most myocytes have no channels of the T system [5, 10, 11], and the sarcoplasmic reticulum is poorly developed [9]. These features of the atrial myocytes are evidently responsible for the fact that during general hyperfunction of the heart caused by muscular work the atria are subjected to a greater additional load, and in turn, this leads to a higher intensity of functioning of structures of the working myocytes and to greater probability of their hypertrophy than in the ventricles. Predominant hypertrophy of the atria during long-term adaptation to physical exercise may perhaps also be facilitated by the fact that the atrial cardiomyocytes differ fundamentally.

LITERATURE CITED

1. A. P. Amvros'ev, A. P. Kirilyuk, and L. M. Lobanok, Neurohumoral Regulation and Motor Activity during Aging [in Russian], Minsk (1984).
2. L. Komadel, E. Barta, and M. Kokavec, Physiological Enlargement of the Heart [in Russian], Britislav (1968).
3. P. L. Kyrge, "Cationic exchange of the myocardium and its hormonal regulation during exhausting physical exercise and training," Author's Abstract of Dissertation for the Degree of Doctor of Medical Sciences, Tallin (1975).
4. F. Z. Meerson, The General Mechanism of Adaptation and Prophylaxis [in Russian], Moscow (1973).
5. P. P. Rumyantsev, Arkh. Anat., No. 6, 115 (1972).
6. P. P. Rumyantsev, Cardiomyocytes during Reproduction, Differentiation, and Regeneration [in Russian], Leningrad (1982).
7. D. S. Sarkisov and B. V. Vtyurin, Electron-Microscopic Analysis of Increased Endurance of the Heart [in Russian], Moscow (1969).
8. A. S. Chinkin, Fiziol. Zh. SSSR, 68, No. 7, 1016 (1977).
9. C. E. Challice and W. G. Tatton, Electron Microscopy 1964, Vol. B, Prague (1964), pp. 101-102.
10. R. G. Hibbs and V. J. Ferrans, Am. J. Anat., 124, 251 (1969).
11. R. Hirakow, Am. J. Cardiol., 25, 195 (1970).
12. N. Külbs, Arch. Exp. Path. Pharm., 4, 228 (1906).
13. J. R. Marie, H. Guillemot, and P. V. Hatt, Pathol.-Biol., 24, 548 (1976).
14. E. Page, J. Earley, and B. Power, Circulat. Res., 34-35, Suppl. 2, II12 (1974).
15. N. E. Pratt, Anat. Rec., 157, 303A (1967).
16. R. Zak, Circulat. Res., 34-35, Suppl. 2, II17 (1974).

EFFECT OF CONDITIONS OF HYPERBARIC OXYGENATION ON STRUCTURAL CHANGES INDUCED IN THE LUNGS

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Hyperbaric oxygenation (HBO) is being increasingly widely used in clinical practice in various diseases. The wide range of application of HBO, on account of the universal character of hypoxia as a typical pathological process, and the specific features of this therapeutic technique are such that hyperbaric medicine can be regarded as a new trend in medical science [1]. Considering the possible toxic action of oxygen, the further spread of this method necessitates a detailed study of the effect of HBO on vitally important organs. The The most interesting aspect is the study of the action of HBO on the tissues of the lungs, which by virtue of their specific functions as organs of gas exchange, and of the method of oxygenation generally used, are exposed to a relatively higher partial pressure of oxygen under an increased total pressure. This has led some workers [3] to regard the lungs as a

