These investigations thus demonstrated that HBO is an effective method of treatment of ischemic injuries in a graft of small intestine intended for esophagoplasty.

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# ANTIATELECTATIC FUNCTION OF LUNG SURFACTANT

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The results of numerous investigations show that certain pulmonary complications are connected with a disturbance of the surface activity of the surfactant [1]. In particular, replacement of surfactant  $in\ vivo$  by a component with less surface activity leads to atelectasis of the lung [5]. However, there are as yet no sufficiently reliable and informative criteria with which to determine relationships of cause and effect between the properties of the surfactant and the pathological state of the lung. Moreover, results throwing doubt on the role of surfactant in themaintenance of normal alveolar structure have been published [4]. Accordingly theoretical studies of the properties of the surfactant and its role in lung function are particularly important.

The writers previously suggested a mathematical model of the surface activity of surfactants. They showed that the basic properties of surfactant (change in surface tension, relaxation hysteresis) can be well described by a system of differential equations:

$$\begin{cases} \frac{d\sigma}{dt} = f(\sigma) \frac{1}{S} \frac{dS}{dt} + (\sigma_0 - \sigma) \frac{1}{\tau} \\ \frac{d\sigma_0}{dt} = \varkappa (\sigma - \sigma_0) + \eta (\sigma_1 - \sigma_0), \end{cases}$$

where  $\sigma$  is the surface tension;  $f(\sigma)$  a function of the state of the surfactant; S the surface area;  $\tau$ ,  $\kappa$ ,  $\eta$ ,  $\sigma_1$  are constants.

The critical condition for normal surface activity of the surfactant  $f(\sigma) > \sigma/2$  was calculated for use with the model. When this condition is disturbed, an alveolus of spherical shape will be unstable and will quickly collapse, and this could cause atelectasis of the lung.

KEY WORDS: lung surfactant; surface activity; atelectasis of the lung.

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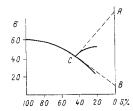


Fig. 1. Graphic determination of function of state of surfactant. Length of segment AB gives numerical value of  $f(\sigma)$  for  $\sigma$  = 40 dynes/cm.

The object of the present investigation was to assess the possibility of predicting atelectasis of the lungs from the value of the surface activity of lung surfactant.

#### EXPERIMENTAL METHOD

Rats weighing 130-150 g were used. The surface activity of surfactant of the animals of the principal group was modified by halothane anesthesia [3]. For this purpose the rats were placed in a chamber through which oxygen with 2 vol. % halothane was passed for 4-6 h. Intact animals kept under normal animal house conditions served as the control. Surfactant was obtained by washing out the lungs. The animals were autopsied (the controls under phentobarbital anesthesia) and the heart—lung complex was removed. A ligature was applied to the upper right lobe of the lung, which was subsequently fixed with 10% formalin and used for histological study. The remainder of the lung was washed out through the bronchii seven times to obtain surfactant.

The surface activity of the surfactant was determined in a modified Wilhelmy's apparatus [2]. A new feature in this measurement was that values of a function of the state of the surfactant  $f(\sigma)$  were obtained. For this purpose, when the area of the test monolayer was measured, not only were traditional hysteresis loops recorded, but a graph of surface tension as a function of time also was plotted. When a definite surface tension (for example,  $\sigma = 40$  dynes/cm) was reached during compression of the test monolayer, the moving barrier was stopped. In that case, an inflection due to relaxation of surface tension was observed on the graph of surface tension as a function of time (Fig. 1). Tangents were drawn to the segments of the curve on the right and left sides of the inflection. These tangents were continued to intersect the vertical line drawn through a point corresponding to the completely compressed monolayer, i.e., to an area of 0%. The length of the segment contained between the two tangents, on the scale used to measure surface tension, gives the value of  $f(\sigma)$ . Measurement of  $f(\sigma)$  in this manner was carried out within the range of  $\sigma$  from 30 to 60 dynes/cm at intervals of 5 dynes/cm.

In each concrete case the state of surface activity of the surfactant was compared with the results of microscopic analysis — the presence and severity of atelectatic changes in the lungs.

# EXPERIMENTAL RESULTS

In five of the seven microscopically investigated structures of the lung parenchyma of control rats no pathological changes were found: The lumen of the alveoli was well expanded. The surface activity of the surfactant of these animals was sufficient to ensure alveolar stability. An example of the lung parenchyma and function of the state of the surfactant of a control animal is given in Fig. 2A. The function of the state of the surfactant did not enter the zone of instability, i.e., over the whole range of surface tension the inequality  $f(\sigma) > \delta/2$  was satisfied. In two control animals diffuse dysatelectasis was found in the central sections of the upper lobe of the lungs. The function of the state of these animals was in a critical position, as shown by Fig. 2B which illustrates the case of one of the animals.

Normal surface activity of the surfactant, determined in agreement with the critical condition thus actually agreed with the normal structure of the lung.

