MECHANISM OF LOWERING OF THE TISSUE OXYGEN PARTIAL PRESSURE DURING HYPEROXIA AND CRITERIA FOR HYPEROXYGENATION DOSAGE

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The partial pressure of oxygen (pO_2) in the tissues depends to a certain extent on its concentration in the surrounding medium [3]. Under oxygen pressure of up to several atmospheres changes in its partial pressure in the tissues occur in phases: a marked increase initially followed by a progressive decrease in the course of a continuing stay under hyperbaric conditions. This phenomenon is explained by the vascular reaction which restricts the entry of oxygen into the tissues [1]. Sokolyanskii [8] regards the lowering of pO_2 in the tissues in hyperbaric hyperoxia as an adverse factor and has introduced the concept of correction of pO_2, embracing a system of measures aimed at maintaining it at a high level.

One cause of the change in the degree of oxygenation of the tissues in hyperoxia may be an increase in the intensity of oxidation-reduction processes in the cell. The aim of the present investigation was to study the role of the metabolic factor in the mechanism of the lowering of the tissue pO_2 in hyperbaric hyperoxia.

EXPERIMENTAL METHOD

Experiments were carried out on albiono rats bred at the A. A. Bogomolets Institute of Physiology, Academy of Sciences of the Ukrainian SSR. The animals were exposed to oxygen in increased concentration at atmospheric and above-atmospheric presure (3-5 kgf/cm^2) for 15-90 min. The value of pO_2 in the liver and muscles was determined by a polarographic method using open platinum electrodes [5]. The total oxygen consumption was recorded in a closed system immediately before and after exposure to hyperoxia. The functional state of the mitochondrial respiratory chain was judged from the results of polarographic determination of the velocity of oxygen consumption by mitochondrial preparations from liver tissues of animals exposed to hyperoxia [4]. The intensity of tissue oxidation-reduction processes was modified by injecting 2,4-dinitrophenol (stimulator) and sodium amytal (inhibitor) into the animals [2, 9].

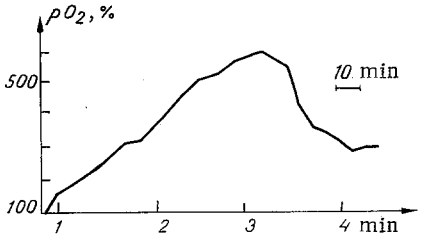

Fig. 1. Time course of pO_2 changes in physiological saline under local oxygen pressure of 4 kgf/cm^2. Exposure of hyperoxygenation for 3 h. Abscissa: 1) compression, 2) "plateau," 3) decompression, 4) normal pressure; ordinate, pO_2 (in %).

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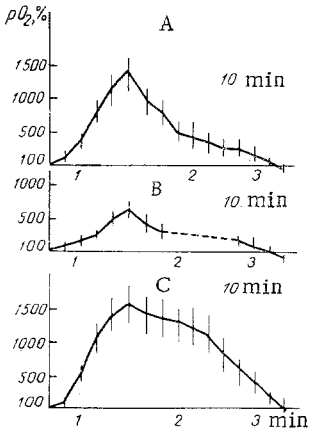

Fig. 2

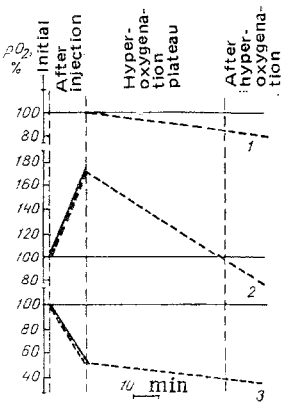

Fig. 3

Fig. 2. Time course of changes in pO_2 in muscle tissue of rats rexposed to hyperbaric oxygenation (4 kgf/cm^2). A) Control, B) DNP, C) sodium amytal. Remainder of legend as to Fig. 1.

Fig. 3. Effect of DNP and sodium amytal on total oxygen consumption of rats exposed to hyperbaric oxygenation (4 kgf/cm^2 for 1 h). 1) Control; 2) DNP; 3) sodium amytal.

TABLE 1. Effect of Normobaric Oxygenation (1 kgf/cm^2, 90 min) on Intensity of Oxidation-Reduction Processes in Rat Liver Preparations (M ± m)

Group of animals	Body weight, g	Metabolic states and velocity of oxygen consumption, g-atoms O_2/min/mg protein				Respiratory control	
		I endogenous	4_{II} rest	3 active	4_O after active	after Chance and Williams	after Lardy and Wellman
Control (n = 9)	182±5,3	20,3±1,40	28,9±2,21	35,4±3,68	31,8±7,15	1,49±0,12	1,72±0,07
Experiment (n = 10)	175±3,4	18,2±1,70	26,7±2,57	44,0±4,15*	21,4±5,60	1,67±0,13*	1,98±0,09
Control (n = 7)	194±2,8	15,3±2,00	24,6±3,99	43,5±7,67	23,9±4,82	1,53±0,15	1,94±0,26
Experiment (n = 7)	193±4,9	18,9±2,19*	28,4±4,26*	47,0±8,31*	22,1±5,36	2,09±0,35	1,77±0,27

*Differences significant with respect to direction of changes ($P < 0.05$).

