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**FUNCTIONAL MORPHOLOGY OF LUNG TISSUE CELLS IN
EXPERIMENTAL PNEUMONIA**

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ABSTRACT

Introduction. Extramural pneumonia - is one of the most common infectious and inflammatory diseases in the world. The main etiological cause of extramural pneumonia in both children and adults is the bacteria *Streptococcus pneumoniae*. Staphylococcal pneumonia is observed in patients older than 60 years, contributes to the exacerbation of chronic diseases, often becomes the causative agent of nosocomial pneumonia. *Klebsiella pneumoniae* is

considered the most common cause of severe nosocomial pneumonia, causing the disease in most cases in patients suffering from alcoholism, diabetes and immunodeficiencies.

Objective. To study of functional morphology of lung tissue cells in experimental pneumonia.

Material and methods. Used white outbred rats of the Wistar line. Experimental inflammation was caused by introducing into the tracheal cavity a bacterial suspension containing cultures of virulent strains of pneumococcus, Staphylococcus and Klebsiella against the background of cold factor. General morphological and electron microscopic studies of lung tissue were carried out on 5, 10, 15, 21, 30, 60 and 90 days of the experiment.

Research result. The effect of virulent cultures of staphylococcus, streptococcus and Klebsiella against the background of hypothermia causes the formation of an active inflammatory process in the lungs with subsequent transition to a subacute and protracted form. In our case, the transition of the acute stage (5-10 days) to subacute (or prolonged) fluctuated between 15 and 21 days of the experiment. The following lines were dominated by atrophic and sclerotic changes in lung tissue. Violations of the epithelial stromal relationships in the lung tissue cause destructive, atrophic and sclerotic processes.

Conclusion. Under the influence of virulent strains of pneumotropic bacteria in the lung tissue, the processes of inflammation, destruction with extensive destruction of both the epithelial cover and the interstitium, as well as the processes of pneumosclerosis prevail. Disproportion between epithelial and immunocompetent cells leads to a decrease in the functional state of alveolar epithelial cells.

Keywords: leukocyte, lymphocyte, macrophage, alveolocytes, endothelial cell, bronchi, alveolus, perivascular and peribronchial tissue, lungs.

INTRODUCTION

Bronchopulmonary pathology occupies a leading place in the structure of morbidity, first place as the cause of morbidity with temporary disability and 3-4th place as the cause of disability and mortality of the population of the whole world, and is a complex and relevant public health problem both in industrialized and developing countries [1].

Extramural pneumonia is one of the most common infectious and inflammatory diseases worldwide [2,3]. In older age groups, the frequency and mortality due to pneumonia increase significantly [4] and remains one of the most common diseases in young children [5]. In Europe and North America, the incidence of pneumonia in children under 5 years of age is 34–40 cases per 1000 children. Annually, on an outpatient basis, from 16.9 to 22.4 cases of community-acquired pneumonia are recorded per 1000 children, at the age of 1–5 years, the highest incidence of community-acquired pneumonia is recorded (32.3–49.6 cases

per 1000 people) [6]. For several decades, pneumonia has been the leading cause of death in young children in the world [7].

The spectrum of leading microbial pathogens is mainly represented by *Streptococcus pneumoniae*, *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Mycoplasma pneumonia* and *Legionella pneumophila* [8]. *Streptococcus pneumoniae* bacteria are the main etiological cause of the development of extramural pneumonia in both children and adults [9]. In the United States, more than 500,000 cases of pneumococcal pneumonia are reported annually [10]. Pneumococcal infection remains an urgent public health problem due to the high morbidity and mortality rates among children of the first years of life, the elderly and people with chronic diseases [11]. The main factors of pathogenicity of pneumococcus are the capsule and substance C (teichoic acid of the cell wall containing choline) [12], which, interacting with the C-reactive protein, leads to the activation of a complementary cascade and the release of mediators of the acute phase of inflammation with subsequent migration of the polymorphic nuclear phagocytes [13].

