mine and serotonin from the depots at the beginning of the inflammatory reaction. We know [6] that lithium reduces the release of catecholamines from adrenergic endings. Since in the second model of inflammation the pain syndrome (pain stress) was dominant [11], during which the secretion of catecholamines from the adrenals and adrenergic endings is increased [10], lithium hydroxybutyrate may perhaps depress this process and thus inhibit prostaglandin synthesis in the second phase of inflammation. Consequently, lithium hydroxybutyrate, together with other preparations, may prove to be effective in the treatment of both early and late stages of inflammatory processes, in which prostaglandin synthesis is disturbed.

LITERATURE CITED

1. P. N. Aleksandrov and T. V. Speranskaya, Byull. Éksp. Biol. Med., No. 2, 188 (1987).
2. G. N. Kryzhanovskii, New Data on Pharmacology and Clinical Application of Lithium Salts [in Russian], Moscow (1984), pp. 49-57.
3. E. V. Montsevichyute-Eringene, Patol. Fiziol., No. 4, 71 (1964).
4. T. V. Speranskaya, Patol. Fiziol., No. 6, 71 (1971).
5. A. M. Chernukh, Inflammation [in Russian], Moscow (1979).
6. O. Beaty, M. G. Collis, and J. Shepherd, J. Pharmacol. Exp. Ther., 218, 309 (1981).
7. P. H. Chanh, Prostaglandins Leukotriens Med., 22, 295 (1986).
8. E. Cullen, J. Pharm. Sci., 73, 579 (1984).
9. M. Di Rosa, J. P. Giroud, and D. A. Willoughby, J. Pathol., 1, 15 (1971).
10. H. Selye, The Story of the Adaptation Syndrome, Montreal (1950).
11. R. Vinegar, J. Truax, and J. Selph, Fed. Proc., 35, 2447 (1976).
12. R. B. Zurier, Mediators of Inflammation, London (1974), p. 163.

CHANGES IN THE AIR-BLOOD BARRIER OF THE LUNGS DURING HYPERTHERMIA

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KEY WORDS: hyperthermia; air-blood barrier of the lungs; mean arithmetic thickness; mean harmonic thickness.

It is generally considered that the response of lung tissue to exogenous and endogenous influence is realized in the form of a stereotyped response of cells composing the air-blood barrier (ABB) of the lungs. This response is based on a change in permeability of the ABB of the lungs and, in particular, of the biological membranes composing its structures, and this ultimately leads to an increase in the degree of hydration of lung tissue and to edema of the lungs [1, 4, 8, 13]. This type of picture is observed during the development of anoxic stages of varied genesis in the body [7, 10, 12]. The disturbances observed may have a significant influence on the effectiveness of oxygenation of the blood in the lungs; the effect of a rise of body temperature on ultrastructure and function of the ABB has received less study. In that state disturbances of the ABB may arise, on the one hand, as a result of the development of an anoxic state of predominantly circulatory genesis, whereas on the other hand the direct action of a high temperature on the lung tissues cannot be ruled out. Whereas edema and dystrophic changes have been shown to take place in the structures of the cardiovascular system during hyperthermia [5, 6], the respiratory apparatus has been inadequately studied from this standpoint.

The aim of this investigation was to study the effect of hyperthermia on the ultrastructure and morphometric characteristics of ABB of the lungs.

EXPERIMENTAL METHOD

Experiments were carried out on six mongrel dogs weighing 14-18 kg and anesthetized with chloralose (80 mg/kg) and urethane (300 mg/kg). Hyperthermia was induced in a hot and humid

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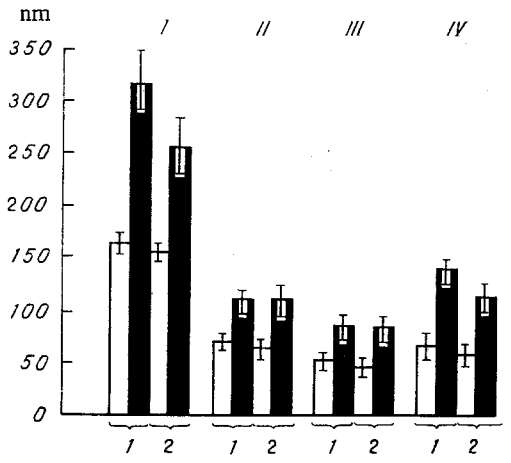

