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EFFECT OF AN ASSISTED CIRCULATION ON THE STATE OF THE ERYTHROCYTES AND MICROCIRCULATION

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KEY WORDS: microcirculation; assisted circulation; erythrocyte morphology

An important cause of hypoxia arising during an assisted circulation (AC) is a disturbance of the microcirculation (MC) [2]. Meanwhile the damaging action of AC on erythrocytes is well known [1, 3].

The aim of the investigation described below was to study the character of the blood flow in the mesentery of the small intestine, morphology of the erythrocytes, and their ability to aggregate in arterial and venous blood during the course of an assisted circulation in order to establish the role of the changes in the state of the erythrocytes in the disturbance of MC.

EXPERIMENTAL METHOD

Experiments were carried out on 12 mongrel dogs weighing 14-42 kg. After premedication with trimeperidine intravenous pentobarbital (30 mg/kg) and endotracheal ether-oxygen anesthesia were used, supplemented by neuroleptanalgesia during perfusion. Hypothermic perfusion was carried out by means of the AIK-5M apparatus, with a countercurrent foam-film oxygenator for 3 h. The apparatus was filled with fresh donors' blood. The hemodilution was 25-30%. The volume velocity of perfusion was maintained at 2.4-2.6 liters/m^2/min. The MC in the mesentric vessels was examined intravitally by means of an apparatus mounted on the MBR-1 microscope and MFN-12 photographic attachment. Blood for investigation was taken from the femoral artery and vein. Morphological changes in the erythrocytes and their ability to aggregate were assessed by means of the phase-contrast system of the MBI-15 microscope. The usual method was used for electron-microscopic study of the erythrocytes. Ultrathin sections were ex-

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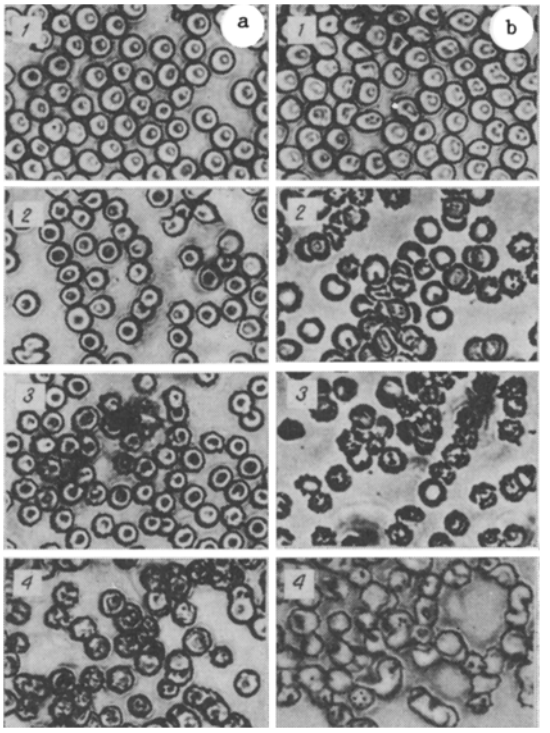

Fig. 1. Erythrocytes of dog during AC (phase-contrast microscopy). a) Arterial blood; b) venous blood. 1, 2, 3, 4) 1st, 2nd, 3rd, and 4th-5th stages, respectively. 280×.

amined under the EMV-100 A electron microscope. Investigations were carried out in the course of the experiments at five stages: 1) the initial state, during ether-oxygen anesthesia, 2) before the beginning of AC, and 3, 4, and 5) after 1, 2, and 3 h of perfusion, respectively.

EXPERIMENTAL RESULTS

In the initial state the erythrocytes had the appearance of normal discocytes (Fig. 1). The electron micrographs showed a uniform distribution of the contents of the erythrocytes in the form of fine-grain material of average electron density (Fig. 2). The blood flow in the mesenteric vessels was rapid and finely granular. Movement of the blood was axial and linear, and the distribution of the cells in the lumen of the vessels was uniform. There were many functioning capillaries (Fig. 3).

In the second stage the appearance of single echinocytes, erythrocytes with single outgrowths, and biconcave forms was observed in arterial and venous blood. A tendency toward aggregation was found in the venous blood (Fig. 1).

Stage 3 was characterized by a marked increase in the number of echinocytes and destructive forms of erythrocytes (Fig. 1). Small aggregates of 2-5 cells were found in the arterial blood. In the venous blood, besides small aggregates in the form of rouleaux, shapeless formations consisting of agglutinated cells appeared. Marked aggregation of erythrocytes was observed in many small venules and single capillaries in the mesentery. The ratio of cells to plasma was shifted in favor of plasma and the number of functioning capillaries was reduced (Fig. 3).

