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EFFECT OF HYPOXEMIA ON ERYTHROPOIETIC ACTIVITY OF ORGANS DURING PERFUSION

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The effect of hypoxemia in vivo for 45 min on erythropoietic activity of the kidney, liver, spleen, and sternum was investigated by the method of normoxic perfusion of isolated organs. An increase in erythropoietic activity was found after perfusion of the liver for 6 h, confirming that this organ participates in the extrarenal excretion of erythropoietic factor.

KEY WORDS: *hypoxemia; erythropoietic activity; perfusion of isolated organs.*

Erythropoietic activity of the organs after hypoxemia was studied. Because of the possible role of several organs in the production of erythropoietic factor (EPF), the study of the site of its formation in the intact organism is difficult. With a combination of hypoxemia in vivo followed by normoxic perfusion of isolated organs, the role of individual organs in the formation of the erythropoietic response can be investigated.

EXPERIMENTAL METHOD

Mongrel dogs aged 3-5 years and weighing 13-18 kg were used. Operations were performed under intravenous thiopental sodium anesthesia with the use of listhenon as relaxant and with controlled intubation respiration. Hypoxemia was produced in the anesthetized animal by bleeding (40% of the blood volume) from the femoral artery for 5 min. To prevent hydremia and hypovolemia, after bleeding the animals were given an intravenous injection of an equal volume of Ringer–Locke solution. The liver, kidney, or spleen was removed 40 min after bleeding, rinsed with Ringer–Locke solution, and connected to the hemodynamic part of an apparatus for controlled perfusion of isolated organs [1]. The medium for perfusion of the organs consisted of a mixture of 40% heparinized autogenous plasma (10 units heparin/1 ml plasma) and 60% medium No. 199. The sternum was perfused as a control, for neither bone marrow nor muscle tissue is known to secrete EPF. Perfusion was carried out under normothermic (38 ± 0.1°C) and normoxic (pO_2 of the arterial perfusion fluid 130-150 mm Hg) conditions, at pH 7.36-7.4. The hemodynamic perfusion parameters (arterial pressure P, volume velocity of the blood flow Q, and arterio-venous difference for pO_2 A-V) were as follows: for the kidney, P = 60-90 mm Hg, Q = 1.5-2 ml/g/min, A-V = 50-75 mm Hg; for the liver, P = 50-70 mm Hg in the hepatic artery and 20 mm water in the portal vein, Q = 0.4-0.8 ml/g/min, A-V = 50-70 mm Hg; for the sternum, P = 40-60 mm Hg, Q = 0.15-0.3 ml/g/min, A-V = 50-65 mm Hg; for the spleen, P = 40-70 mm Hg, Q = 1.0-0.7 ml/g/min, A-V = 30-50 mm Hg. Each variant of the experiment was repeated four times and the results were subjected to statistical analysis [2]. The erythropoietic activity was determined in mice with posttransfusional polycythemia [7].

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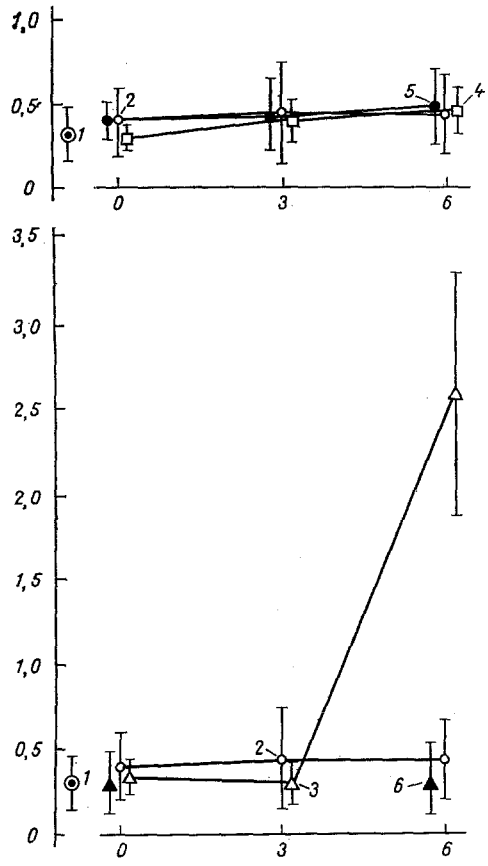

