EFFECT OF HYPEROXIA ON RATE OF RESTORATION OF THE BLOOD COMPOSITION AFTER BLOOD LOSS

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Regeneration of the peripheral red blood is considerably inhibited in rabbits with anemia (caused by blood loss equivalent to 2% of body weight) exposed to hyperoxia (98% oxygen in the inspired air at a pressure of 2 atm) for 5 h.
KEY WORDS: hyperoxia; anemia; hematopoiesis.

Because of the widespread use of oxygen in medicine, aviation, astronautics, aquanautics, and so on the need has arisen for a detailed study of the physiological and toxic action of oxygen on the systems of the body, including the blood system. The writers showed recently that under the influence of hyperoxia erythropoietins disappear from the plasma of animals, and inhibitors of erythropoiesis may appear in their blood [6, 7]. This naturally raises the question of how the peripheral red blood regenerates after blood loss under conditions of an increased partial oxygen pressure in the inspired air.

EXPERIMENTAL METHOD

Experiments were carried out on 28 male rabbits weighing 2-3 kg. Blood was taken from all the animals in a volume equivalent to 2% of the body weight by puncture of the left ventricle. Immediately after bleeding 13 of the rabbits were kept for 5 h in a hyperbaric chamber containing 98% O_2 and 2% N_2 at a pressure of 2 kg force/cm^2 (CO_2 and water vapor were absorbed by soda lime and silica gel).

The remaining rabbits with anemia were kept under normal atmospheric conditions. The hemoglobin concentration, erythrocyte and reticulocyte counts, and hematocrit index were determined in all animals before bleeding, 12 h after bleeding, and thereafter daily for 9 days.

EXPERIMENTAL RESULTS AND DISCUSSION

After bleeding the hematocrit index was reduced on average by half. In the control rabbits it began to rise again 3 days after bleeding, but in the experimental rabbits this did not happen until 5 days after bleeding ($P < 0.01$; Fig. 1).

The erythrocyte count in the rabbits fell sharply after blood loss. In animals exposed to hyperoxia as well as blood loss it started to rise again only after 5 days ($P < 0.01$). In the control rabbits, however, this index began to rise as early as 3 days after blood loss ($P < 0.01$). The hemoglobin concentration 12 h after blood loss fell sharply, on the average by 49%. The hemoglobin concentration (like the erythrocyte count), in animals exposed to hyperoxia showed a small increase after 24 h, but for several days it continued at a low level; only after 5 days did this index begin to rise steadily ($P < 0.01$). In the control animals the hemoglobin concentration began to increase earlier, 3 days after blood loss ($P < 0.01$).

The reticulocyte count in the peripheral blood of the control animals began to rise 24 h and, in particular, 3 days after blood loss, but in the experimental animals this process was delayed by 24 h and was less marked.

The increase in the reticulocyte count in the peripheral blood indicates that the observed recovery of the hemoglobin, erythrocytes, and hematocrit indices after blood loss was the result of true formation of new red

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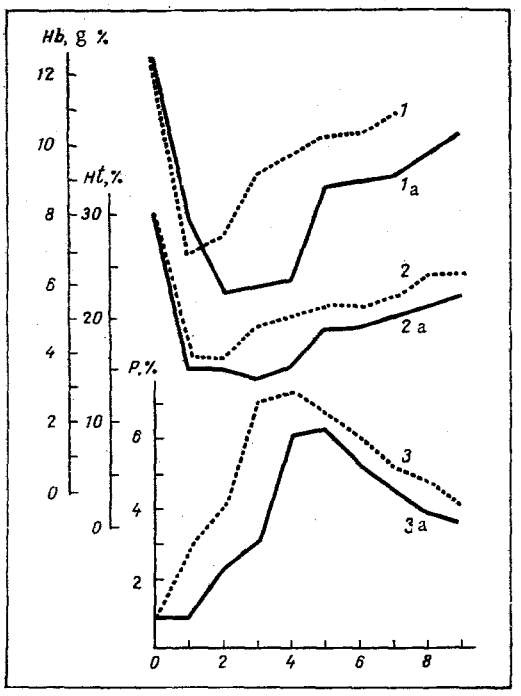

Fig. 1. Changes in hemoglobin concentration (1, 1a), hematocrit index (2, 2a), and reticulocyte count (3, 3a) in peripheral blood of rabbits after blood loss (2% of body weight). 1, 2, 3 – Animals kept under normal atmospheric conditions (control); 1a, 2a, 3a – animals kept under hyperoxic conditions (experiments). Ordinate, hemoglobin concentration (Hb), hematocrit index (Ht), and reticulocyte count (R); abscissa, time after bleeding (in days).

blood cells and not the result of hemodynamic changes in the body which could have arisen after exposure to a high partial pressure of oxygen.

In rabbits with anemia exposed to hyperoxia, regeneration of the red blood was thus considerably inhibited. In other words, an excess oxygen supply to the animals disturbs the stimulation of erythropoiesis that usually arises after acute blood loss to compensate the anemia.

