7. C. Clarke and R. Hill, Brit. J. Pharmacol., 44, 435 (1972).
8. D. Curtis and G. Johnston, Ergebn. Physiol., 69, 97 (1976).
9. D. Curtis, C. Game, G. Johnston, et al., Brain Res., 43, 242 (1972).
10. R. Davidoff, Science, 175, 531 (1972).
11. R. Davidoff, Brain Res., 45, 638 (1972).
12. G. Bernardi, V. Floris, M. Marciani, et al., Brain Res., 114, 134 (1976).
13. J. Ferguson and H. Jasper, Electroenceph. Clin. Neurophysiol., 30, 377 (1971).

EFFECT OF HYPERBARIC HYPEROXIA ON HUMAN PLASMA ERYTHROPOIESIS INHIBITORS

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In persons unadapted to hyperbaric hyperoxia, 24 h after exposure in a pressure chamber to an increased pressure corresponding to a depth of 63 m (with 25% O_2 in the inspired air), erythropoietins completely disappeared from the plasma, but erythropoiesis inhibitors appeared instead.

KEY WORDS: hyperbaric hyperoxia; erythropoiesis inhibitor; erythropoietin; erythropoiesis.

Few investigations have been undertaken of the action of hyperbaric hyperoxia on erythropoietic activity of the blood in various species of animals [3,10,13]. The answer to the question of how hyperbaric hyperoxia affects the erythropoietic properties of human plasma is not only of theoretical, but also of great practical importance, for nowadays man frequently has to stay and work under conditions of increased partial oxygen pressure both under water and elsewhere.

The object of this investigation was to study the erythropoietic properties of the plasma and composition of the peripheral red blood in persons exposed for the first time to the action of hyperbaric hyperoxia.

EXPERIMENTAL METHOD

Tests were carried out on ten healthy male students aged 18-19 years before and 24 h after a stay in a continous-flow decompression chamber under a pressure of 7.3 kgf/cm^2, equivalent to a depth of 63 m. During their stay at this "depth" the subjects breathed (by means of a special breathing apparatus) an atmosphere consisting of 25% oxygen, 15% helium, and 60% nitrogen. The pressure in the chamber was raised from 1 to 7.3 kgf/cm^2 in the course of 5 min (the partial oxygen pressure – pO_2 – rose to 1.83 kgf/cm^2, i.e., about 1400 mm Hg). The subjects remained under these conditions for 10 min. Pressure in the chamber was then lowered to 2.6 kgf/cm^2 and the subjects started to breathe almost pure oxygen – 98% O_2 (pO_2 2.5 kgf/cm^2), while decompression continued. The whole "lifting" of the subjects from a "depth" of 63 m to sea level occupied about 40 min. None of the subjects had ever previously been exposed to either hyperbaric conditions or hyperoxia.

The erythropoietic activity of the plasma and the hemoglobin concentration, erythrocyte count, and hematocrit index of the peripheral blood were determined before and 24 h after the beginning of the experiment. Erythropoietic factor was determined by studying the mitotic activity of a bone marrow culture in liquid medium in the presence of colchicine [8,11] (from the difference between the stathmokinetic indices of the erythroblasts after addition of the test plasma and of Hanks' solution to the culture) and expressed in conventional units.

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TABLE 1. Mean Plasma Erythropoietic Activity and Composition of Peripheral Red Blood in Subjects before and 24 h after Exposure to Hyperbaric Hyperoxia

Index	Before hyperoxia		24 h after hyperoxia		
	n	$M \pm m$	n	$M \pm m$	P
Plasma erythropoietic activity, conventional units	10	+61±29	6	−5±8	<0.05
Hemoglobin, g%	10	15,5±0,4	8	14,1±0,2	<0,01
Erythrocytes, millions/mm^3	10	4,7±0,1	8	4,4±0,1	<0,05
Hematocrit, %	10	53±1	8	48±1	<0,01

EXPERIMENTAL RESULTS

In all subjects before exposure to hyperbaric hyperoxia the blood plasma possessed marked erythropoietin activity. Its mean level was 61 ± 29 conventional units (Table 1).

Erythropoietins disappeared completely from the blood plasma of all subjects (except one) 24 h after their stay in the continuous-flow decompression chamber at a "depth" of 63 m. The plasma of half of the subjects not only possessed no erythropoietic activity, but actually began to induce inhibition of mitotic activity of erythroblasts in a bone marrow culture, i.e., erythropoiesis inhibitors appeared in the plasma. The mean erythropoietic activity of the blood plasma 24 h after exposure to increased pressure in the chamber was −5 ± 8 conventional units ($P < 0.05$), i.e., the plasma possessed erythropoiesis-inhibiting properties. This change in the erythropoietic properties of the plasma as a result of exposure to hyperbaric hyperoxia (pO_2 in the inspired air was 1.83 kgf/cm^2, or about 1400 mm Hg) was due, on the one hand, to cessation of erythropoietin production and, on the other hand, to the appearance of erythropoiesis inhibitors in the blood.

It is considered that erythropoiesis inhibitors inhibit the differentiation of erythroid precursors [14], delay the formation of erythropoietin from its precursor — erythrogenin [12] — and form an erythropoietin-inhibitor complex, which inhibits erythropoiesis in the earliest stages [5].

