LITERATURE CITED

1. G. N. Kryzhanovskii, Zh. Nevropat. Psikhiatr., No. 11, 1730 (1976).
2. G. N. Kryzhanovskii, Zh. Nevropat. Psikhiatr., No. 7, 1090 (1976).
3. G. N. Kryzhanovskii, Tetanus [in Russian], Moscow (1966).
4. G. N. Kryzhanovskii, V. N. Grafova, E. Z. Danilova, et al., Byull. Eksp. Biol. Med., No. 7, 15 (1974).
5. G. N. Kryzhanovskii, V. N. Grafova, E. Z. Danilova, et al., Byull. Eksp. Biol. Med., No. 9, 31 (1973).
6. G. N. Kryzhanovskii and V. K. Lutsenko, Neirofiziologiya, No. 3, 234 (1975).
7. G. N. Kryzhanovskii (G.N. Kryshanovsky) and F. D. Sheikhon, Exp. Neurol., 38, 110 (1973).
8. G. N. Kryzhanovskii (G. N. Kryzhanovsky) and F. D. Sheikhon, Exp. Neurol., 50, 387 (1976).
9. G. N. Kryzhanovskii, F. D. Sheikhon, and M. B. Rekhman, Neirofiziologiya, No. 6, 608 (1975).
10. Yu. S. Sverdlov, Neirofiziologiya, No. 1, 25 (1959).
11. V. B. Brooks, D. R. Curtis, and J. C. Eccles, J. Physiol. (London), 136, 655 (1957).
12. D. R. Curtis and W. C. De Groat, Brain Res., 10, 208 (1968).
13. J. C. Liebeskind, G. Guilbaud, J. M. Besson, et al., Brain Res., 50, 441 (1973).
14. J. C. Liebeskind, D. J. Mayer, and H. Akil, Adv. Neurol., 4, 261 (1974).
15. D. S. Mayer and J. C. Liebeskind, Brain Res., 68, 73 (1974).
16. D. J. Mayer, T. L. Wolf, H. Akil, et al., Science, 174, 1351 (1971).
17. R. Melzack and P. D. Wall, Science, 150, 971 (1965).
18. J. L. Oliveras, J. M. Besson, et al., Exp. Brain Res., 20, 32 (1974).
19. L. J. Pellegrino and A. J. Cushman, A Stereotaxic Atlas of the Rat Brain, New York (1967).
20. D. V. Reynolds, Science, 164, 444 (1969).

EFFECT OF HYPERBARIC OXYGENATION ON SOME FUNCTIONAL AND MORPHOLOGICAL PROPERTIES OF THE HEART AND ON CATECHOLAMINE METABOLISM IN COMPENSATORY HYPERTROPHY OF THE MYOCARDIUM

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Less-marked hypertrophy and signs of myocardial degeneration developed in rabbits exposed for one month to hyperbaric oxygenation (HBO) after the formation of stenosis of the ascending aorta, and the contractile power of the left ventricle was increased more than in animals with stenosis of the aorta kept under ordinary conditions. In rabbits with hypertrophy of the heart developing under conditions of HBO increased powers of adaptation of the myocardium to physical exertion were accompanied by an increase in the functional reserve of the sympathetic control apparatus. HBO evidently favors the development of optimal adaptation of the heart to an increased pressure load.

KEY WORDS: *hyperbaric oxygenation; myocardial hypertrophy; catecholamines.*

In recent years hyperbaric oxygen has been used on an increasingly wide scale in the treatment of various heart diseases. The action of hyperbaric oxygenation (HBO) is based not merely on its protective effect against hypoxia, but also on its ability to cause modification to the activity of the energy-forming structures and enzyme systems of the cells and

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TABLE 1. Effect of HBO on Changes in Weight and Some Indices of Contractile Activity of the Left Ventricle in Rabbits at Different Times after Aortic Stenosis (M ± m)