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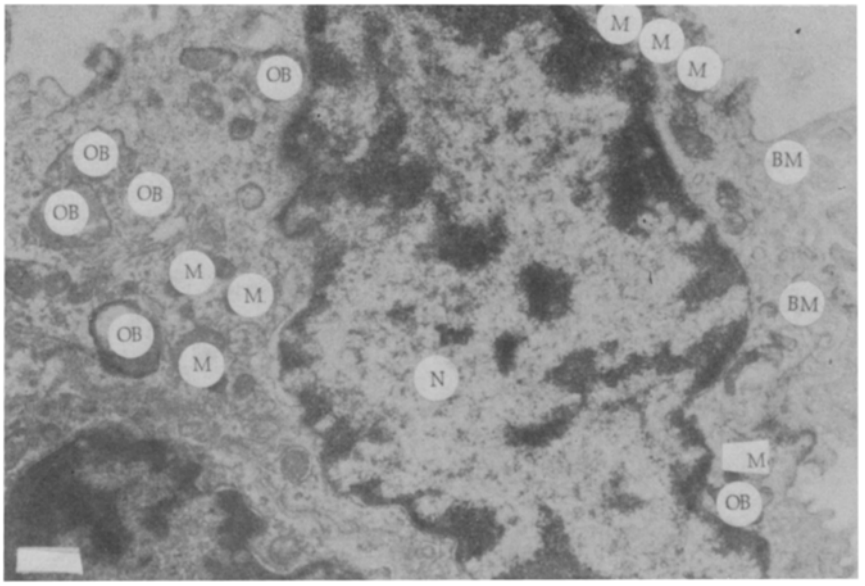

Fig. 1. Type II pneumocytes under the influence of HBO in a dose of 2.5 atm for 1 h daily for 3 weeks. Nucleus (N) has uneven outlines and is festooned, marginal distribution of chromatin; mitochondria (M) are electron-dense, homogeneous, and swollen: osmiophilic bodies (OB) have lost their typical laminar structure; basement membrane (BM) is edematous. 8000×.

target organ for the toxic action of oxygen [3, 4, 8]. Morphological changes in the lungs during continuous exposure to normobaric oxygenation have been described in the literature [2, 5-8].

Early morphological changes in the healthy lungs during intermittent exposure to HBO were studied in the investigation described below, in order to determine safe treatment schedules.

EXPERIMENTAL METHOD

Experiments were carried out on 30 chinchilla rabbits, placed in a BKI-191 pressure chamber, filled with 100% O_2. The rate of compression and decompression was 0.1 atm/min. The animals were kept for 1 h daily for 1, 2, and 3 weeks at the height of the assigned pressure (2, 2.5, 3, and 4 atm). At the end of the assigned period, the rabbits were killed 20 min after removal from the chamber by intravenous injection of hexobarbital. Pieces of tissue were taken from different parts of the lungs. Histological sections stained with hematoxylin and eosin and by Van Gieson's method and semithin sections stained with toluidine blue were studied. An electron-microscopic investigation was undertaken.

EXPERIMENTAL RESULTS

During the action of HBO in doses of 2 atm for 1, 2, and 3 weeks and of 2.5 atm for 1 h daily for 1 week, uneven aeration of the lung tissues was observed: alternation of areas of acinar dystelectasis with areas of increased aeration. In the zones of dystelectasis the alveolar septa were thickened because of closer packing of the cells; the elastic and collagen fibers of the alveolar septa were twisted. Emphysematous areas were found mainly beneath the pleura. Hypersecretion of mucus was observed in the large bronchi, while many small bronchi, and also small and medium-sized branches of the pulmonary artery were constricted. These changes can evidently be interpreted as compensatory and adaptive, in response to increased oxygenation. No significant ultrastructural changes were found under these circumstances in the lung tissue.

Under the influence of HBO in a dose of 2.5 atm for 2 and 3 weeks, besides the morphological changes described above, changes at the ultrastructural level also were observed in cells of the air–blood barrier. In the type I alveolocytes the number of micropinocytotic