Staphylococcal pneumonia is observed in patients older than 60 years, contributes to the exacerbation of chronic diseases [14]. *Staphylococcus aureus* more often becomes the causative agent of nosocomial pneumonia (20–50%) [15]. Necrotizing pneumonia characterized by high mortality due to the development of hemorrhagic necrosis and extensive destruction of the lungs, occurs mainly in healthy children and young people as a result of the production of Pantone – Vilecain leukocidin by *S. aureus* strains [16]. Lethal cases of pneumonia during an influenza epidemic are associated with *S. aureus*, for example, the cause of most deaths in an influenza pandemic in 1918-1919. and in 1957-1958. Superinfection of *S. aureus* has become precisely. At the same time, bronchopneumonia with extensive lung infiltration developed during radiography, leukopenia, hemoptysis and a large number of cocci in sputum.

Klebsiella pneumoniae is considered the most common cause of severe nosocomial pneumonia, causing the disease in most cases in patients with

alcoholism, diabetes mellitus and immunodeficiency. The relevance of *K. pneumoniae* sharply increases in a hospital setting; in general, the proportion of Klebsiella in the structure of all causative agents of nosocomial pneumonia is 11.8% [17]. The frequency of pathogens in the Russian Federation exceeds 58% [18]. In experimental studies, endotracheal administration of *K. pneumoniae* caused massive inflammation, accompanied by severe edema, and the significance of chronic alcoholism, obesity, diabetes mellitus, and viral infection in the development of Friedlander pneumonia was established.

Pseudomonas aeruginosa is the main causative agent of nosocomial infections and was found in 9 (18%) of 41 patients with pneumonia. It is characterized by natural resistance to most antimicrobial agents - ceftazidime, cefepime, piperacillin, aztreoname and gentamicin [19].

Decrease or damage to the protective (non-specific and specific) mechanisms of the macroorganism, the massive dose of microorganisms and / or their increased virulence leads to the development of an inflammatory reaction. Therefore, the pathogenesis of pneumonia is mainly associated with the composition of the microflora of the respiratory tract, the impact of the external environment, the age of the patient and the general condition of the macroorganism [20].

Thus, the picture of inflammatory diseases of the bronchi and lungs largely depends on the features of the action of the causally significant agent and the structural and functional features of the broncho-pulmonary system involved in the pathological process.

Purpose of research: to study the functional morphology of lung tissue cells in experimentally induced inflammation of bacterial origin.

MATERIALS AND METHODS

White outbred Wistar rats of both sexes weighing 170-200 g from the laboratory animal nursery of the Tashkent Medical Academy were used in the experiments in accordance with the 1977 «Rules for Working with Experimental Animals». The experimental animals were kept under normal vivarium conditions.

The study was conducted on 150 animals. Experimental inflammation was caused by introducing into the tracheal cavity a bacterial suspension containing in 1 ml of a 2×10^6 daily culture of virulent strains of *St. pneumoniae*, *St. aureus* and *Klebsiella pneumoniae*. For this, a bacterial suspension was prepared from standard dilutions containing 1 ml of 2×10^6 streptococcus, staphylococcus and Klebsiella bacteria, which was injected into the tracheal cavity under light ether anesthesia at the time of inhalation. Before the introduction of virulent bacterial strains of bacteria into the respiratory tract, all animals were preliminarily kept for 4 hours in a cold chamber at a temperature of -10°C . The cultures of virulent bacteria staphylococcus, streptococcus and Klebsiella used in the work were selected from museum strains of the Department of Microbiology, Virology and Immunology of the Tashkent Medical Academy (Professor I.M. Mukhamedov).

A general morphological study of lung tissue was performed at 5, 10, 15, 21, 30, 60, and 90 days after infection. Animals were slaughtered under mild ether anesthesia by opening the abdominal cavity and cutting the abdominal aorta. At 3, 5, 15 and 30 days, 1 g of lung tissue was taken, homogenized and 5% blood agar was plated to determine the microbial number in the lung.

Histological changes in the lungs were studied on sections stained with hematoxylin and eosin according to van Gieson. For electron microscopic examination, lung pieces were fixed in a 2.5% solution of glutaraldehyde in phosphate buffer, followed by additional fixation in a 1% solution of osmium tetroxide. After conventional processing, the material was poured into epon-araldite. Ultrathin sections were obtained on an LKB-4800 ultra-microtome, contrasted with uranyl acetate and lead nitrate and examined under a JEM-100S electron microscope.