Time of investigation	Experimental condition		Relative weight of left ventricle, g/kg body weight	Dry residue of tissue of left ventricle, percent	Maximal systolic pressure in left ventricle, mm Hg	Coefficient of potential working capacity of left ventricle, percent
3rd day	Mock operation	(I)	1,14±0,004 (8)	20,8±0,3 (8)	208±12 (5)	—
	Mock operation+HBO	(II)	1,11±0,11 (5)	19,8±0,7 (6)	209±14 (6)	101
7th day	Aortic stenosis	(III)	1,50±0,10* (5)	15,5±0,5* (6)	216±11 (5)	108
	Aortic stenosis+HBO	(IV)	1,34±0,07* (10)	19,6±0,3† (8)	262±23* (7)	158*
	Mock operation	(I)	1,15±0,08 (7)	21,3±0,3 (8)	203±5 (6)	—
	Mock operation+HBO	(II)	1,16±0,04 (7)	21,3±0,2 (4)	198±6 (6)	95
	Aortic stenosis	(III)	1,62±0,07* (9)	20,9±0,4 (10)	210±8 (8)	107
	Aortic stenosis+HBO	(IV)	1,40±0,02‡ (7)	20,8±0,5 (5)	254±13‡ (12)	157‡
25th-28th day	Mock operation	(I)	1,12±0,06 (7)	21,3±0,6 (4)	209±7 (9)	—
	Mock operation+HBO	(II)	1,15±0,07 (4)	21,3±0,5 (5)	191±6 (5)	84
	Aortic stenosis	(III)	1,78±0,05* (10)	22,3±0,1 (4)	250±15* (6)	143*
	Aortic stenosis+HBO	(IV)	1,52±0,04‡ (10)	21,1±0,5 (7)	280±7* (6)	180*

Legend. Number of animals shown in parentheses.
*P_{I-III}, $P_{I-IV} < 0.05$; †$P_{III-IV} < 0.05$; ‡P_{I-IV}, $P_{III-IV} < 0.05$.

also of the neuroendocrine regulation of the body. It is stated in the literature that HBO stimulates regeneration of mitochondria [5], stimulates protein synthesis in the myocardium [7], has a positive inotropic effect on the heart [6], and increases the activity of the sympathico-adrenal system regulating the heart [3]. These facts suggest that HBO may have a substantial effect on the mechanism determining the formation of adaptation of the myocardium to an increased load.

In the investigation described below the effect of HBO on the dynamics of some functional and morphological properties of the heart and some stages of catecholamine metabolism was studied during compensatory hypertrophy induced by stenosis of the ascending aorta.

EXPERIMENTAL METHOD

Compensatory hyperfunction and hypertrophy of the heart were induced in male rabbits weighing 2.5-3.3 kg by reducing the diameter of the ascending aorta by half its initial value by means of a tantalum coil. The operation was performed under hexobarbital anesthesia and artificial respiration under aseptic conditions. Some of the experimental animals were exposed to HBO (2 atm) for 1 h daily for 25-28 days. Another group of rabbits was kept under ordinary conditions after the production of aortic stenosis. Rabbits undergoing a mock operation served as the control. Some of the control animals received the same sessions of HBO as the experimental animals. The ECG and the real and maximal (during complete occlusion of the ascending aorta for 5 sec) systolic pressure in the left ventricle (P_{max}) were recorded in all animals on the "Hellige" polygraph. The coefficient of potential working capacity of the myocardium (η) was determined by a special formula [4]. Some of the experimental and control rabbits were subjected to enforced physical exertion by swimming in water at a temperature of 33-34°C for 3-5 min, with intervals of 5 min, on the 25th-28th day after the operation, until clinical signs of cardiac failure appeared, when they were sacrificed. The weight of the left ventricle was determined as wet tissue and as its dry residue in all the animals. The concentrations of noradrenalin, adrenalin, and dopa [2] also were determined in the myocardium of the left ventricle. Morphological and histochemical investigations of the myocardium were carried out by the usual methods.