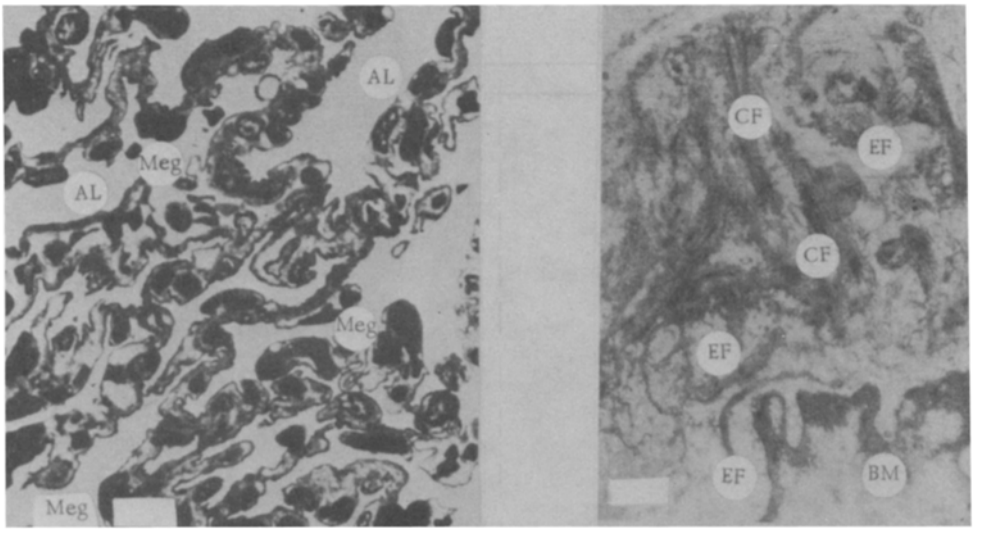

Fig. 2 Fig. 3

Fig. 2. Action of HBO in a dose of 4 atm for 1 h daily for 1 week. Capillaries distended by megakaryocytes (Meg), lumen completely occluded. AL) Alveolar lumen. 1500×.

Fig. 3. Edema of interstitial alveolar stroma: swelling, loosening of structure, and disorganization of collagen fibers (CF), vacuoles with edema fluid (EF) appear in cytoplasm of fibroblasts. 10,000×.

vesicles were reduced, and in individual cells large micropinocytotic vesicles containing edema fluid appeared. In the type II alveolocytes changes were observed in the osmiophilic bodies: They appeared homogeneous because of loss of their laminar structure, and some of them were expelled from the cells and replaced by vacuoles. Nuclei of the pneumocytes had an uneven, festooned surface, with marginal distribution of their chromatin. The mitochondria were swollen, electron-dense, and homogeneous, with no outlines of cristae. The basement membrane was edematous and convoluted (Fig. 1). Vacuoles containing edema fluid appeared in the cytoplasm of the endotheliocytes, with separation of certain areas of cells from the basement membrane.

The action of HBO in a dose of 3 atm for 1 week caused considerable changes in the lungs. Compared with the previous series, the uneven aeration of the lung tissue was more marked. In areas of lobular atelectasis many macrophages, edema fluid, and solitary erythrocytes were found, evidence of increased permeability of the air–blood barrier. The small bronchi and branches of the pulmonary artery were greatly constricted. Cytoplasmic outgrowths of type I pneumocytes were detached from the basement membrane, vesicles formed beneath them, and large vacuoles with edema fluid were found in their cytoplasm. These changes in the cells can be interpreted as edema, hydrophic dystrophy, and the onset of desquamation. Hypertrophy of the mitochondria and of the osmiophilic bodies was observed in the type II pneumocytes. The latter were enlarged to 2.5-3 μ (normally 1-1.5 μ) and located in the apical part of the cells: Many reticular structures were visible in the alveoli, an indirect sign of hyperfunction of these cells. The basement membranes of the alveoli were edematous and twisted. The uneven distribution of chromatin in the endotheliocyte nuclei and the large vacuoles in their cytoplasm are evidence of dystrophic changes in these cells. Changes in the air–blood barrier described above were more marked in areas of atelectasis.

