REGULATION OF RESPIRATION AND THE PULMONARY CIRCULATION IN EXPERIMENTAL PNEUMONIA

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There is clinical and experimental evidence to show that the appearance and development of inflammatory foci in the lungs are closely connected with disturbances of the activity of individual formations of the CNS [2, 3, 9, 10, 12-15]. Most authorities reduce the role of the nervous system in inflammation to vasodilatation in the inflammatory focus and to active hyperemia, and consider that hyperemia creates the necessary preconditions for exudation, emigration, capillary permeability, and tissue edema. Clinicians and experimental research workers are agreed that, on the one hand, increased activity of the nervous system is responsible for development of the inflammatory process in successive stages and, on the other hand, biologically active substances, which correlate activity of the respiratory and circulatory systems under these conditions, are activated, inhibited, or appear *de novo* in the lungs [5, 6]. Meanwhile, the nervous and humoral mechanisms of disturbance and compensation of the disturbed functions of respiration and the pulmonary circulation are usually judged on the basis of indirect data.

The aim of this investigation was to study mechanisms corresponding activity of the respiratory and macro- and microvascular systems of the lungs, using a model of experimental inflammation of the respiratory passages and lungs.

EXPERIMENTAL METHOD

In experiments on 26 cats 0.3 ml of turpentine was introduced into the trachea. Tests were carried out 24, 48, and 72 h after injection of the turpentine. The methods used involved a combination of microelectrode, stereotaxic, and electromyographic techniques. For intravital investigation of the pulmonary microcirculation, biomicroscopy (MBI-15 microscopy) was used. The time course of the volume velocity of the blood flow in the pulmonary macrovessels was recorded by an ultrasonic method. The blood gas composition and acid-base balance (ABB) were determined by the micromethod of Astrup and Siggard-Andersen. Pathological and histological investigations of the lung tissue were undertaken in experimental and spontaneously developing pneumonia.

EXPERIMENTAL RESULTS

Comparative analysis of the pathological and histological findings showed common pathological features in the location and course of experimental and spontaneous inflammation. In both cases discrete large or multiple small foci of inflammation were observed (most frequently on the right side or near the hilus). Histological investigation showed that each focus of inflammation, regardless of its size, was surrounded by a "belt" of emphysema. In most of the emphysematous areas the alveolar septa were ruptured and formed an air cushion around the inflammatory focus, in which virtually no gas exchange or circulating blood was present. The air cushion around the inflammatory focus consists not only of pathologically changed lung tissue, but at the same time it serves as a natural barrier preventing the spread of inflammation. Its protective role is thus expressed.

Biomicroscopy revealed the time course of functional changes in the capillary system of the normal lung and the lung with experimental pneumonia (Fig. 1). As stated previously

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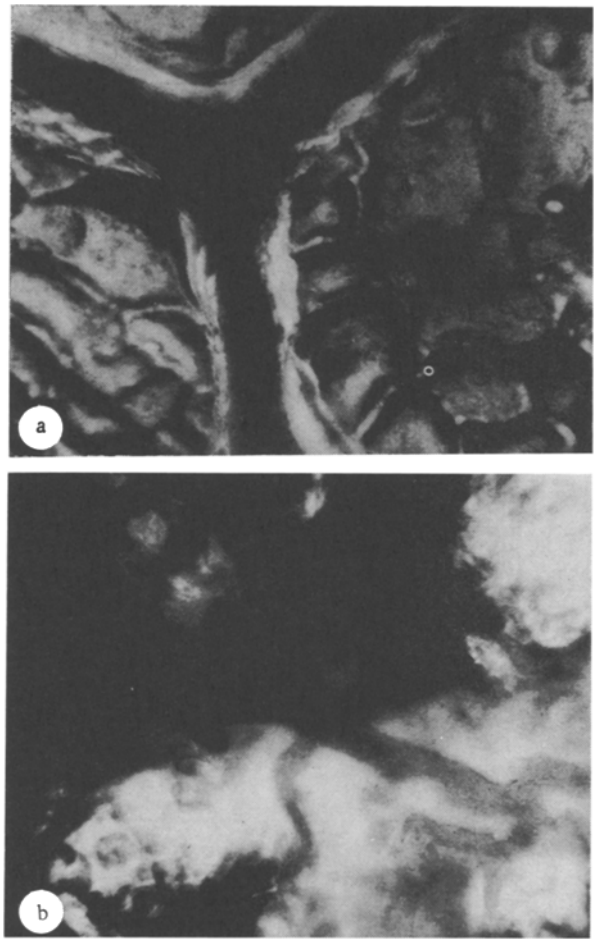

Fig. 1. Microvascular bed of the lung: a) wide and narrow pulmonary capillaries during natural breathing with the chest closed; b) wide and narrow capillaries, immersed in turbid exudate, in an inflammatory focus during artificial respiration with the chest open. Ocular 4, objective 25.