EXPERIMENTAL RESULTS

In the determination of tissue pO_2, experiments on animals were preceded by model experiments to study the time course of pO_2 in physiological saline under a local oxygen pressure of 4 kgf/cm^2. The results of one such experiment are given in Fig. 1. Throughout the "plateau" period there was a progressive rise in pO_2 in the solution. The fall of pO_2 began only in the decompression period. These experiments ruled out any role of physicochemical factors in the lowering of pO_2 observed in the animals' tissue during exposure to hyperbaric oxygen.

In experiments on animals exposed to oxygen at atmospheric pressure in most cases pO_2 in the tissues rose by 50-100%. This level also remains virtually unchanged throughout the period of observation. The results confirm the pattern of the time course of changes in tissue pO_2 described previously under the corresponding conditions of normobaric oxygenation [3].

In experiments in which oxygen was used at a pressure of 3-5 kgf/cm^2 pO_2 in the tissues showed a marked rise (up to 1215 ± 181%) at the beginning of exposure to oxygen, followed by a fall as the experiment continued. By the end of the "plateau" period pO_2 in the tissues was usually 200-400% compared with its initial level. These results on the whole also agree with data in the literature [3, 7].

To study the intensity of oxidation-reduction processes in the tissues during changes in their pO_2, appropriate experiments were carried out in which exposure to hyperbaric oxygen was accompanied by stimulation or inhibition of oxidation-reduction processes in the tissues by injection of 2,4-dinitrophenol (DNP) or sodium amytal. After injection of DNP the

TABLE 2. Effect of Hyperbaric Oxygenation (4 kgf/cm^2) on Intensity of Oxidation-Reduction Processes in Liver Preparations from Albino Rats (M ± m)

Preparation	Group of animals	Body weight, g	Metabolic states and velocity of oxygen consumption, g-atoms O_2/min/mg protein				Respiratory control	
			I endogenous	4_{II} rest	3 active	4_O after active	after Chance and Williams	after Lardy and Wellman
			Exposure 15 min					
Mitochondria	Control (n=9)	119±7,5	—	29,7±4,0	40,4±3,1	—	—	2,60±0,43
	Exp. (n=18)	127±4,9	—	44,0±3,1*	38,4±4,6†	—	—	1,79±0,17
			Exposure 60 min					
Homogenate	Control (n=13)	143,9±6,0	—	30,9±2,6	47,7±4,2	—	—	1,86±0,17
	Exp. (n=18)	140±4,9	—	35,6±2,10†	49,6±5,4†	—	—	1,51±0,18†
	Control (n=18)	158±8,6	—	43,1±2,3	107,6±9,7	—	—	2,29±0,15
	Exp. (n=24)	155±6,0	—	50,4±1,8*	81,2±8,0*	—	—	1,82±0,14*
Mitochondria	Control (n=13)	177±6,6	26,4±2,8	73,3±3,7	129,7±15,8	59,2±6,2	2,27±0,16	2,10±0,21
	Exp. (n=14)	176±6,3	18,3±2,5*	80,1±3,6†	106,7±11,4†	32,5±3,6*	2,09±0,15†	1,83±0,20†

*$P < 0.05$.

†Differences significant with respect to direction of changes ($P < 0.05$).

rise of pO_2 in muscle tissue was smaller, and toward the time of decompression it was 100-150% higher than initially in the tissues (Fig. 2). Inhibition of oxygen reduction by sodium amytal was accompanied by a greater increase in pO_2 and by a slower decrease in its level during exposure to hyperbaric oxygen (Fig. 2).

The results of these experiments confirm the view that the velocity of oxygen utilization plays the leading role in the maintenance of its partial pressure at a given level in the tissues. Under these circumstances the conditions of supply of oxygen to the tissues were evidently the same in all series of experiments described.

The results of investigation of the intensity of the total oxygen consumption indicate that, independently of the efficiency of oxidation-reduction processes in the tissues, the oxygen consumption of the animals fell after exposure to hyperbaric oxygen (Fig. 3). This reaction of the body may perhaps be aimed at limiting the intake of excess oxygen and may be one of the mechanisms protecting the body against hyperoxygenation.

