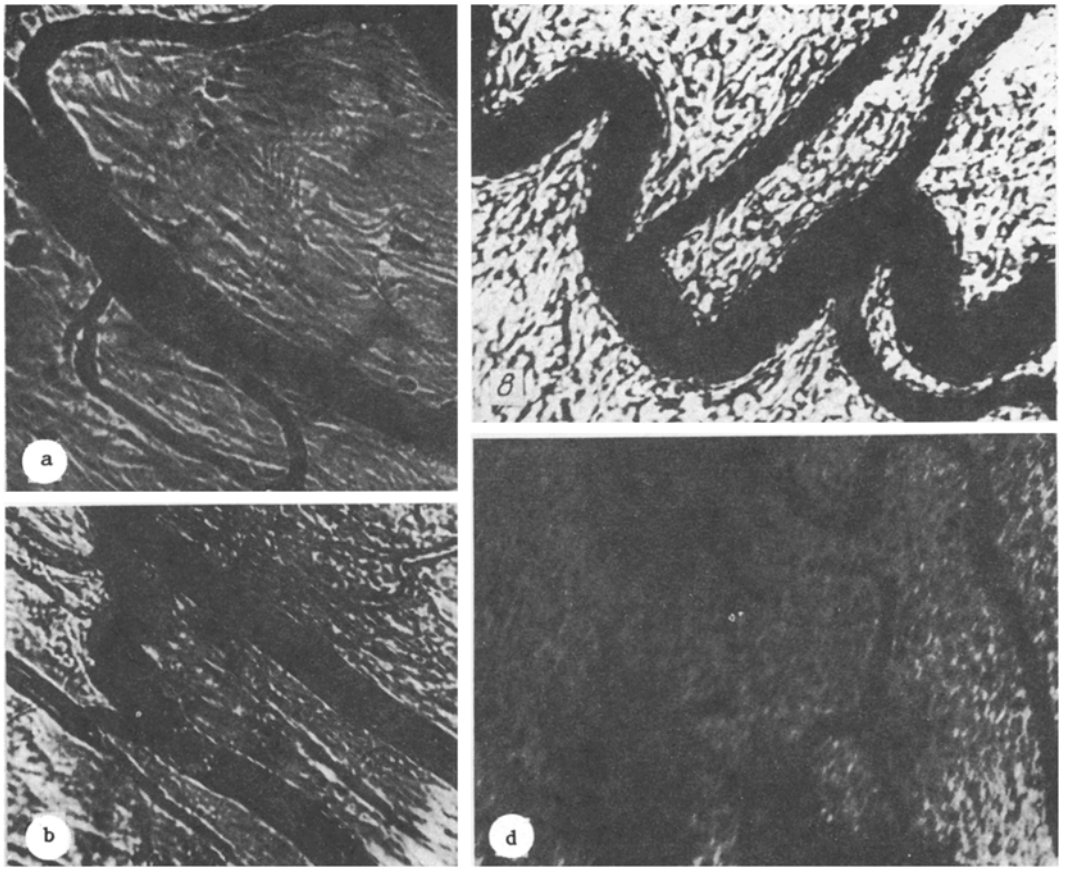

Fig. 2. Disturbances of microcirculatory processes in the mesentery. a) Arteriolo-venular anastomosis of the "hemishunt" type (6th day of dehydration); b) aggregation of erythrocytes in lumen of a venule (6th day); c) adhesion of leukocytes to luminal surface of a venule (12th day of dehydration); d) focal hemorrhages around capillaries and postcapillaries (12th day). Magnification: a, b, c) 140 ×; d) 63 ×.

anastomoses (Fig. 2a). The greatest juxtacapillary discharge of blood was observed on the 6th day of dehydration. On the 12th day of the experiment these processes were less marked due to the spread of the intravascular disturbances to the communicating shunts.

The intravascular changes took the form of slowing of the velocity of the blood flow, its exclusion from certain vascular territories of distribution, aggregation of erythrocytes (Fig. 2b), and adhesion of leukocytes to the luminal surface of the walls of the microvessels (Fig. 2c). These changes developed until the sublethal stage of dehydration. Maximal fluctuations of blood flow were discovered in the capillaries. Changes in the capillary blood flow were characterized by a decrease in the relative number of vessels with a continuous, homogeneous blood flow and an increase in the proportion of vessels with a continuous, granular type or a discontinuous, granule type of flow, as well as an increase in the number of plasmatized capillaries. The development of extravascular disturbances was observed after the 6th day of dehydration. These took the form of local hemorrhages (Fig. 2d), which became widespread in character at the sublethal stage of the experiment.