In rats with anemia exposed to hyperoxia (PO_2 in the inspired air about 640 mm Hg for 4 days) the utilization of ^{59}Fe and the reticulocytosis also were lower than in control "anemic" animals [11].

The inhibitory effect of hyperbaric oxygenation on erythropoiesis can be explained by the disappearance of erythropoietin and also, possibly, by the secretion of inhibitors of erythropoiesis by the kidneys into the blood stream [7]. Under these circumstances differentiation of erythropoietin-sensitive cells into erythroblasts is evidently delayed also [5]. Restoration of the composition of the peripheral red blood may probably also be inhibited to some degree by damage to the enzyme systems of the erythrocytes by oxygen [3] and by an increase in the rate of their destruction [2, 10].

A respiratory mixture with an increased partial pressure of oxygen is now extensively used [1, 4, 8, 9]. However, as the results of this investigation show, oxygen therapy in patients with anemia caused by blood loss must be used with care, and the process of natural regeneration of the red blood must be monitored.

LITERATURE CITED

1. Zh. I. Abramova, B. R. Glants, S. G. Germane, et al., in: Emergency Oxygen Barotherapy (ed. by Zh. I. Abramova and B. R. Glants) [in Russian], Riga (1973), p. 29.
2. F. I. Bakulina and A. S. Vidmanova, in: Hypercapnia and Hyperoxia in Clinical and Experimental Medicine [in Russian], Kuibyshev (1970), p. 45.
3. F. I. Bakulina, N. P. Kalabornova, and A. S. Vidmanova, in: Hypercapnia and Hyperoxia in Clinical and Experimental Medicine [in Russian], Moscow (1974).

4. I. P. Berezin, Hyperbaric Oxygenation [in Russian], Moscow (1974).
5. V. I. Voitkevich, Chronic Hypoxia (adaptive reactions of the organism) [in Russian], Leningrad (1973).
6. V. I. Voitkevich and A. M. Volzhskaya, Dokl. Akad. Nauk SSSR, 191, No. 3, 723 (1970).
7. V. I. Voitkevich, A. M. Volzhskaya, and A. P. Myasnikov, Byull. Éksp. Biol. Med., No. 4, 44 (1975).
8. G. L. Ratner (editor), Hyperbaric Oxygen Therapy [in Russian], Kuibyshev (1970).
9. A. G. Zhironkin, The Physiological and Toxic Action of Oxygen [in Russian], Leningrad (1972).
10. C. J. Lamdersten, in: Handbook of Physiology, Section 3, Respiration (ed. by W. O. Fenn and H. Rahn), Vol. 2, American Physiological Society, Williams and Wilkins, Baltimore (1965), p. 1027.
11. E. Nečas and J. Neuwirt, Am. J. Physiol., 216, 800 (1969).

ROLE OF THE INCRETORY FUNCTION OF THE PANCREATIC ISLETS IN THE MECHANISMS OF DEVELOPMENT OF HYPOTHALAMIC OBESITY

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Administration of alloxan, which injures the β cells and depresses insulin secretion, to animals with experimental hypothalamic obesity prevented any further increase in body weight despite an excessive food intake by the animals. It is concluded that the most important mechanism of development of obesity following injury to the ventromedial hypothalamic nuclei is the hypersecretion of insulin caused by such injury.
KEY WORDS: hypothalamic obesity; insulin; pancreatic islets; alloxan diabetes.

Destruction of the ventromedial hypothalamic nuclei (VMHN) or deafferentation of that region in rats is accompanied by hyperphagia, obesity [2, 4], and a raised blood insulin level [1, 4, 9]. Changes developing under these circumstances in the pancreatic islets have been attributed to hyperstimulation of the β cells as a result of overeating [2, 3]. However, the increased secretion of insulin after injury to VMHN could be the cause of the hyperphagia and obesity, and not its effect [9]. If this hypothesis is true, weakening of the insulin-producing function of the pancreatic islets ought to stop the increase in weight of animals after destruction of VMHN.

To study this problem the development of hypothalamic obesity after injury to the pancreatic β cells by alloxan was investigated.

EXPERIMENTAL METHOD

Symmetrical bilateral destruction of VMHN in sexually mature female rats was carried out by means of a stereotaxic apparatus with a direct current of 2 mA for 15 sec [3]. Two weeks after the operation diabetes was produced in the animals by subcutaneous injection of 100 mg/kg alloxan in buffer solution, pH 4.0, into each animal after starvation for 16-18 h. The controls were intact rats, animals with alloxan diabetes but without destruction of VMHN, and animals with destruction of VMHN but without alloxan diabetes. For 2 months, during which all the rats were kept on the same balanced diet ad libitum, regular determinations were made of their body weight, their blood sugar (by the method of Hagedorn and Jensen), and sugar in their urine (by Benedict's method). At the end of the experiments the concentration of immunoreactive insulin (IRI) in the plasma was determined [8]. The presence of obesity was established from the index:

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