RESULTS

On the 5th day after the intratracheal administration of virulent strains of *Staphylococcus aureus*, streptococcus and *Klebsiella*, a pool of neutrophils and leukocytes is determined in the lumen of small vessels. There is a sharp expansion and blood vessels filling. Perivascular, mainly in the area of the inflammatory

focus, marked swelling and accumulation of cells. The nuclei of the vascular endothelial cells are large, protrude into the lumen.

The lumen of the bronchial tubes of small and medium caliber contains mucous secretions, desquamated epithelial cells and white blood cells. The epithelium of the bronchi and bronchioles has a corrugated structure, in some places it is represented by low-cylindrical epithelium, areas of damage to the cilia of epithelial cells are noted in large bronchi. The epithelial layer of the bronchi contains a large number of hyperplastic goblet and secretory cells. In the own plate of the bronchial mucosa, pronounced edema and numerous diffusely scattered lymphoid cells are observed. In some areas, accumulations of lymphoid cells reach the submucosa (Fig. 1). The wall of the bronchi and bronchioles is swollen and infiltrated by lymphocytes, neutrophils and macrophages.

On electron microscopic patterns, the apical surface of the secretory cells of the bronchial mucosa is enlightened, the cytoplasm is poor in organelles, some ciliated cells lack cilia, and in other cilia are replaced by microvilli. In the supranuclear zone, as well as on the apical surface of secreting cells, numerous secretory granules are determined. Between epithelial cells macrophages, plasma cells and T-lymphocytes are visible. The process of their cooperation indicates antigenic stimulation of lymphocytes. In plasma cells, an expansion of the tubules of the granular endoplasmic reticulum is noted. Own plate of the bronchial mucosa contains macrophages and lymphocytes. In the peribronchial lymph nodes, there are many mitotically dividing lymphoblasts and poorly differentiated as well as proliferating cells.

The respiratory department of the lungs is characterized by microcirculatory disorders. In the interalveolar septa, dilated capillaries swell into the lumen of the alveoli, their lumen contains basophilic leukocytes, neutrophils and lymphocytes. Alveolar septa are strongly swollen and hypertrophied. An increased transition of transcapillary fluid into the interstitium and into the lumen of the alveoli due to microcirculatory disorders and disturbances in the structure of the basement membrane of the endothelial cells of the airborne barrier is noted. In areas of

collapsed alveoli in their cavity, alveolar macrophages, single lymphocytes and desquamated alveolocytes of type II are found, which are in different functional states: active type II alveolocytes secreting surfactant and cells in which osmiophil-laminated bodies are emptied.

Thus, on the 5th day after exposure to virulent strains of pneumotropic bacteria against the background of the cold factor, microcirculatory disorders develop, expansion and plethora of capillaries of the alveolar septa and peribronchial tissue, exudation and edema of the connective tissue stroma. In the bronchial epithelium, the number of goblet and serous-mucous cells increases, cilia of ciliary cells are damaged, which leads to exposure of the epithelial layer. In the own plate of the bronchial mucosa, lymphoid infiltration is noted. The detected cooperation of macrophage and lymphocyte indicates an increase in the local immune response. In the peribronchial lymph nodes and broncho-associated lymphoid tissue, activation and transformation of B-lymphocytes is noted.

By the 10-day period of the experimental inflammatory process, the microvasculature was characterized by plethora, strong perivascular edema, the release of blood cells into the interstitial tissue, and the appearance of mast cells at the vessel walls. In the lumens of the bronchi, desquamated epithelial cells, mucous secretions and pus, polymorphonuclear leukocytes are found. The epithelial cover contains hypertrophied epithelial cells, as well as active macrophages and neutrophils, lymphocytes and plasma cells. In the own plate of the bronchial mucosa, mainly around the foci of destruction and microabsceding, functionally active fibroblasts appear. On the periphery of inflammatory foci, there is a seal of the connective tissue basis. In the lymphoid follicles of the submucosal basis there are a lot of blast, mitotically dividing cells. Peribronchial – a large number of lymphoid follicles and lymphoid clusters, the presence of plasma cells.