Fig. 1. Change in τ (1) and τ_h (2) of thickness of ABB of the lungs (I) and of endothelial (II), interstitial (III), and epithelial (IV) layers during hyperthermia (black columns) and in control (white columns).

chamber, in which the temperature and humidity of the ambient air could be changed within fairly wide limits and assigned parameters could be maintained automatically at the required level. The degree of hyperthermia was judged from the animal's body and blood temperatures measured by the rectal transducer of the TPÉM-1 electrothermometer and by a second electrothermometer with transducer introduced into the arch of the aorta. Samples of lung tissue for electron-microscopic investigation were taken after the animal's body temperature had reached 42°C and was maintained at that level for 3 h. Pieces of tissue from peripheral regions of the lower lobes of the lungs were fixed in glutaraldehyde and OsO_4 and subsequently embedded in Epon by the standard technique [9]. Ultrathin sections 40-60 mm thick were stained in uranyl acetate and lead citrate and examined in an electron microscope of the JEM-7A and JEM-100CX type. Random samples were taken by Weibel's method [3]. Morphometric determination of the arithmetic mean (τ) and harmonic mean (τ_h) thickness of ABB of the lungs was carried out on photomicrographs [15]. To monitor the degree of the anoxic state developing during hyperthermia, pO_2 and pH of arterial and mixed venous blood were determined by means of a biological microanalyzer (Radelkis, Hungary).

EXPERIMENTAL RESULTS

When the action of hyperthermia was studied considerable changes were found in ABB of the lungs. The degree of hydration of the lung tissues was increased. Morphometric determination of τ and τ_h of ABB revealed a significant increase in the value of both these parameters (Fig. 1). The degree of the increase corresponded to that observed in anoxic states of varied genesis, evidence of the nonspecific effect of different external factors, including hyperthermia, on lung tissue, leading to an increase in its water content. Both the total thickness of ABB of the lungs and the number of thickened areas in the overall distribution of thicknesses were increased, as shown by the increase in τ_h. The epithelial, interstitial, and endothelial layers of ABB contributed unequally to the increase in thickness of ABB (Fig. 1), for they underwent changes of different magnitude (Fig. 2).

The endothelium of the lung capillaries was the layer of ABB to undergo the greatest degree of thickening, as reflected in both τ and τ_h; this evidently confirms once again the existing view that the endothelial cells respond earliest to different kinds of external influence [2, 14]. Thickening of the endothelium, moreover, was accompanied by a sharp rise in the intensity of micropinocytosis in the cytoplasmic processes of the endothelial cells, up to the stage of "extreme vesicle formation" [11], when the number of micropinocytotic vesicles per unit surface area increased up to 15-20 (Fig. 2). The vesicles were virtually homogeneous in size and were located mainly near the capillary and interstitial borders, opening into the capillary lumen and the interstices. It can be tentatively suggested that this pinocytic mechanism is responsible for the excessive intake of fluid from the blood plasma, causing increased hydration of the tissue and edema of the lungs during hyperthermia. Considerable divergence of the cytoplasmic processes of the endothelial cells also was observed at the sites of the intercellular junctions, causing denudation of the basement membrane of the interstitial layer (Fig. 2d, e). This type of response can be regarded as a compensatory reaction, aimed at improving the conditions of O_2 supply from the alveolar air into the blood in the pulmonary capillaries.