These data are evidence that structural changes in the microcirculatory bed and transformations of the microcirculatory blood flow in the mesentery develop gradually during dehydration and they are definitely interconnected. The low intensity of the changes discovered on the 3rd day of dehydration is evidence of minimal involvement of the vascular sector in the initial elimination of intracorporeal water, in agreement with the results of physiological investigations [13]. After the 6th day of dehydration the vascular changes in all components of the microcirculatory bed attained a significant level. These data are in full agreement with the results of our previous investigations [8]. In the intermediate and late stages of dehydration three interconnected groups of morphological and functional mechanisms responsible for regulating the microcirculatory blood flow under conditions of an

increasing water deficiency can be distinguished. These include contraction of the smooth muscle cells of the arterioles and precapillaries, activation of arteriolo-venular shunting, and reduction of the capillary blood flow. The last of these, in our opinion, is the key mechanism. Changes in the geometry of the capillary bed, in the hemodynamic parameters of the capillary blood flow, and also in blood rheology must be distinguished among the morphological and functional factors that determine its development. At certain stages many of these changes are adaptive in character. They are aimed primarily at maintaining new levels of matching between the reduced circulating blood volume and the capacity of the microcirculatory bed [10]. In this connection the exclusion of a certain part of the capillary bed from the blood flow, accompanied by increased discharge of blood through arteriolo-venular anastomoses, can be interpreted as responses aimed at maintaining the systemic hemodynamics at adequate levels [2, 8]. Under these circumstances slowing of the blood flow must be considered to be an essential hemodynamic mechanism. The adaptive role of this process consists not only of maintenance of the balance of the circulation when the circulating blood volume is reduced, but also of lengthening of the exposure of the blood in the exchange sectors of the microcirculatory bed [8, 14]. Intensification of these changes at the sublethal stages of dehydration leads to an increase in the proportion of unperfused capillaries and of capillaries blocked by stasis. All this leads to the development of a state of tissue hypoperfusion [10].

Comparison of the microcirculatory disorders typical of the final stages of dehydration, which we have distinguished, with known schemes of development of microvascular disturbances when the organism is exposed to other extremal factors indicates their similarity with the patterns of shock. In this connection our evaluation of the states studied in this paper agrees with conclusions drawn by workers [4, 12] who regard the sublethal stages of dehydration as a special, hypovolemic form of shock.

The acceptance of this fact opens up new ways for the prevention and treatment of these disturbances. Efforts in this direction must be concentrated mainly on normalization of matching the capacity of the microcirculatory bed to the volume of blood circulating in it. Intensive infusion therapy must be supplemented by treatment aimed at lowering the increased tone of the resistive vessels and diminishing arteriolo-venular shunting, which ultimately must favor recovery of the capillary microcirculation.

A special role in the set of therapeutic measures for use in dehydration must be played by disaggregants and angioprotectors, whose action is aimed at correcting intravascular and extravascular disturbances.

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QUANTITATIVE CHANGES IN CELL COMPOSITION AND VASCULARIZATION OF ASEPTIC SKIN WOUNDS HEALING IN RATS WITHOUT TREATMENT AND WITH STIMULATION OF REPAIR BY EXOGENOUS COLLAGEN

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Histochemical and electron-microscopic investigations on experimental and clinical material have demonstrated the beneficial effect of collagen preparations on healing of wounds of varied etiology [2, 3]. However, no quantitative morphological investigations, marked by a shift from the descriptive level to the level of objective mathematical analysis of the phenomena studied [1, 7], have hitherto been undertaken.

The aim of this investigation was to compare the dynamics of the quantitative changes in the cell composition and vascularization of aseptic skin wounds healing in rats without treatment and with stimulation of repair processes by collagen powder.

EXPERIMENTAL METHOD

Experiments were carried out on 40 male Wistar rats. A teflon ring, covered above with perforated cellophane, was inserted into full-thickness skin wounds on the animals' back, with an area of 3 cm^2, in order to exclude any effect of contraction and drying of the wound. The wounds in control animals healed without the use of any preparations. The wound surface of the rats of group 2 was treated with 20 mg of collagen powder, obtained from a solution of collagen dissolved in alkali. The animals were anesthetized with ether and killed 3, 5, 7, and 10 days after the operation (five animals at each time in each group). Histological sections were stained with hematoxylin and eosin, by Van Gieson's method and with toluidine blue, by Brachet's method, and the PAS reaction. A Stefanov's ocular grid containing 10 squares, with a side of 1 mm, was used for the investigations. In 30 randomly chosen fields of vision of the microscope, and under a magnification of 600, the neutrophilic leukocytes (NL), macrophages (Mp), fibroblasts (Fb), endotheliocytes (En), and other tissue and vascular cells present on the grid were counted. Vessels with no vertical orientation (V_{nv}), vertical vessels (V_v), and the total number of vessels (V_t) were counted. Mean values and relative percentages of cells and vessels were calculated. The results thus obtained were subjected to statistical analysis by Student's test. The results of the quantitative investigation of the cell composition and vascularization of the granulation tissue (GT), calculated per standard unit of area of the measuring grid, are given in Table 1.

EXPERIMENTAL RESULTS

In the animals of group 1 in the stage of inflammation on the 3rd day the principal cells in both absolute and relative terms were NL, and the predominant blood vessels were V_{nv}. Between the 3rd and 5th days the most rapid increase in the numbers of Mp, En, and Fb took place. For instance, the absolute number of Fb by the 5th day compared with the 3rd

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