Electron microscopically, the cytoplasm of secretory cells is poor in organelles, there is a picture of increased secretion by clasmotosis and microapocrine secretion. Some ciliated cells lack cilia. In the own plate of the bronchial mucosa, cooperation of macrophages with polymorphonuclear

leukocytes and lymphocytes is more often detected. In peribronchially located lymphatic follicles, mitotic dividing lymphoblasts are noted, along the periphery of which there are poorly differentiated and proliferating cells. In peribronchial tissue, lymph vessels are moderately dilated.

In the respiratory part of the lung tissue marked areas of atelectasis and distelectasis, around which-lymphocytic infiltrates with centers of reproduction, containing both young and Mature forms of lymphocytes. Vessels of dilated and infiltrated interalveolar septa are full-blooded (Fig. 2). In the blood capillaries, violations of the structure of the basal membranes and endothelial cells are detected, the latter are sharply swollen, the gaps between them are expanded, and some areas of the aerogematic barrier do not contain endothelial cells at all. Strongly expressed perivascular and peribronchial edema. The alveoli are filled with fluid, desquamated epithelial cells, macrophages, lymphocytes.

Electron microscopically on the apical surface of alveolocytes II-type visualized a lot of cytoplasmic outgrowths and microvilli in the cytoplasm of mitochondria, endoplasmic reticulum, Golgi complex, different severity osmophilic lamellar bodies. These data indicate the activity of type II cells. But along with this, there are also low-activity alveolocytes of type II, which were characterized by a small number of mitochondria and osmiophilic lamellar bodies in the cytoplasm, most of which were devastated. The cytoplasm of alveolar macrophages contains a large number of electron-dense inclusions, phagolysosomes. The nucleus is large with invaginations, the cell surface is uneven. There are macrophages in the division stage.

Thus, on the 10th day of experimental inflammation, morphological changes in the bronchi were characterized by serous-purulent effusion, damage to the walls of small bronchi by the inflammatory process, proliferation of goblet cells and small foci of peribronchial inflammatory processes with microabsorption patterns. The picture of acute catarrhal purulent bronchitis and focal pneumonia developed. Quantitative and qualitative changes of type II alveolocytes are noted.

On the 15th day of simulation of the experimental inflammatory process, the lumen of the bronchi and bronchioles is crowded with Muco-purulent secret, desquamated epithelial cells, neutrophils, leukocytes. Epithelial cells of the bronchial mucosa are swollen, enlarged in volume, with a light cytoplasm. Goblet and secretory cells are hypertrophied. The own plate of the bronchial mucosa is infiltrated by macrophages, lymphocytes, eosinophils. Plasma cells and fibroblasts are also detected here. Peribronchial tissue is strongly edematous, contains large lymphoid follicles with a center of reproduction, in the peripheral zones of which there are active, large cells. The loose connective tissue between the follicle and lung tissue is infiltrated by lymphocytes.

Electron microscopically, the epithelial layer of the bronchi is characterized by a large number of serous-mucous and goblet cells, the apical part of the cytoplasm which contains many secretory granules, actively released into the lumen of the bronchi. In ciliated cells, localized in the foci of inflammation and near it completely absent cilia, if there were, they were disoriented. The cytoplasm of these cells contain destructively altered mitochondria and vacuolated endoplasmic network. Diffusely scattered lymphoid cells, macrophages, as well as a large number of lymphoid follicles, which occupied an extensive area, are visible in the own plate of the bronchial mucosa. Lymphoid follicles contain many blast, dividing cells, around which are localized poorly differentiated, differentiating and proliferating cells. Peribronchial lymphoid follicles have a hermetic center, with the presence of many sinuses filled with lymphocytes. Borders follicles clear, within and on the edges of the differ lymphatic capillaries. The cytoplasm of macrophages has a large number of phagosomes and phagolysosomes (Fig. 3). In the own plate of the bronchial mucosa among lymphocytes and macrophages are plasma cells with different functional States (Fig. 4). And their number is significantly increased.