The well-marked response of the body to hyperbaric hyperoxia, in the form of the appearance of erythropoiesis-inhibiting properties of the plasma (erythropoiesis inhibitors) in the subjects in these experiments was undoubtedly attributable to the fact that they were exposed to an increased partial oxygen pressure for the first time and were not adapted to these conditions. On the other hand, in subjects repeatedly exposed to hyperoxia [4], the plasma erythropoietic activity was lower between each successive experiment, i.e., some decrease in the plasma erythropoietin concentration as a result of previous exposure to hyperoxia persisted for a long time, Furthermore, in these same subjects after repeated exposure to an increased partial oxygen pressure (after "lowering" to a "depth" of 100 m, equivalent to pO_2 of 2.3 kgf/cm^2, or about 1800 mm Hg) the concentration of erythropoietic factor in the blood was considerably reduced but the blood plasma did not possess inhibitory properties, i.e., it did not contain erythropoiesis inhibitors.

As regards the peripheral blood, the hemoglobin concentration, erythrocyte count, and hematocrit index fell statistically significantly (Table 1) 24 h after exposure to an increased pressure in the chamber. This fact can evidently not be regarded as the result of inhibition of erythropoiesis through the action of the erythropoiesis inhibitors which had started to appear, for a longer time is required for the erythrocytes to mature. A more likely explanation of this decrease is the displacement of tissue fluid into the blood and of blood into the parenchymatous organs [6, 7], an increase in the rate of erythrocyte destruction [1, 9], and injury to the enzyme systems of the erythrocytes [2] under the influence of hyperoxia.

The development of inhibition of erythropoiesis and, consequently, of anemia as a result of exposure to a definite degree of hyperoxia can accordingly be predicted on the basis of determination of the erythropoietic activity of the blood plasma and steps can be taken to prevent it. In particular, the results show that it is desirable that persons submerged to great depths (63 m or more) should be first adapted to hyperbaric hyperoxia. If it is necessary to immerse subjects unadapted to hyperbaric hyperoxia to such depths, appropriate measures aimed at preventing the development of posthyperoxic anemia must be taken beforehand.

LITERATURE CITED

1. F. I. Bakulina and A. S. Vidmanova, in: Hypercapnia and Hyperoxia under Clinical and Experimental Conditions [in Russian], Kuibyshev (1970), p. 45.
2. F. I. Bakulina, N. P. Kalabornova, and A. S. Vidmanova, in: Hypercapnia and Hyperoxia under Clinical and Experimental Conditions [in Russian], Kuibyshev (1970), p. 47.

3. V. I. Voitkevich, A. M. Volzhskaya, and A. P. Myasnikov, Byull. Éksp. Biol. Med., No. 4, 44 (1975).
4. V. I. Voitkevich et al., Byull. Éksp. Biol. Med., No. 11, 1299 (1976).
5. E. N. Mosyagina, N. A. Fedorov, V. I. Gudim, et al., in: Normal Hematopoiesis and Its Regulation, N. A. Fedorov, ed. [in Russian], Moscow (1976), p. 341.
6. A. J. Anthony and H. Biedenkopf, Z. Ges. Exp. Med., 103, 451 (1938).
7. A. Hitzenberger and H. Molenaar, Klin. Wschr., 13, 1599 (1934).
8. L. G. Lajtha, J. Clin. Path., 5, 67 (1952).
9. C. J. Lambertsen, in: Handbook of Physiology, Section 3, Respiration, Vol. 2, Washington (1965), p. 1027.
10. J. W. Linman and R. V. Pierre, Ann. N.Y. Acad. Sci., 149, 25 (1968).
11. Y. Matoth and E. B. Porath, J. Lab. Clin. Med., 54, 722 (1952).
12. Y. Moriyama, Israel J. Med. Sci., 7, 1012 (1971).
13. J. Ramos and C. Reynafarje, Arch. Inst. Biol. Andina, 2, 216 (1968).
14. W. H. Whitcomb, in: Kidney Hormones, J. W. Fisher, ed., New York (1971), p. 461.

NEUROPATHOLOGICAL EFFECTS OF INJECTION OF TETANUS TOXIN INTO CERTAIN STRUCTURES OF THE RAT BRAIN

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The neuropathological effects of local injection of tetanus toxin (TT) into various structures of the brain were studied in experiments on rats. Definite neuropathological changes were observed in the animals, different from those found after injection of TT elsewhere. As a rule the action of TT in a given region of the brain was local. The experiments confirm the theory of generator mechanisms of neuropathological syndromes, according to which specific manifestations of the corresponding syndrome are determined by the location of a generator of pathologically enhanced excitation in a certain brain structure.

KEY WORDS: subcortical brain structures; lateral geniculate body; tetanus toxin; neuropathological syndromes.

Previous experiments showed that after injection of tetanus toxin (TT) into the lateral geniculate body (LGB) of animals specific pathophysiological effects characterizing a syndrome of photogenic epilepsy arise [1,3,6]. These effects were the result of functional changes evoked by TT in LGB, i.e., they were the result of the formation of a generator of pathologically enhanced excitation (GPEE) in that nucleus [2]. However, in order to explain the role of this mechanism in the formation of the neuropathological syndrome, an answer must be found to the question: Could not these phenomena be the result of spread of TT into other regions of the brain? Data in the literature of the ability of TT to spread in the brain [7, 8] do not provide an unequivocal answer to this question.

It was accordingly necessary to investigate the effects of creation of appropriate GPEE in neighboring structures connected anatomically with LGB. Such experiments would, on the one hand, provide fresh evidence on the character of spread of TT in different regions of the brain and, on the other hand, they would show whether corresponding neuropathological syndromes can be obtained by injection of TT into various structures of the animal brain.

EXPERIMENTAL METHOD

Under hexobarbital anesthesia TT was injected into various subcortical structures of 66 noninbred albino

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