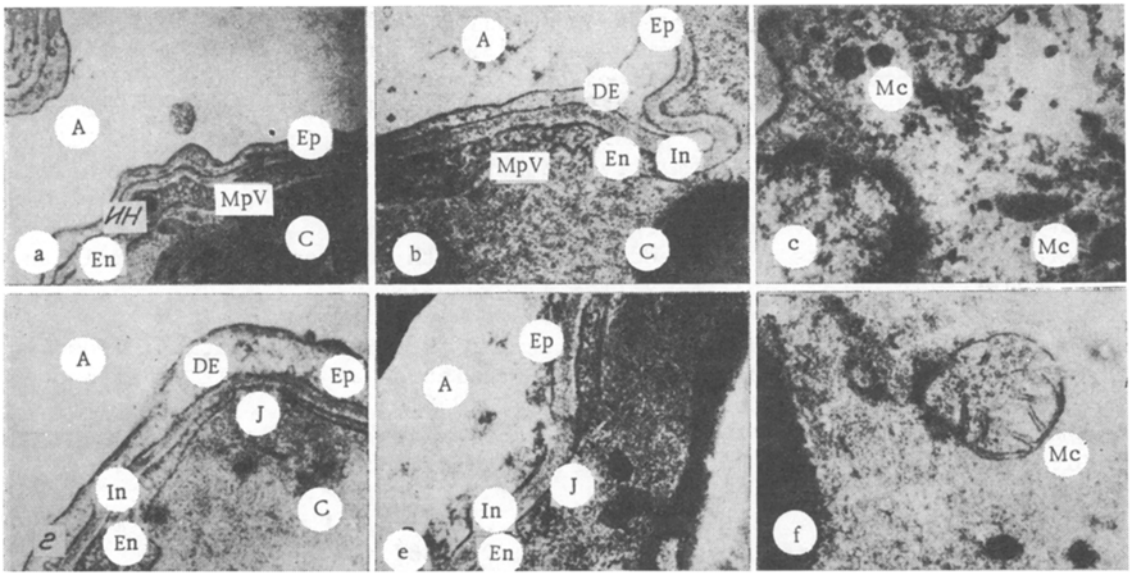

Fig. 2. Ultrastructure of ABB of lungs during hyperthermia: a) intact ABB; b-f) ABB during hyperthermia. A) Alveolus; C) capillary lumen; En) endothelial layer; In) interstitial layer; Ep) epithelial layer; MpV) micropinocytotic vesicles; DE) diffuse edema of cytoplasm; J) site of intercellular junction; Mc) mitochondria. 48,000 ×.

Under conditions of hyperthermia the interstitial layer was the least changed and made the smallest contribution (compared with the other layers) to the increase in thickness of ABB. Thickened and dehydrated areas with translucent contents were found extremely rarely in this layer (Fig. 2b, d, e).

The epithelial layer underwent the most pronounced and widespread destructive ruptures (Fig. 2b, d, e).

The increase in τ and τ_h of the epithelium took place mainly because of the predominance of areas with electron-translucent contents, i.e., of considerably hydrated areas. Micropinocytotic vesicles were rare and were situated mainly along the border with the interstitial layer, into which they opened. Meanwhile, larger vacuole-like formations with translucent contents were observed. Areas of total destruction of the epithelial layer with escape of their contents into the alveolar lumen and with denudation of the basement membrane of the interstitial layer were observed (Fig. 2e).

It can be concluded from these findings that the development of marked changes in all layers of ABB, including the alveolar epithelium, regardless of the cause, is accompanied by the development of arterial anoxemia. Hyperthermia is no exception, for it was shown that pO_2 in the arterial blood is reduced on average by 21% during a rise of body temperature to 42°C. This evidently reflects the general rule that even under normoxic conditions, when the role of the diffusion factor in maintenance of the alveolo-arterial O_2 gradient is negligibly small, some connection, possibly indirect, exists between the morphological and functional state of ABB and the level of oxygenation of the blood in the lungs.

The investigations revealed a considerably mosaic pattern of changes in the mitochondria of the cells composing ABB (in particular, type II pneumocytes; Fig. 2c, f), with the simultaneous coexistence of unchanged mitochondria, juvenile mitochondria with an electron-optically dense matrix, and partly swollen mitochondria, which in the modern view lies at the basis of adaptation of cells to new conditions of existence, in the tissues studied [1, 11].

The ultrastructural changes discovered in ABB of the lungs were more marked than those observed during the development of an anoxic state of circulatory type in vivo, and this confirms the hypothesis that a rise of temperature in the external environment and (or) in an animal's blood has a marked effect on the morphological and functional state of ABB of the lungs.