After 2 and 3 h of perfusion an increase in the destructive changes in the erythrocytes was observed (Fig. 2). Besides swelling and disturbance of the integrity of the membranes, examination of the electron micrographs also showed regrouping of the electron-dense material, and as a result, the cells became "spotted" in appearance. Nonhomogeneous formations (globules) were composed of a denser nucleus and a less dense halo. Under magnification of 60,000 the single globules could be seen to consist of smaller granules, comparable in size with single hemoglobin molecules (5-7 nm). The possibility therefore cannot be ruled out that these nonhomogeneities are centers of crystallization of methemoglobin, which readily con-

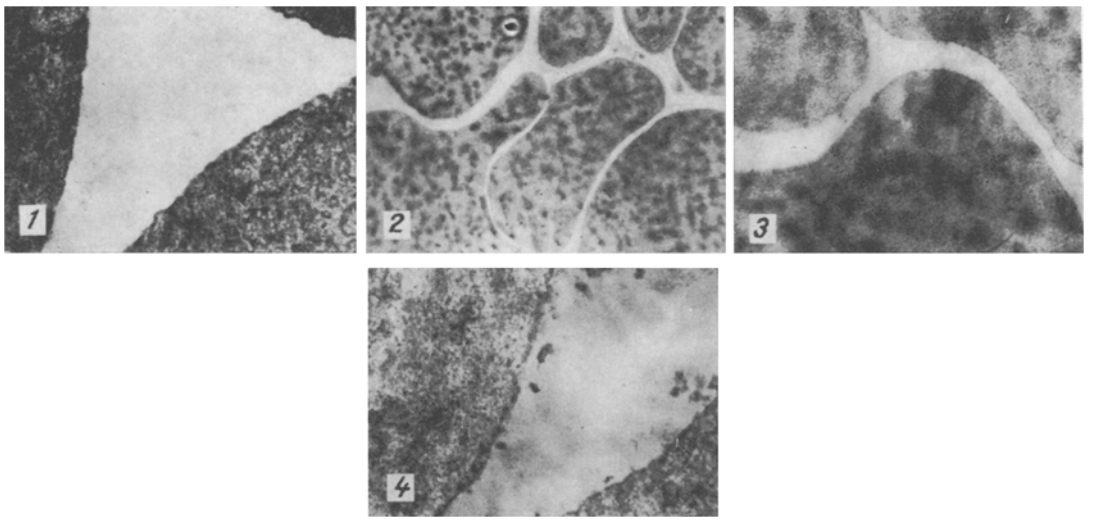

Fig. 2. Electron micrograph of erythrocytes of a dog during AC. 1) Stage 1; 2-4) stage 5. Magnification: 1, 4) 60,000; 2) 15,000; 3) 27,000.

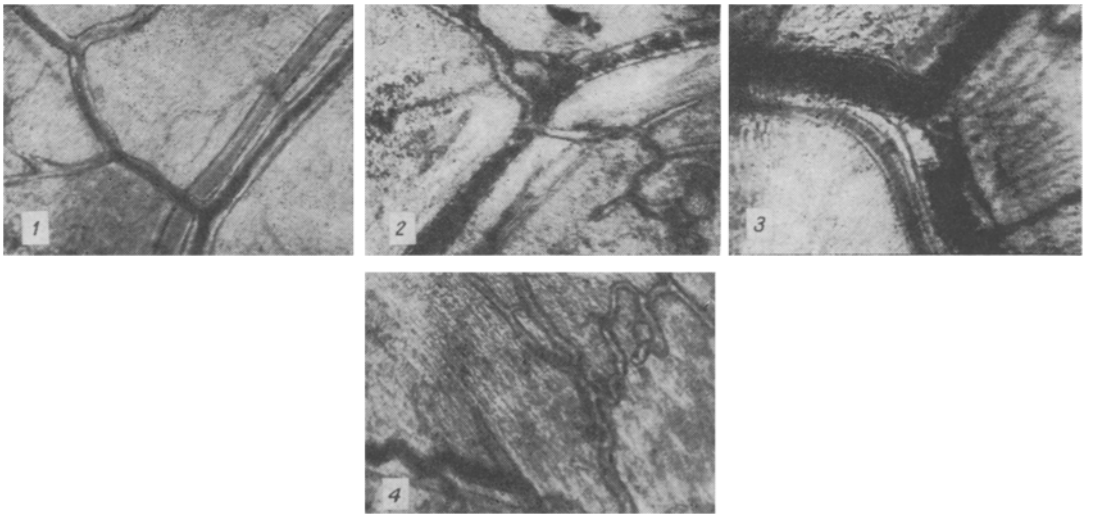

Fig. 3. Biomicroscopy of mesentery of dog's small intestine during AC. 1) Stage 1; 2) stage 3; 3, 4) stages 4 and 5. Magnification 35.