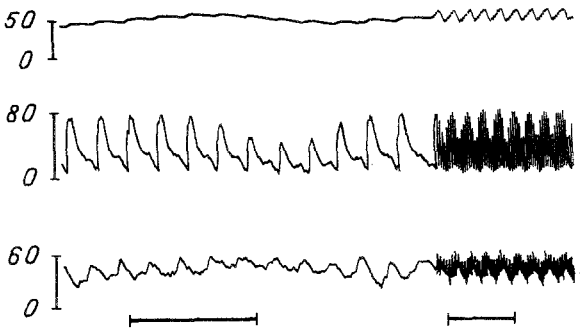

Fig. 2. Blood flow in pulmonary artery and vein of lower lobe during development of inflammatory focus in that same lobe. From top to bottom: mean blood flow in pulmonary artery of lower lobe (in ml/min), phasic blood flow in pulmonary artery (in cm/sec), mean blood flow in pulmonary vein of lower lobe (in ml/min). Time markers 1 and 10 sec.

[8], under normal conditions the wide capillaries form a network in which the cells move one after the other in a continuous stream. In narrow capillaries, on the surface of the alveoli, single blood cells move one after the other at high speed and in different directions (Fig. 1a).

The picture is drastically disturbed in inflammation of the lungs (both in and near to the focus) [1]. In the focus of inflammation the blood cells can be seen to accumulate in the turbid exudate. Narrow lung capillaries are masked in this mass and cannot be seen. Only separate dilated regions of wide capillaries can be seen on the surface of the alveoli (Fig. 1b). Aggregation and stasis of the blood cells take place in these capillaries. During inflammation of one lobe or even of one lung, the gas exchange in the alveoli and microcirculation in the affected lung tissue cease not only in the inflammatory focus itself, but also in the neighboring areas of lung tissue [1]. Meanwhile, ultrasonic investigations showed that the blood flow in the macrovessels of the affected lobe is not interrupted. Moreover, the inflow of blood along the arteries from the heart and its outflow along the veins from the affected lobe of the lung show very little change (Fig. 2).

As a result, blood unsaturated with oxygen evidently travels to the heart, bypassing wide and narrow alveolar capillaries, along macrovessels and arteriovenous anastomoses of the lungs. The previous correlation between the alveolar gas exchange and circulation of the blood in the pulmonary macro- and microvessels is disturbed, giving rise to increasing hypoxemia in the systemic circulation, tissue hypoxia, and metabolic and respiratory acidosis [8, 11, 15].

As the inflammatory focus spreads, a combination of factors thus arises which not only stimulates the respiratory center, but at the same time, causes excitation of nervous structures involved in regulation of the activity of the cardiovascular system. Nervous control of respiration and the circulation becomes pathological in character. This is shown by the fact that during extremely intensive excitation of the true repsiratory neurons of the dorsal and ventral respiratory nuclei in the medulla, electrical activity of the principal respiratory muscles at the periphery not only is not increased, but may be actually reduced, especially in the case of the external intercostal muscles [9]. Meanwhile electrical activity of the accessory respiratory muscles (dilator naris, posterior crico-arytenoid, cricothyroid, scaleni, and

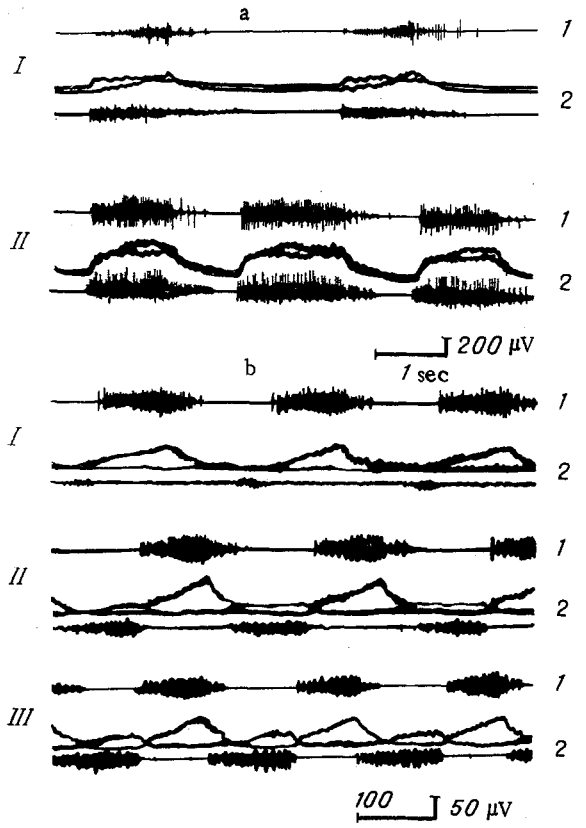

Fig. 3. Electrical activity of the diaphragm and accessory respiratory muscles. *a*: 1) Electromyogram (EMG) of diaphragm; 2) EMG of posterior crico-arytenoid muscle: I) in normal animal, II) in unilateral inflammation; b: 1) EMG of diaphragm; 2) EMG of constrictor muscles of the pharynx: I) in normal animal, II) in unilateral inflammation, III) in bilateral inflammation.