Fig. 1. Dynamics of erythropoietic activity of isolated organs during normoxic perfusion after hypoxemia for 45 min in vivo (M ± m). Abscissa, time of perfusion (in h); ordinate, uptake of ^{59}Fe into erythrocytes of mice with posttransfusional polycythemia (in %): 1) blood of intact animal; 2) sternum; 3) liver; 4) kidney; 5) spleen; 6) liver without hypoxemia.

EXPERIMENTAL RESULTS

As is clear from Fig. 1, during perfusion of the kidney and spleen, and also of the liver taken from intact animals, no increase was observed in the EPF level; a significant increase in the EPF level was found only after perfusion of the liver taken from animals with hypoxemia.

The connection of the kidneys with EPF production is known, but after total nephrectomy ability to produce EPF is not lost [4, 6, 10]. Among the sources of extrarenal EPF production great importance is attached to the liver. Conflicting views are held on its role in EPF metabolism. According to some workers, the liver is the site of destruction and inactivation of EPF [9, 12], whereas others state that EPF is secreted by the liver [3, 5, 8, 11, 13]. In the present investigation secretion of EPF by the liver also was observed. The increase in the EPF concentration could be due both to its extrarenal biosynthesis and to the liberation of renal EPF accumulated in the liver under the influence of hypoxemia in vivo. The absence of an increase in the EPF level after normoxic perfusion of the posthypoxemic kidney can probably be explained by the inadequate duration of perfusion or the inappropriateness of the experimental model (inability to take up the activating substrate produced by the liver, etc.). The results of the investigation thus confirm the hypothesis that the liver is a site of extrarenal secretion of EPF.

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PROPERDIN AND THE PROTEIN COMPOSITION OF THE LYMPH AND BLOOD DURING RESUSCITATION

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Experiments on dogs showed that terminal blood loss followed by resuscitation by injection of autologous blood into the bone marrow causes a regular redistribution of proteins between the blood, limbs, and tissues. Retention of properdin and α-globulins is observed in the interstitial tissue and is not abolished by the resuscitation measures; a stress discharge of γ-globulins is also found from the lymph nodes.

KEY WORDS: *properdin; proteins; lymph; resuscitation.*

The properdin content and protein composition of the lymph and blood were studied before and after resuscitation of dogs from clinical death caused by acute massive blood loss.

EXPERIMENTAL METHOD

Experiments were carried out on 19 dogs of both sexes weighing 15 ± 5 kg. Under thiopental anesthesia the thoracic duct and cervical lymphatic trunk were cannulated. In 12 dogs a terminal state was induced by free bleeding from the femoral artery up to the extent of 60 ml/kg body weight. Resuscitation was started 1-3 min after the onset of clinical death (as shown by spirography, electrocardiography, and measurement of the arterial blood pressure) by injection of autologous blood, stabilized with sodium citrate, into the bone marrow until normal respiration, cardiac activity, and blood pressure were restored. Samples of lymph and blood were taken before and 3 h after bleeding and subsequent reinfusion. Seven dogs served as the control. The properdin concentration was determined by binding it with inulin, followed by mineralization of the properdin—inulin complex and isometric distillation of ammonia in Conway dishes; the protein composition was studied by electrophoresis in agar gel. The results were subjected to statistical analysis by the Nairi-2 computer.

EXPERIMENTAL RESULTS

The results are given in Table 1. After resuscitation the properdin level was found to be lowered in the blood (by 23.4%), and the thoracic (by 18.9%) and cervical lymph (by 28.1%) of the experimental dogs. This decrease probably indicates retention of properdin in the tissues and not its redistribution between the blood and lymph. The writers previously found

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