The study of the ability of mitochondria to undertake biological oxidation and coupled phosphorylation is exceptionally important, because the mitochondria are the main oxygen consumer in the body. The investigations revealed different effects of normo- and hyperbaric hyperoxia on the functional state of the mitochondrial respiratory chain (Tables 1 and 2). Analysis of these observations showed that exposure to normobaric oxygenation is accompanied by an increase in the intensity of phosphorylation and in the degree of coupling of free and phosphorylating oxidation in the mitochondrial preparations tested. A characteristic result of hyperbaric oxygenation even after an exposure of only 15 min was intensification of free oxidation, inhibition of phosphorylation, lowering of the respiratory control, and stimulation of respiration by an exogenous phosphate acceptor (respiratory control after Chance and Williams and after Lardy and Wellman respectively).

A dominant feature of hyperbaric oxygenation is thus stimulation of the biological mechanisms aimed at lowering the degree of saturation of the cell with oxygen. The most effective of them are evidently processes leading to reduction of oxygen in the course of free oxidation. The development of the reaction of the mitochondrial respiratory chain to hyperoxygenation, as described above, with time coincides with the onset of the fall in tissue pO_2. It can accordingly be concluded that an important role in the mechanism of the lowering of pO_2 in the tissues in hyperoxia is played by activation of oxygen reduction processes in the mitochondria. This conclusion is confirmed by the fact that components of the respiratory chain are highly resistant to oxygen. This means that they are capable of carrying on electron transport and reducing oxygen under conditions of hyperoxygenation of the body and they constitute a natural mechanism of defense against excess oxygen.

The development of the reaction described above is preceded by a latent period [10], accompanied by saturation of the body with oxygen. It is at this time that the therapeutic

effect of hyperoxygenation is exhibited. Oxygen poisoning then develops: the ultrastructure and function of the mitochondrial and cytoplasmic membranes are damaged, free and phosphorylating oxygenation processes are uncoupled, and the efficiency of biological oxidation is reduced [6]. An oxygen concentration of up to 100% under a pressure of not more than 1 kgf/cm^2 with an exposure of up to a few tens of minutes may have a beneficial effect on the course of oxidative processes in the tissues in the presence of moderate degrees of hypoxia. Hyperbaric conditions of oxygenation (3-5 kgf/cm^2) with an exposure of 15-20 min ought to be maximally effective for producing urgent recovery from a state of deep hypoxia. To prevent the development of oxygen poisoning, fractional schedules of oxygenation are preferable.

LITERATURE CITED

1. V. Y. Berezovskii, The Tissure Oxygen Partial Pressure in Animals and Man [in Russian], Kiev (1973).
2. M. Dixon and E. Webb, Enzymes, Academic Press (1964).
3. E. A. Kovalenko and I. N. Chernyakov, in: Problems in Space Biology [in Russian], Vol. 21, Moscow (1972).
4. M. N. Kondrashova and A. A. Ananenko, in: A Manual for the Study of Biological Oxidation by the Polarographic Method [in Russian], Moscow (1973), pp. 106-128.
5. V. V. Matsynin, in: Polarographic Determination of Oxygen in Biological Objects [in Russian], Kiev (1968), pp. 64-69.
6. V. V. Matsynin, Dokl. Akad. Nauk Ukr. SSR, Ser. B. No. 12, 1117 (1978).
7. I. F. Sokolyanskii, in: Polarographic Determination of Oxygen in Biological Objects [in Russian], Kiev (1974), pp. 232-237.
8. I. F. Sokolyanskii, in: Mechanisms of Injury, Resistance, Adaptation, and Compensation [in Russian], Vol. 1, Tashkent (1976), pp. 450-451.
9. A. A. Sharaf, "A study of the mechanism of action of uncouplers of oxidative phosphorylation," Author's Abstract of Candidate's Dissertation, Moscow (1968).
10. C. J. Lambertsen, in: Treatment with Hyperbaric Oxygen [Russian translation], Moscow (1968), pp. 9-11.

LIPID PEROXIDATION IN MYOCARDIAL MEMBRANES AND ITS CONTROL DURING AGING

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Accumulation of lipofuscin in cells, mainly in hypertrophied muscle fibers, is one of the characteristic changes in the myocardium during aging [1, 6, 8, 13, 14]. Lipofuscin and fluorescent lipopigments like it are end products of free-radical lipid peroxidation (LPO) in biological membranes as a result of interaction of free amino groups of phospholipids and proteins with aldehydes formed during LPO in the membranes [6, 8]. An important role is ascribed to LPO in the pathogenesis of diseases frequently associated with age, such as atherosclerosis [4]. Accordingly it is interesting to study age changes in the intensity of LPO in myocardial membranes and the character of its cytoplasmic regulation in mammals during aging. Investigations previously carried out in this direction [7, 10-14] do not provide a complete age picture of LPO in myocardial membranes.

In the investigation described below the intensity of accumulation of lipofuscin and of lipofuscin-like pigments in the myocardium, the intensity of membrane LPO in homogenates and mitochondria, and also the activity of several enzymes of the antioxidant system of the myocardial cytosol and mitochondria were studied in rats of different ages.

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