constrictor muscles of the pharynx) increases intensively [4]. Analysis of the trend of electrical activity of the principal and accessory respiratory muscles showed that in animals with severe (bilateral) pneumonia the efferent flow of impulses between the principal respiratory muscles and accessory muscles possessing a common innervation with the principal muscles undergoes redistribution [9]. New typologic features of respiration are formed with redistribution of the efferent impulsation. For instance, in animals with bilateral inflammation of the lungs pathological respiration arises, in which the main participants are the accessory respiratory muscles — nasopharyngeal, laryngotracheal (Fig. 3). This pathological respiration resembles the evolutionarily primitive type of respiration found in the lung-breathing amphibians [14]. Respiration of this kind in pneumonia is an important adaptive reaction. Nasopharyngeal and laryngotracheal respiration facilitates repair processes in lung tissue, because the mobility of the chest is reduced in regions in contact with the affected zone in the lungs [10]. Characteristically, a marked increase in electrical activity of the expiratory internal intercostal muscles was observed under these circumstances [9]. The chest of the affected animal thus assumes the expiratory position, and this also protects the lungs from injury during respiratory excursions. The increased electrical activity of the accessory respiratory muscles and the characteristic pathological respiration, arising in pneumonia, confirm L. L. Shik's hypothesis that in such cases the gas exchange may actually take place at the level of the respiratory dead space.

The results of these investigations, together with previous data [7-9], showed that at the beginning of the disease in the respiratory passages the first adaptive reactions, which are highly effective, are reflex stimulation of respiration and an increase in the respiratory waves of the blood flow in the macrovessels of the lungs as a result of an increase in the additional resistance to respiration [10]. During development of an inflammatory focus in the lungs, in its central part the microcirculation ceases initially in the narrow capillaries and alveolar ventilation is impaired. This leads to the development of a combination of factors which have a simultaneous excitatory action on the respiratory and vasomotor centers. There is reason to suppose that in severe bilateral pneumonia adaptive reactions develop on the basis of reserve regulatory systems of respiration and the circulation, arising in the body at an early stage of evolution, and which are not exhibited in healthy animals under the ordinary conditions of life.

LITERATURE CITED

1. N. K. Bogolepov, Zh. Nevropatol. Psikhiat., No. 9, 1291 (1975); No. 11, 1628 (1977).
2. M. S. Vovsi, Ter. Arkh., 18, 6 (1940).
3. V. M. Gul'yan, Patol. Fiziol., No. 4, 50 (1984).
4. V. A. Goncharova and N. V. Syromyatnikova, Ter. Arkh., No. 9, 143 (1975).
5. V. A. Goncharova et al., in: Metabolism of the Lungs in Nonspecific Diseases of the Respiratory Organs [in Russian], Leningrad (1979), pp. 19-21.
6. A. M. Kulik, L. N. Kondrat'eva, and L. N. Lebedeva, in: Abstracts of Proceedings of the 3rd All-Union Congress of Pathophysiologists [in Russian], Moscow (1982), pp. 205-206.
7. A. M. Kulik, A. I. Bartyzel', and P. S. Aref'ev, Byull. Éksp. Biol. Med., No. 3, 19 (1982).
8. A. M. Kulik and L. N. Kondrat'eva, Byull. Éksp. Biol. Med., No. 10, 37 (1982).
9. M. E. Marshak, Regulation of Respiration in Man [in Russian], Moscow (1961).
10. N. V. Sanotskaya and D. D. Matsievskii, Byull. Éksp. Biol. Med., No. 12, 119 (1982).
11. D. S. Sarkisov, On the Effect of Disturbances of Brain Morphology and Function on the Course and Outcome of Experimental Pneumonia [in Russian], Leningrad (1956).
12. A. D. Speranskii, Lobar Pneumonias [in Russian], Moscow (1942).
13. Ts. V. Serbenyuk and P. S. Ippolitova, Nauch. Dokl. Vyssh. Shkoly, Biol. Nauki, No. 2, 38 (1965).
14. I. A. Tarakanov, "The protective action of gas and tissue hypercapnia on the organism in hypoxic hypoxia," Author's Abstract of Dissertation for the Degree of Candidate of Biological Sciences, Moscow (1984).
15. A. V. Tonkikh, Nervous and Humoral Factors in the Genesis of Pneumonias and Edema of the Lungs [in Russian], Moscow (1949).