In foci with an active inflammatory process, the interalveolar septa are thickened, the small vessels located here are expanded, full-blooded. The lumen of the expanded venules contains a large number of leukocytes and neutrophils, in

some vessels these cells are concentrated mainly parietally, forming a pool of polymorphonuclear leukocytes. The muscular sheath of the vessels is thickened, and the adventitial connective tissue fibers are loose. Perivascular tissue is highly edematous, often revealed perivascular lymphoid infiltration. The endothelial cells of these vessels are swollen, protrudes into the lumen, which is why the lumen of the capillaries is sharply narrowed in places. The nucleus of the endothelial cell is oval with evenly distributed chromatin. The perinuclear zone contains mitochondria, a poorly developed Golgi complex, single tubules of the endoplasmic network, as well as free ribosomes and polysomes. The basal membrane of endothelial cells is well contoured, although in places it looks swollen.

Pulmonary tissue is characterized by foci of half-asleep and sleeping alveoli, around which there are areas of hypertrophied and normal alveoli. The lumen of the first two alveoli contain serous fluid, exfoliated and destructively altered type II alveolocytes, alveolar macrophages and lymphocytes in different functional states. Red blood cells are found in the lumen of the alveoli. In the cavity of the half-asleep alveoli, purulent contents with a large number of polymorphonuclear leukocytes and clusters of neutrophils are revealed. In the interstitial tissue of expanded interalveolar septa, neutrophils, lymphocytes are noted, which are present in large numbers near inflammatory foci, perivascular and peribronchial zones.

In the perinuclear cytoplasm of most alveolar I-type epithelial cells located in the half-asleep and sleeping alveoli, there are swollen mitochondria with disorganized crystals, their nuclei with an uneven membrane. The tubules of the smooth endoplasmic reticulum are poorly developed and expanded. Nuclei of alveolar epithelial cells II-type spherical shape, in the cytoplasm – numerous edematous mitochondria, with disoriented crystals, tubules granular endoplasmic reticulum expanded. Osmiophilic-lamellar corpuscles in cells of type II round or oval, contain lamellar material of high electron density, their location and degree of osmiophilicity are variable. Some alveolocytes of type II contain a small number

of osmiophilic-lamellar bodies, and in others-osmiophilic-lamellar bodies are not detected. In the cytoplasm of alveolar macrophages differ nuclei with scalloped edges and nucleolus, organelles are well developed, a large number of polymorphic lysosomes and phagosomes.

Thus, this period of experimental inflammation of bacterial Genesis is characterized by microcirculatory disorders, expansion and fullness of capillaries, both peribronchial zones and interalveolar partitions, as well as expansion of lymphatic vessels. In the foci of active inflammatory process, there is the development and strengthening of edema of interstitial, perivascular and peribronchial tissue. In the course of the bronchi, a large number of lymphatic follicles are formed and massive lymphoid-plasmacytic infiltrations appear. The activity of newly formed lymphatic follicles is evidenced by the presence of hermetic centers and lymphoid sinuses filled with lymphocytes. Lymphoid-plasmacytic infiltration in this period is mainly due to plasma cells. Mirabiliandia the presence of lymphocytes in the mucosa of the bronchial tree, which are mostly T-lymphocytes, should be considered a manifestation of cellular immune response to numerous antigens in the bronchial lumen and absorbed through the mucosa. A thorough immunological armament of the bronchial tree mucosa is provided by a more pronounced infiltration of its own plate by lymphocytes, plasma cells and macrophages.

On the 21st day of experimental pneumonia prevailed mainly the picture of perivascular, peribronchial lymphohistocytic infiltration, thickening of the walls and swelling around the vessels, sharp blood filling, as well as vascular spasm (Fig. 5). Perivascular tissue is highly edematous, connective tissue is compacted in places and contains single fibroblasts and fibrocytes.

Muco-purulent secret fills not only the small bronchi, but also the bronchi of medium caliber. There are areas of exfoliation of epithelial cells at large distances. Epithelial cells are heterogeneous in density and color, between the ciliated and accessory cells are a lot of goblet cells, which strenuously produce a secret. Severe swelling of the submucosal layer. The own plate of the bronchial mucosa is

infiltrated by lymphocytes, fibroblasts and macrophages. There are also elastic fibers. In the areas of the own plate of the bronchial mucosa, where the lymphatic follicle is located, the surface of the epithelial layer is smoothed, strongly protrudes into the lumen of the bronchus, and the basal membrane is intermittent. There are foci of microabsceding, sclerosis, hemorrhage and pronounced lymph-leukemia-histiocytic infiltration, both in the bronchial wall and in the peribronchial zones.