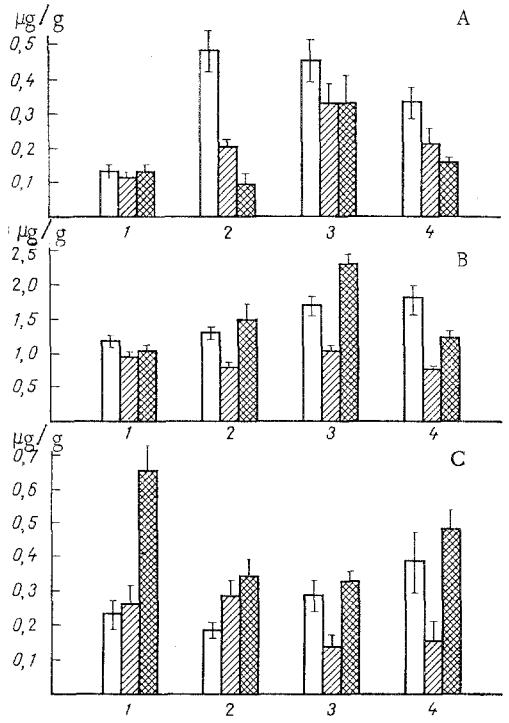

Fig. 1. Change in concentration of adrenalin (A), noradrenalin (B), and dopa (C) in left ventricle of rabbit during development of cardiac hypertrophy: 1) 3rd day; 2) 7th day; 3) 25th–28th day of experiment; 4) physical exertion. Unshaded columns indicate mock operation; obliquely shaded columns aortic stenosis without HBO; cross-hatched columns aortic stenosis + HBO. Values of M ± 2m given.

EXPERIMENTAL RESULTS

As Table 1 shows, the relative weight of the left ventricle increased progressively for one month after application of the coil to the aorta. The dry residue of the tissue of the left ventricle three days after stenosis of the aorta was reduced, but later it was almost the same as in the control. After exposure to HBO the increase in the relative weight of the left ventricle during the development of hypertrophy was less marked and no decrease in the dry residue of the tissue of the left ventricle was observed in the early stages of cardiac hypertrophy, indicating the absence of edema of the myocardium.

On the third and seventh days after stenosis of the aorta P_{max} in the left ventricle and η were the same as in the control, but on the 28th day they were increased. In rabbits with aortic stenosis and treated with HBO, P_{max} and η started to rise earlier during the investigation, and by the 28th day they were higher than their values in rabbits with aortic stenosis but without HBO.

During the development of hypertrophy of the heart a progressive decrease was found in the catecholamine concentration in the myocardium of the left ventricle, mainly on account of noradrenalin (Fig. 1). This is in agreement with data in the literature [1] and, judging from the change in the dopa concentration, it is probably connected with a decrease in catecholamine synthesis. In rabbits with hypertrophy of the heart developing during exposure to HBO, after a certain decrease in the noradrenalin level on the third day it rose gradually. The dopa concentration in the myocardium of the left ventricle remained high throughout the period of observation. This could indicate that under HBO conditions the mechanisms for the maintenance of the noradrenalin reserves in the heart are preserved.

Rabbits with hypertrophy of the myocardium developing under HBO conditions were more resistant to the development of acute heart failure during physical exertion. After sessions of swimming of equal duration, they developed less marked hypodynamia, dyspnea, and tachysystole than rabbits with hypertrophy not exposed to HBO. Physical exertion in the control rabbits was accompanied by an increase in the dopa concentration and with preservation of the noradrenalin reserves in the heart whether or not they were exposed to HBO. In the rabbits with aortic stenosis and not exposed to HBO, the dopa concentration in the myocardium did not rise after swimming, but the noradrenalin reserves fell sharply. In rabbits with myocardial hypertrophy developing under HBO conditions, the noradrenalin concentration also fell after swimming, but still remained higher than in rabbits with aortic stenosis but without HBO, and the dopa concentration in the myocardium rose. This could indicate that the increase in the

