The results indicate that toxic action on the vascular bed of the lungs causes redistribution of the blood flow into the pulmonary circulation. In a situation when the pulmonary vascular permeability is already disturbed, changes in the balance normally existing between the ejection volumes of the right and left ventricles may aggravate the degree of pulmonary edema.

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REGULATION OF RESPIRATION AND THE CIRCULATION IN MICROEMBOLISM OF PULMONARY VESSELS

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Microembolism has been discussed mainly by clinicians, who have studied this phenomenon at various levels — from clinical observations to bioclinical investigations [2, 4, 6]. Pulmonary embolism in clinical practice is manifested in several different forms, depending on the rate and intensity of its development. It has been shown that in response to microembolism of the pulmonary vessels, both the pulmonary and the systemic branches of the circulation are involved [9, 11-13]; in microembolism of the pulmonary vessels a threatening complication, namely pulmonary edema, develops.

The aim of this investigation was to compare the time course of the functional state of the respiratory center with the features of pulmonary macro- and microcirculation during microembolism of the pulmonary vessels, with the subsequent development of edema of the lungs.

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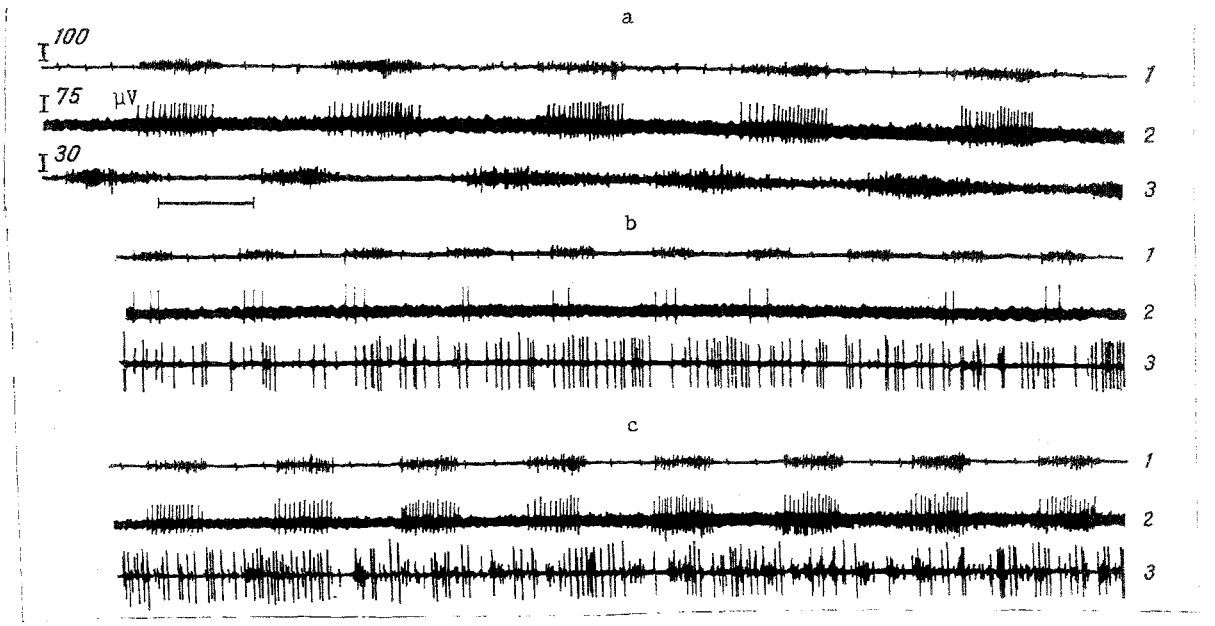

Fig. 1. Electrical activity of respiratory neurons and muscles after injection of olive oil. 1) Electromyogram (EMG) of diaphragm (calibration: 100 μV); 2) spike discharge or inspiratory neurons in dorsal respiratory nucleus (calibration: 75 μV); 3) EMG of obliquus abdominis muscle (calibration: 30 μV); time marker 1 sec. a) Initial state, b) 1 min, c) 5 min after injection of olive oil.