A variety of ciliated cells with an enlightened cytoplasm and fragmentation of cilia are determined electron-microscopically. In some areas, all stages of extrusion of epithelial cells are observed. The epithelial lining of the bronchi is infiltrated by interepithelial lymphocytes. Functionally active eosinophils, mast cells, macrophages, fibroblasts and plasma cells appear in the lamina propria mucosa. In plasma cells, signs of an active functional state. In the peribronchial tissue, lymphatic vessels are determined, their lumen is dilated.

In the respiratory part of the lung tissue, foci of atelectasis, distelectasis, and alveolar hypertrophy are observed in large numbers. Hypertrophy of the alveoli is more signified in the subpleural parts and around the foci of atelectasis. In the foci of distelectasis, there is a lymphocytic infiltration, expansion of capillaries, diapedesis of blood cells, in the foci of hypertrophy are the areas of destruction and thinning of the interalveolar septa. Around necrotic altered foci, and areas of abscess formation, signified lympho-leuko-histiocytic infiltration with hemorrhage, on the periphery of which severe edema is noted.

Electron-microscopically in the lumen of the bronchi and alveoli, particles of destroyed macrophages and type II alveolocytes, in addition, erythrocytes, leukocytes, which had the appearance of active and collapsing cells, are visible. In some places, the lumen of the alveoli is completely filled with desquamated cells. Type II alveolocytes are found with destructive phenomena in the cytoplasm. The number of osmiophil-plate bodies is reduced in them. The cytoplasm of alveolar epithelial cells of type I is more enlightened, the mitochondria in them are swollen, and the profiles of the smooth endoplasmic reticulum are expanded. The peripheral parts of these cells in some places protrude towards the lumen of the

alveoli. Part of the I-type alveolocytes in a state of destruction. Endothelial cells with swelling. As a result of swelling of the endothelial cell, the lumens of some vessels are narrowed and stasis is determined in them. The basement membrane is swollen in places. The airway barrier in the area of dilated and full-blooded capillaries is thickened.

Thus, this period of experimental inflammation was characterized by a picture of purulent panbronchitis, as well as focal purulent pneumonia. In the lumen of the bronchi, accumulations of mucopurulent masses are noted, the wall of the bronchi and peribronchial tissue are infiltrated by a large number of neutrophils and lymphoid-macrophage elements. Among the accumulations of cells are fibroblasts. The interalveolar walls are also infiltrated, in some areas there is a picture of the development of fibrosis, in the cavity of the alveoli, serous-purulent-fibrinous exudate mixed with desquamated epithelial cells, macrophages. The inflammatory process with a pronounced perivascular and peribronchial lymphocytic reaction, as well as atelectasis, hypertrophy and the appearance of sclerotic changes predominate.

On the 30th day of the experiment, huge sections of the destruction and hemorrhage of the lung tissue, a sharp expansion and blood filling of the vessels are microscopically revealed. A large number of atelectasis sites along the periphery of which hypertrophied alveoli are visible. Along the bronchi, there is a pronounced lymphocytic and macrophage reaction, and a picture of purulent-catarhal bronchitis. A marked depletion of B-dependent zones in the tissue of the lymph nodes is noted. There are plots of multiple bronchiectasis with purulent contents and foci of abscesses with perifocal inflammation of the lung tissue. In the abscess zone there is a large number of collagen fibers.

In the epithelium of the mucous membrane of the bronchi, cells with destructively modified cilia are found. Epithelial cells are located in one row, their apical part is enlightened and contains light granules. The number of goblet cells is increased, which also contain a large number of granules of secretion. The basement membrane is thickened and contains a large number of collagen fibers.