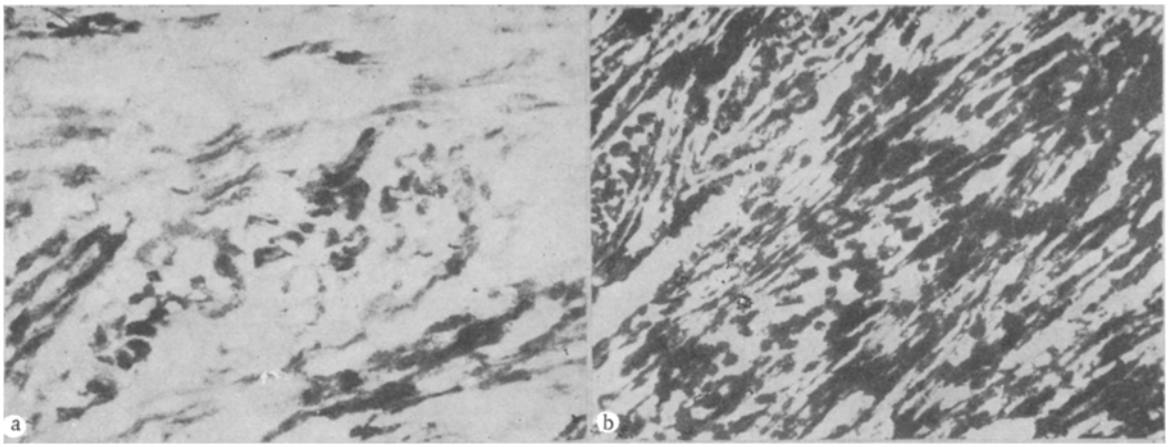

Fig. 2. Succinate dehydrogenase activity in myocardium of left ventricle of rabbits on third day after stenosis of aorta: a) rabbits not exposed to HBO: irregular decrease, foci of absence of enzyme activity; b) rabbits exposed to HBO: uniform distribution of high enzyme activity. Ocular 7, objective 20. Reaction by Nachlas's method.

adaptive powers of the heart in rabbits with hypertrophy of the myocardium developing under HBO conditions is accompanied by an increase in the functional reserves of the sympathetic control system.

Morphological and histochemical investigations of the myocardium of the left ventricle on the third day after aortic stenosis revealed marked hyperemia, small hemorrhages, signs of cloudy swelling and fatty degeneration, interstitial and intercellular edema, and a sharp decrease in activity of succinate, malate, and lactate dehydrogenases. On the subsequent day progressive development of cardiosclerosis and a tendency toward normalization of enzyme activity and for the degenerative changes to diminish were observed. In rabbits with hypertrophy of the myocardium developing under HBO conditions the severity of the degenerative changes at all periods of the investigation, and especially on the third day, was much less: Foci of micronecrosis were absent, only solitary fibers were in a state of granular degeneration, the myofibrils were more compactly arranged, and marked activation of malate, lactate, and succinate dehydrogenases was found (Fig. 2).

The conditions of HBO chosen thus have a significant effect on the dynamics of the morphological and functional properties of the myocardium and activity of the sympathetic control system during the development of hypertrophy of the heart. In rabbits exposed to HBO, despite the less marked hypertrophy of the myocardium, P_{max} and η were higher than in animals with hypertrophy developing under ordinary conditions. Considering the less marked changes in the enzymes of tissue respiration in the experimental animals subjected to HBO and also the ability of HBO to stimulate regeneration of mitochondria [5], it can be postulated that HBO improves the energy metabolism of rabbits with aortic stenosis. The greater activity of the sympathetic control system of the heart and its higher functional reserves under these circumstances help to maintain the contractile function of the heart at a higher level.

It can tentatively be suggested that HBO favors the development of optimal adaptation of the heart to an increased pressure load when high functional activity is combined with moderate hypertrophy of the heart [1].

LITERATURE CITED

1. F. Z. Meerson, Adaptation of the Heart to High Loads and Cardiac Failure [in Russian], Moscow (1975).
2. V. V. Men'shikov, in: Investigation of the Functional State of the Adrenal Cortex and the Sympatho-Adrenal System under Clinical and Experimental Conditions [in Russian], Moscow (1963), p. 149.
3. G. V. Troshikhin and F. G. Shalyapina, Fiziol. Zh. SSSR, No. 1, 119 (1970).
4. V. A. Frolov, T. A. Kazanskaya, G. A. Drozdova, et al., in: Predisease [in Russian], Part 1, Moscow (1969), p. 93.

5. L. L. Shimkevich, "Functional morphological investigations during hyperbaric oxygenation," Author's Abstract of Doctoral Dissertation, Moscow (1973).
6. B. Pelld, Y. Seki, F. Ramsey, et al., in: Fifth International Hyperbaric Congress. Proceedings, Vol. 2, Vancouver (1974), pp. 691-698.
7. S. S. Schreiber, C. Evans, M. Oratz, et al., Am. J. Physiol., 212, 35 (1967).

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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