EXPERIMENTAL METHOD

Acute experiments were carried out on 40 male cats weighing 3-4 kg under pentobarbital anesthesia (40 mg/kg, intraperitoneally). Two models of microembolism of the pulmonary vessels were used: fat and mechanical. A model of fat microembolism of the pulmonary vessels was created by intravenous injection of olive oil (1.2 ml/kg) into the animals for 2 min. Mechanical microembolism was induced by intravenous injection of a 2.5% suspension of lycopodium spores (1 ml/kg body weight). Microelectrode and stereotaxic techniques were used [10], together with intravital microscopy of the capillary bed of the lungs [1, 3]. The linear and volume velocity of the blood flow in the artery and vein of the lower lobes of the lungs and the blood pressure in the pulmonary and systemic circulation [8] was studied by means of an ultrasonic method [7]. The severity of pulmonary edema in some animals was estimated quantitatively by determining the pulmonary coefficient (PC) and dry residue (DR) [5].

EXPERIMENTAL RESULTS

The experiments showed that PC for fat microembolism was 11.89 ± 1.98 (normally 5.5-6.0), whereas DR was 13.98 ± 0.41% (normally 18-20%). Analysis of the bursting discharge and spike activity of the respiratory neurons and of electromyographic activity of the respiratory muscles shows that their intensity during and immediately after injection of olive oil decreased. However, 2-3 min after the injection, neuronal and muscular activity intensified (Fig. 1). At the periphery this was manifested as quickening or respiration, which increased from 26-30 to 50-60 cycles/min. Quickening of breathing was accompanied by a decrease in its depth. As a result the respiratory minute volume remained virtually unchanged compared with the initial value, at about 600 ml. There is reason to suppose that rapid superficial breathing is an important adaptive reaction under these conditions. This is confirmed by the fact that in animals which died quickly from edema, this reaction was absent. Rapid and stronger breathing evidently leads to pulverization of large fat emboli into microemboli, which pass from the large pulmonary vessels into the capillary bed of the lungs (Fig. 2a). Simultaneously with a change in the character of respiration soon after injection of olive oil there was a distinct rise of pressure in the pulmonary artery by 2-2.5 times compared with its initial level. In the course of the experiment the pressure in the pulmonary artery gradually fell, but nevertheless it still remained persistently higher than initially. The resistivity of the pulmonary vessels remained high until death of the animal (Fig. 3a). There is reason to suppose that the apparent normalization of pressure in the pulmonary artery was the result of increasing weakness of activity of the right side of the heart. Immediately after the end of olive