In the own plate of the bronchial mucosa, there is a focal increase in the number of connective tissue fibers, between which macrophages, mast cells and fibrocytes are visible. There are areas with lymphoid infiltration, consisting of lymphocytes, monocytes, plasma cells. The own plate of the bronchial mucosa is thickened due to infiltration and the appearance of collagen fibers on the background of swelling. The muscular membrane of the bronchi is hypertrophied, the connective tissue of the bronchi is edematous. Peribronchial diffuse and focal perivascular lymphoid infiltration is noted.

In the respiratory department of the lung tissue, the alveoli and alveolar sacs are dormant, around such altered areas, hypertrophied and half-asleep alveoli are visible. On the atelectated and distelected areas of the lung, the lumen of the alveoli is filled with exfoliated destructively altered epithelial cells, macrophages. Inter-alveolar partitions contain expanded and blood-filled capillaries and venules, in the lumen of which there are many leukocytes, lymphocytes. There is swelling around such dilated and full-blooded vessels. Endothelial cells are light, edematous. The nuclei of endothelial cells protrude into the lumen of the vessel (Fig. 6).

Electron microscopy in the bronchi revealed a large number of epithelial cells with light cytoplasm, lying on the thickened and containing collagen fibers of the basal membrane. The apical part of the ciliated cells are exposed due to the destruction and destruction of their cilia. Goblet cells are increased in volume, their cytoplasm contains a large number of light secretory granules. The own plate of the bronchial mucosa is infiltrated by lymphocytes, macrophages, plasma cells, eosinophils. It should be noted the presence of fibroblasts and mast cells, as well as many collagen fibers.

Electron microscopically detected the presence of active fibroblasts in interstitial tissue, mainly around the foci of destruction, atelectasis and distelected areas. Alveolar epithelial cells of type I are dropsical, mitochondria in them are swollen, their cytoplasm is enlightened. Alveolar epithelial cells of type II contain immature forms and fragments of osmiophilic lamellar bodies, smooth

endoplasmic reticulum, mitochondria with rare crystals. Aerogemata barrier thickened. The interbasal space is expanded and contains collagen fibers.

Thus, on the 30th day of experimental inflammation, perivascular and peribronchial infiltration, swelling, expansion and fullness of blood vessels, the appearance of foci of purulent inflammatory process both in the walls of the bronchi and peribronchial tissue, and in the respiratory department of the lung tissue are preserved. In own plate of the mucous membrane – massive infiltration of cellular elements, and collagenization of it. The respiratory Department is represented by areas of hypertrophy of the alveoli, atelectases and distelectases, foci of destruction of lung tissue, expansion of the interbasal space of the aerogemata barrier with signs of colonization by collagen fibers. Changes in epithelial cells are noted: alveolocytes of type I are edematous, and alveolocytes of type II are in a state of passive functioning and exhaustion.

In late terms (60 days) of the experiment - the presence of spasm of small arterial vessels, perivascular sclerosis and perivascular lymphoid infiltration. In the cavity of the small bronchi - mucous secretion with an admixture of different types of cells, hyperplasia of goblet and mucus-secreting cells. There are areas of atrophy of the epithelial cover of the bronchioles. The own plate of the bronchial mucosa is somewhat edematous, contains compacted collagen fibers, as well as lymphoid clusters with centers of reproduction. Around the focus of destruction occurs accumulation of metabolically active fibroblasts, macrophages, lymphoid cells, and the appearance of collagen fibers. Due to sclerotic changes, some areas of the bronchi are deformed.

On electronograms, ciliated cells are cylindrical, the cytoplasm of secreting epithelial cells of the bronchi is filled with secretory granules, mitochondria have shortened crystals, a well-developed Golgi complex localized in the perinuclear zone. The own plate of the bronchial mucosa contains collagen fibers, as well as fibrocytes, fibroblasts, lymphocytes, macrophages. Around many small vessels of the own plate of the bronchial mucosa, mast cells are visible. It should be noted the active cooperation of these cells with each other. In the peribronchial lymph node

there are lymphocytes of varying degrees of maturity, here lymphatic vessels with thickened walls are detected, their lumen is somewhat narrowed.