verts into a crystalline state. Evidently, during conditions of increasing hypoxia in the erythrocytes structural changes can take place and cause changes both in the rheology of the blood and the state of the gas exchange. Large collections of agglutinated cells appeared in the venous blood. The agglutinates were smaller in arterial blood (Fig. 1). Profound disturbances of MC corresponded to these changes in the erythrocytes: stasis of the blood flow was observed in many venules and capillaries, the number of functioning capillaries was considerably reduced, whereas their diameter was increased, and multiple diffuse hemorrhages and many plasmatic capillaries were found, together with functioning arteriovenous shunts (Fig. 3).

In the course of the AC marked changes were thus observed in the erythrocytes, as shown by the appearance of pathological cell forms, disturbances of integrity of the membranes, and reorganization of the internal structure. The degree of damage to the erythrocytes corresponded to the progressive disturbances of MC. It can accordingly be postulated that damage to the erythrocytes during AC occupies an important place in the pathogenesis of microcirculatory disturbances, for they lead to changes in their hydrodynamic properties [4] and to the appearance of pathological aggregation [5]. The fact will be noted that the first signs of injury to the erythrocytes appeared before the beginning of perfusion, in the period of operative procedures (thoracotomy, connection of the arterial and venous lines of the AC apparatus). To

prevent disturbances of MC during AC, substances (antihypoxants, antioxidants) prolonging the period of reversible changes in the erythrocytes must be administered both before the operation and during perfusion.

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FUNCTIONAL STATE OF PORTAL VEIN SMOOTH MUSCLES IN SPONTANEOUSLY HYPERTENSIVE RATS

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KEY WORDS: smooth muscles; portal vein; spontaneous hypertension

The important role of changes in the functional state of vascular smooth muscles in the regulation of vascular tone and of blood pressure is well known. Published data [6], including investigation in the authors' laboratory [2], have shown that the increase of vascular resistance in arterial hypertension arises as the result of disturbances of contractility of the smooth muscles of the arterioles and/or as a result of their structural and functional adaptation to high blood pressure (BP), caused by hypertrophy of the smooth-muscle layer of the arterioles. Changes in smooth muscles of the veins in arterial hypertension have received much less study, and the available data are very contradictory [4, 8-11, 13]. These changes are definitely interesting, considering the importance of venous tone in regulation of the cardiac output and the fact that in arterial hypertension the veins are not subjected to a pressure load. Changes in these smooth muscles, if present at all, may therefore reflect primary disturbances of the functional state of the vascular smooth muscles in arterial hypertension.

The aim of this investigation was to study some parameters of the functional state of smooth muscles of the portal vein and their response to noradrenalin in spontaneously hypertensive rats of different ages, i.e., in the course of the disease.

EXPERIMENTAL METHOD

Experiments were carried out on spontaneously hypertensive Kyoto-Wistar rats — SHR: group 1) young animals (4-6 weeks) with normal or slightly raised BP; group 2) rats aged 3 months with BP of 152 ± 4.3 mm Hg, group 3) rats with chronic hypertension (28 weeks, BP 166 ± 4.7 mm Hg). Normotensive Wistar-Kyoto rats (WKY) of the corresponding age (BP 100-118 mm Hg), also divided into three groups, were used as the control. BP was measured in the caudal artery of the conscious animals by an electroplethysmographic method, using an NK-709 apparatus (Natsume, Japan). The animals were killed by decapitation and the portal vein was removed and transferred into a thermostatically controlled working chamber filled with oxygenated Krebs' solution, at 35°C, and a load of 400 mg was attached. The portal vein preparation was kept under these conditions for 1 h before recording began in order to stabilize the spontaneous contractions, which were recorded on a two-channel (control—experimental) apparatus (Ugo Basile, Italy) under isometric conditions. Spontaneous activity with a load of 500 mg (opti-

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