Under the influence of HBO in a dose of 4 atm for 1 h daily for 1 week the uneven aeration of the lungs was even more marked than in the previous series. Foci of atelectasis and dystelectasis were larger and the emphysema in places was bullous in character. Contraction of the small bronchi and branches of the pulmonary artery waa severe, especially in zones of atelectasis. The capillaries were dilated and contained more megakaryocytes than normally, which completely blocked the lumen (Fig. 2). Permeability of the air–blood barrier was sharply increased, as shown by the marked intra-alveolar edema, and the presence of numerous macrophages and erythrocytes in the edema fluid. In zones of atelectasis there was consider-

able edema of the interstitial alveolar stroma, with swelling and disorganization of elastic and collagen fibers, the formation of electron-translucent areas in the ground substance, and the presence of large vacuoles containing edema fluid in the cytoplasm of the fibroblasts (Fig. 3).

Severe dystrophic changes turned into necrosis were present in cells of the alveolar epithelium and in the endotheliocytes. Outlines of the nuclei in the type I pneumocytes and endotheliocytes were festooned, the chromatin was distributed mainly at their periphery, and electron-translucent regions were visible in the nuclei and cytoplasm, evidence of plasmolysis and karyolysis. The type II pneumocytes contained large vacuoles instead of osmiophilic bodies. The matrix of the mitochondria was swollen, electron-translucent, and contained remnants of cristae. The number of microvilli on the apical surface of the cells was reduced, and those which remained were swollen. The chromatin in the nuclei was distributed peripherally. The basement membrane was loose in structure and thickened. Besides macrophages and erythrocytes, many desquamated type II cells and fragments of reticular structures were found in the lumen of the alveoli, in the edema fluid. Consequently, the action of HBO in a dose of 4 atm for 1 h daily for 2 week can be interpreted as toxic, causing destructive processes in cells of the air–blood barrier, and as a result, leading to a sharp increase in its permeability, causing intra-alveolar and interstitial edema. These morphological changes evidently arise through the cytotoxic action of free oxygen radicals, generated more intensively during hyperoxia. The manifestation of this action is associated with exhaustion of the capacity of the antioxidant system of the lungs [9].

The results of these investigations thus demonstrate clear dependence of the severity of the morphological changes in the lungs on the pressure of oxygen and the duration of its action. A safe HBO schedule, with no destructive action on the lungs of intact rabbits, is 2 atm for 1 h daily for 2 weeks or 2.5 atm for 1 h daily for 1 week. Changes in the lung tissue under these circumstances can be interpreted as compensatory or adaptive. With a higher pressure they become pathological in character, as is shown by disturbances of the microcirculation and dystrophic changes in the air–blood barrier, with an increase in its permeability and with the development of intra-alveolar and interstitial edema. Endotheliocytes and type I alveolocytes are most sensitive to the action of high doses of HBO: Hydropic dystrophy, karyolysis and shrinking of the nuclei, and separation of cells from the basement membranes and desquamation gradually increase in severity among these cells. The type II pneumocytes are more resistant to the harmful action of HBO. In response to intensification of dystrophic changes in other structures of the air–blood barrier, they are observed to undergo compensatory changes, reflecting their high functional activity. The pathological changes described above in the lungs are mosaic in character: They are most marked in areas of atelectasis, and become diffuse only as a result of exposure to toxic doses of HBO.

LITERATURE CITED

1. B. V. Petrovskii and S. N. Efuni, Abstracts of Proceedings of the 7th International Congress on Hyperbaric Medicine [in Russian], Vol. 1, Moscow (1983), pp. 5-11.
2. W. R. Anderson, M. B. Strickland, and S. H. Tsai, Am. J. Path., 73, 327 (1973).
3. G. L. Huber and D. B. Drath, Oxygen and Living Processes, New York (1981), pp. 273-357.
4. S. K. Ludvin, W. H. Northway, and K. G. Bensch, Lab. Invest., 31, 425 (1974).
5. H. Lum, W. Schwartz, D. L. Dungworth, and W. S. Tyler, Am. Rev. Resp. Dis., 118, 335 (1978).
6. M. J. Evans, Environ. Health Perspect., 55, 85 (1984).
7. A. Sladen, M. B. Laver, and H. Pontoppidan, New Engl. J. Med., 279, 923 (1968).
8. T. Yusa, J. D. Crapo, and B. A. Freeman, Biochim. Biophys. Acta, 798, 167 (1984).