Microscopic investigation of the tissue of the upper lobe of the lung in all rats of the main group (12 animals) revealed areas of dysatelectasis and atelectasis. They occupied from 0.1 to 0.5 of the area of section of the lobe. Surface activity of the surfactant of these animals was depressed to different degrees. The results of an investigation of an animal of the main group are shown in Fig. 2C as an example. The function of the state of the

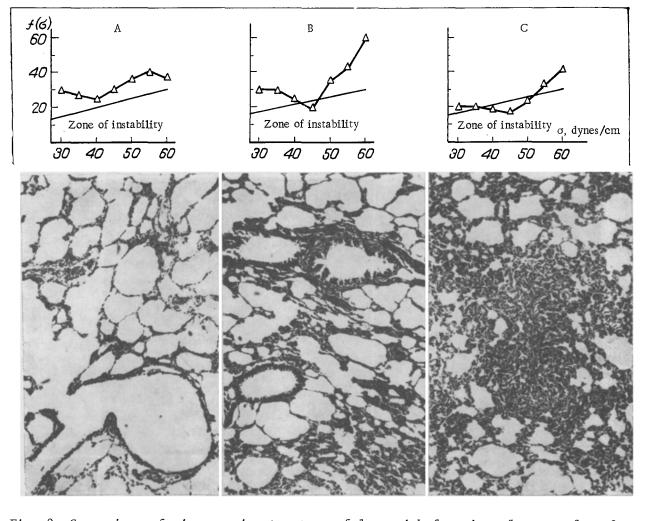


Fig. 2. Comparison of microscopic structure of lung with function of state of surfactant. A) Lung parenchyma of intact rat with homogeneous structure and well-expanded alveoli (photomicrograph); surface activity of surfactant ensures alveolar stability (graph). B) Lung parenchyma of intact rat with diffuse dysatelectasis (photomicrograph); critical position of function of state of surfactant (graph). C) Lung parenchyma of rat after general anesthesia with halothane for 4 h. Extensive atelectasis in center of upper lobe of right lung (photomicrograph); surface activity of surfactant does not ensure alveolar stability (graph). Lung parenchyma stained with hematoxy-lin and eosin;  $140 \times$ .

surfactant of this rat entered the zone of instability, infringing the critical condition. Extensive dysatelectasis was found in the lung parenchyma of the upper lobe. As this example shows, disturbance of the surface activity of the surfactant in accordance with the critical condition is accompanied by the development of dysatelectatic changes in the lung.

Correlation analysis of the results was carried out to assess the informativeness of the suggested method for the study of surfactants. The coefficient of correlation between the microscopic state of the lung and the state of surface activity of the surfactant, determined according to the critical condition, was 0.88. This corresponded to correct prediction of atelectasis in 18 or 19 cases. Meanwhile the use of the traditional index of surface activity of surfactants (minimal surface tension) enabled the state of the lung to be correctly predicted in only 11 of 19 cases, corresponding to a coefficient of correlation of 0.41.

The suggested method of assessment of the properties of a surfactant in accordance with the critical condition for normal surface activity is thus sufficiently informative and reliable.

When conditions of alveolar stability were determined, allowance was made for the force of surface tension but not for the force of tissue elasticity. It can accordingly be con-

cluded that the trigger mechanism for the development of pulmonary atelectasis is disturbance of the surface activity of the surfactant.

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BIOLOGICALLY ACTIVE SUBSTANCES OF LUNG TISSUE IN RABBITS WITH BRONCHOPULMONARY INFLAMMATION

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In recent years the lungs have come to be regarded not only as a respiratory, but also as a metabolic organ. One of the most important manifestations of nonrespiratory function of the lungs is their metabolic function in relation to certain biologically active substances (BAS), with marked vasomotor activity. The question of the physiological role of the lungs in the metabolism of BAS has been widely discussed in the literature [1, 2, 10, 11], but there is an almost total absence of data on BAS metabolism in the lungs under pathological conditions. Investigations of this sort could help to shed light on certain stages of the pathogenesis of lung lesions.

The object of this investigation was to study BAS in blood flowing into and out of the lungs, and also in the lung tissue itself during experimental acute and chronic nonspecific bronchopulmonary inflammation.

## EXPERIMENTAL METHOD

Experiments were carried out on 68 rabbits of both sexes weighing 2.5 kg, of which 34 were intact. In the other 34 animals chronic inflammation was produced in the lungs by a modified method [3]. A length of Kapron thread, 0.5 mm thick and 7-10 cm long, with a metal bob attached to its end, was introduced by operation into the trachea. The anterior end of the thread was fixed to the anterior wall of the trachea, and its posterior end remained free and reached one of the lobar bronchi or (more frequently) became impacted in one of the small bronchial branches. Biochemical tests were carried out between 1 and 5 months after introduction of the Kapron thread into the trachea. Blood flowing into the lungs was obtained by catheterization of the right atrium under hexobarbital anesthesia (35 mg/kg body weight) and blood flowing from the lungs was obtained by catheterization of the left ventricle. After removal from the thorax the lungs were studied in detail macroscopically. Pieces of lobe of the "affected" lung from some of the rabbits were investigated histologically. To study BAS in lung tissue the bronchi and great vessels were separated on ice and shredded pieces of parenchyma were immersed in liquid nitrogen and homogenized to a fine powder. Adrenalin, noradrenalin, and dopa [6], acetylcholine [8], histamine [7], and serotonin [4] were determined in the tissue homogenate. The same determinations were repeated during blood tests. The total catecholamine concentration in the blood was estimated from the level of adrenalinlike substances (ALS) [5]. The content of BAS in the tissues was expressed in  $\mu g/g$  wet weight of tissues and the concentration of BAS in the blood in  $\mu g/ml$ .

KEY WORDS: bronchopulmonary inflammation; content of biologically active substances.

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