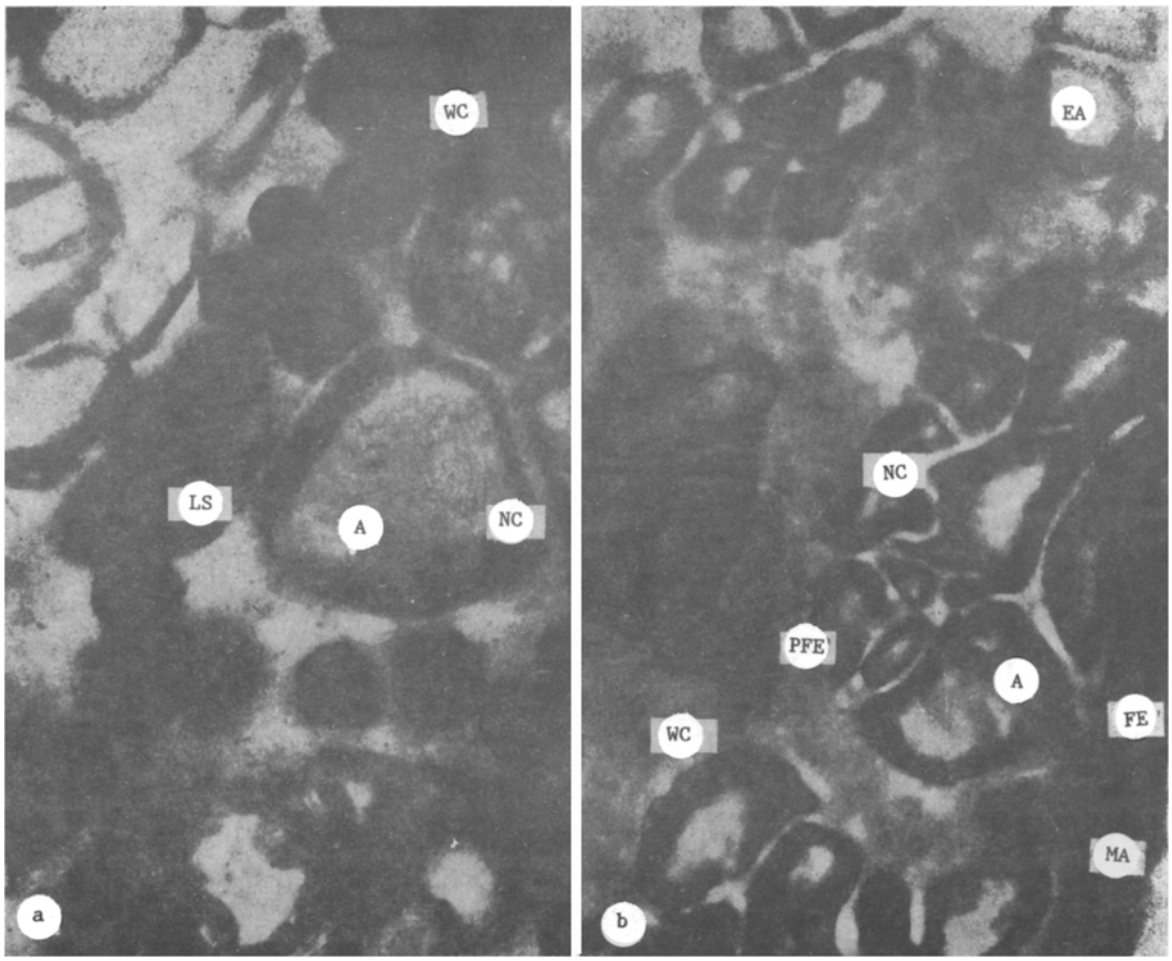

Fig. 2. Microembolism of pulmonary microvessels by lycopodium spores (a) and olive oil (b). a: A) Alveolus, LS) lycopodium spores, NC) narrow capillaries, WC) wide capillaries; b: FE) fat embolus, MA) microaggregate, PFE) particles of fat embolus, EA) edema of alveolus. Magnification: objective 20, ocular 4.

oil injection areas with uneven microcirculation began to appear in the lungs: bloodless capillaries alternated with regions of hyperemia. In hyperemic regions the diameter of the capillaries was increased, many blood cells accumulated in them, and they moved more slowly. In bloodless regions the capillary diameter was reduced. These changes in the blood flow in the capillaries led to a decrease in the outflow of blood along veins to the heart. This led to weakening of cardiac activity, lowering of the systemic blood pressure, and elevation of the pressure in the pulmonary circulation. Respiration was weakened and correlation disturbed between the pulmonary microcirculation and periods of cardiac contractions and phases of the respiratory cycle.

With an increase in frequency of the respiratory movements the blood pressure rose to 100-150 mm Hg. At the same time redistribution of the bloodless and hyperemic regions took place and they decreased in number and size. Extensive fat emboli, taking on the shape of the capillary, appeared in the wide capillaries. The blood flow, on reaching the embolus, instantly changed the direction of its movement and turned into the capillaries of neighboring alveoli. Where the blood collided with a fat embolus, hemoconcentration took place, with the formation of aggregates of blood cells (Fig. 2). The blood flow ceased in narrow capillaries. In these cases the wide capillaries perform the function of shunts. Fat emboli were propelled along the course of the blood flow, broke into fragments, and passed into pulmonary venules. In capillaries freed from microemboli the blood flow was restored, possibly due to normalization of pressure in the large pulmonary vessels of the pulmonary and systemic systems.

During mechanical microembolism PC was 9.56 ± 0.14, and DR was 17.20 ± 0.28%. After injection of a 2.5% suspension of lycopodium spores there was a sharp rise of pressure in the