LITERATURE CITED

1. A. P. Avtsyn and V. A. Shakhlamov, The Ultrastructural Bases of Cell Pathology [in Russian], Moscow (1979).

2. A. K. Biokov, The Lung in Pathology [in Russian], Novosibirsk (1975), p. 71.
3. E. R. Wiebel, Morphometry of the Human Lungs [Russian translation], Moscow (1970).
4. T. N. Kovalenko, "State of the air-blood barrier of the lungs under conditions of a normal and modified gaseous environment in rats of different ages," Author's Abstract of Dissertation for the Degree of Candidate of Biological Sciences, Kiev (1984).
5. A. A. Korchagina, The Pathobiochemistry and Histopathology of Hyperthermia [in Russian], Smolensk (1974), p. 54.
6. K. S. Mustafin, Sov. Zdravookhr, Kirg., No. 6, 3 (1970).
7. M. M. Seredenko, Abstracts of Proceedings of the 9th Congress of the Ukrainian Physiological Society [in Ukrainian], Kiev (1972), p. 332.
8. S. A. Simbirtsev, N. A. Belyakov, and V. B. Serikov, Fiziol. Zh. (Kiev), 30, 696 (1984).
9. B. S. Weakley, Electron Microscopy for Beginners [Russian translation], Moscow (1975).
10. Z. G. Tsagareli and N. S. Durmishidze, The Circulation at High Altitudes and in Experimental Anoxia [in Russian], Dushanbe (1978), p. 246.
11. V. A. Shakhlamov, Capillaries [in Russian], Moscow (1971).
12. C. K. Drinker, The Clinical Physiology of the Lungs, Springfield (1954).
13. J. M. Foult, Tempo Med., No. 182, 33 (1984).
14. S. S. Sobin, H. M. Tremer, J. D. Hardy, et al., J. Appl. Physiol., 55, 1445 (1983).
15. E. R. Weibel and B. W. Knight, J. Cell Biol., 21, 367 (1964).

CHANGES IN G-, ECL- AND EC-CELLS IN THE GASTRIC AND DUODENAL MUCOSA AFTER EXPERIMENTAL SELECTIVE PROXIMAL VAGOTOMY

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Selective proximal vagotomy (SPV), an organ-sparing operation, is widely used in the treatment of diseases of the duodenum and stomach. Its therapeutic effect is connected with abolition of the stimulating influence of the vagus (acetylcholine) on the parietal cells. However, various complications may arise after vagotomy, due to changes in the mechanisms of neurogenic and hormonal regulation of gastric secretion and, in particular, to interaction between the vagus and G-, ECL-, and EC-cells. Information about changes in the G-, ECL-, and EC-cells in the stomach and duodenum after SPC is limited [2-4]. The effect of vagotomy on G-, ECL-, and EC-cells simultaneously has virtually not been studied. In order to examine these problems, the effect of SPV on G-, ECL-, and EC-cells, synthesizing the chief stimulators (gastrin and histamine) and modulators (serotonin) of the gastric secretion, was studied experimentally.

EXPERIMENTAL METHOD

Experiments were carried out on 120 albino rats divided into two groups (60 rats in each group, 10 rats in each series): group 1 (control) rats undergoing laparotomy only; group 2) rats undergoing SPV. The rats were decapitated under superficial pentobarbital anesthesia 24 h, 3, 7, and 15 days, and 1 and 6 months after the operation. Sections of the stomach and duodenum were stained with hematoxylin and eosin, by Grimelius's reaction (for argyrophilic cells), by the Masson–Fontana reaction (for argentaffin cells), and by Sevki's reaction (to detect ECL-cells, which stain blue-violet on account of the presence of histamine). The number of endocrine cells was counted by means of Avtandilov's grid in 1 mm^2 of mucosa under a magnification of 400. The results were subjected to statistical analysis by Student's test. Pieces of tissue for electron-microscopic study were fixed in solutions of glutaraldehyde and osmium tetroxide and then embedded in Epon-812.

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