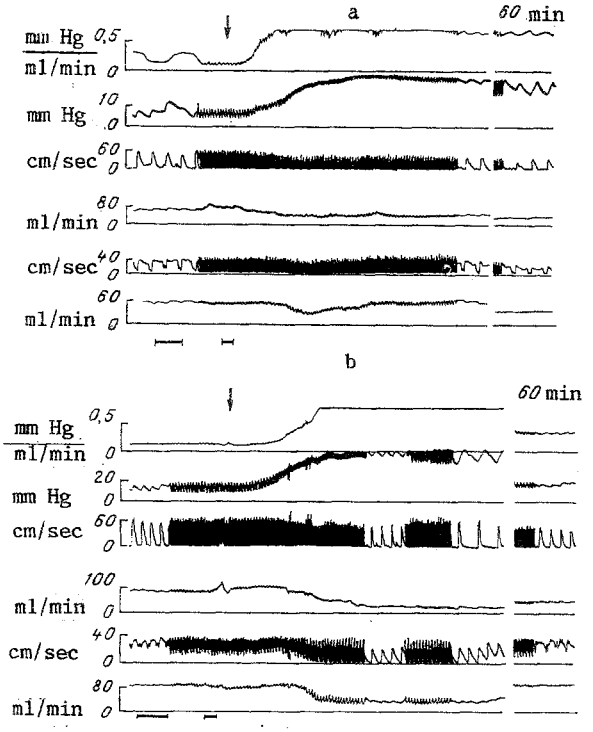

Fig. 3. Pulmonary hemodynamics in fat (a) and mechanical (b) microembolism. From top to bottom: resistance of vascular bed of the lungs, blood pressure in pulmonary artery, phasic blood flow in lower lobar branch of pulmonary artery, mean values of flow in lower lobar branch of pulmonary artery, phasic blood flow in lower lobar pulmonary vein, mean values of flow in lower lobar pulmonary vein. Time scale: 1 and 10 sec. Thin straight lines beneath each trace indicate zero levels; 60 min) time after beginning of embolism. Arrow indicates time of injection of olive oil (a) or lycopodium (b) into femoral vein.

pulmonary artery (by 2.5-3 times compared with initially). Meanwhile the pressure in the systemic circulation fell by 50-56%. In the period from the 2nd to the 5th minute after injection the blood flow in the artery and vein of the lower lobe was reduced (Fig. 3b). The more marked decrease in the blood flow along the pulmonary vein will be noted, reflecting a disturbance of drainage from the affected lobe of the lung. This was accompanied by the development of marked cardiac arrhythmia with slowing of the heart rate by 2-3 times. Characteristically at the 9th-10th minute restoration of the cardiac rhythm was accompanied by a simultaneous increase in the inflow of blood along the lobar branch of the pulmonary artery and in the outflow of blood along the vein. Meanwhile, throughout the experiment (60-90 min) the inflow of blood along the artery exceeded its outflow along the vein. Obstruction to the outflow of blood along the vein to the heart was evidently connected with exclusion of large areas of pulmonary capillaries from the circulation as a result of accumulation of lycopodium spores in them.

It is generally accepted that obstruction of the outflow of blood from the lungs is an important stage in the pathogenesis of development of pulmonary edema when embolism of the pulmonary vessels is present. Under these circumstances permeability of the air–blood barrier increases for blood plasma, protein, and so on. The resistance of the vascular bed of the lungs at the beginning of embolism was considerably increased, but later it fell during the remainder of the experiment, but it remained higher than initially right until the end. A remarkable fact was noted, indicating that death of the animals 1-1.5 h after injection of lycopodium spores most frequently occurred on account of respiratory arrest, the hemodynamic parameters remaining relative good. This may perhaps be connected with the fact that lycopodium spores do not completely occlude the capillary lumen. Part of the lumen was preserved between the spore and capillary wall, capable of transmitting a weak blood flow. Lycopodium spores did not penetrate into the narrow capillaries, but their number in the wide capillaries

increased rapidly. To begin with they formed a chain, but later they were arranged in rows (Fig. 2b). This led to the fact that many pulmonary capillaries were excluded from the microcirculation, and although the parameters of the blood flow were restored, severe hypoxemia developed. At this time, proximally to the embolus, blood plasma passed through into the lumen of the alveoli. Death of the animal took place from established hypoxemia and pulmonary edema. Thus fat and mechanical microembolism differ not only in the character, intensity, and rate of development of pulmonary edema, but also in their final result. Although in mechanical microembolism changes in the hemodynamic parameters are much more severe in character than in fat embolism, in the first case pulmonary edema develops less intensively.

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EFFECT OF ADAPTATION TO ANOXIA ON ANTIOXIDATIVE ENZYME ACTIVITY IN THE LIVER OF STRESSED ANIMALS

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Dyslipoproteinemia of atherogenic nature develops in the blood serum under the influence of emotional—painful stress (EPS), whereas preliminary adaptation of animals to periodic exposure to pressure chamber anoxia prevents disturbances of lipoprotein metabolism [7]. Despite the fact that activation of lipid peroxidation (LPO) in the liver does not change the rate of lipoprotein secretion by hepatocytes [9], an important role for intensification of LPO in the mechanism of stress-induced liver damage seems likely, for damage of this kind can be prevented by gradual adaptation to moderate degrees of anoxia [3, 4].

To test this hypothesis the effect of EPS and of preliminary adaptation to anoxia on the malonic dialdehyde (MDA) concentration and activity of antioxidative enzymes, utilizing active forms of oxygen (superoxide dismutase) and of lipoperoxidases (glutathione peroxidase, glutathione-S-transferase) was studied in the liver of animals.

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