The lumen of the half-apneumatic and apneumatic alveoli are filled with epithelial cells, macrophages, leukocytes, which are in a state of different functional activity. In thickened interalveolar septa – macrophage and lymphoid infiltrates. The nuclei of endothelial cells are somewhat hypertrophied, in the vascular cavity there are electron dense granules and fibrin. There is an expansion of the interbasal space, where collagen fibers appear (Fig. 7).

The surface of alveolar epithelial cells of type I has outgrowths and protrusions, their cytoplasm in some areas is enlightened. In alveolar epithelial cells of type II, the picture of increased functional activity: osmiophil-lamellar bodies is hypertrophied, the number of which is increased relative to the previous period. But along with this, type II alveolocytes with destruction phenomena are found, with a deficiency of osmiophil-lamellar bodies, and if they exist, they are mostly devastated. Active fibroblasts are visualized in the interstitium, around which the development of collagen fibers is noted, in addition, the septal zone contains single alveolar macrophages, mast cells and eosinophils. By this time, the development of the sclerotic process in the interstitial tissue is observed. The interbasal space of the airborne barrier is expanded, contains collagen fibers.

Thus, on the 60th day, a large number of mucus-releasing cells are preserved, epithelial cells are in a state of destruction, connective tissue seals in the form of sclerosis are noted in the bronchial mucosal plate itself. Perivascular and peribronchial fibrosis develops. The respiratory department of the lungs, in particular the airborne barrier, has an uneven structure, collagen fibers appear in the expanded interbasal spaces. The development of massive and focal pneumosclerosis, mainly in areas of collapsed lung tissue, comes to the fore.

On the 90th day of the experimental inflammatory process around the large vessels, moderate lymphoid infiltration and well-packed collagen fibers are noted. Collagen fibers are also detected in the subendothelium of muscle type vessels. Under the epithelial layer of the mucous membrane, a thickened basement

membrane. Own plate of the mucous membrane is moderately infiltrated by lymphocytes, plasmocytes and fibroblasts, between which there are collagen fibers. Many alveoli are hypertrophied, their walls are thinned, around the hypertrophied alveoli there are half-sleeping and sleeping alveoli. The interalveolar septa of the lung tissue are thickened.

Electron microscopically, the mucous membrane of the bronchus is represented by light epithelial cells. Goblet cells are located on the basement membrane, the nucleus is oval, in the cytoplasm there are a large number of ribosomes, polysomes, numerous granules of various shapes surrounded by a thin membrane, a small number of mitochondria. The cytoplasm of serous cells contains granular endoplasmic reticulum, lysosomes, granules of secretion, and in the basal part the nucleus is irregular in shape. Accumulations of lymphocytes and plasma cells, macrophages and fibroblasts are visible in the lamina propria mucosa.

In the lung tissue, the capillaries of the interalveolar septa are moderately narrowed. The aerogematic barrier is sometimes presented as a thin layer, and in some areas the expansion of the interbasal space prevails, where collagen fibers are localized in the form of well-packed clusters. The cytoplasm of the endothelial cell of the airborne barrier contains pinocytotic vesicles. A large number of microvilli can be seen on the surface of type I alveolocytes facing the alveolus. Type II alveolar epithelial cells are hypertrophied, have a large number of emptied osmiophil-lamellar bodies. In the cavity of the alveoli are alveolar macrophages with electron-dense inclusions, lysosomes. In the septal zone, the development of collagen fibers is noted. Here you can see septal cells, fibroblasts, fibrocytes, single mast cells, eosinophils.

Thus, by 90 days of experimental inflammation, a connective tissue densification along the bronchi and blood vessels is observed. Own plate of the bronchial mucosa contains lymphocytes, plasma cells, eosinophils, macrophages and fibroblasts, which form various cooperations among themselves. The respiratory department is characterized by a picture of focal pneumosclerosis. In

the septal zone, the growth of collagen fibers is noted, among which fibroblasts, fibrocytes, single mast cells, and eosinophils are visible.

DISCUSSION

Intercellular interaction plays a very important role in maintaining the constancy of the internal environment of the body, in regulating protective reactions in response to various stimuli of both exogenous and endogenous origin. In this aspect, the epithelial stromal relationship occupies a special place.

Under the conditions of biological aggression and the inflammatory reaction developing at the same time, cells are activated, primarily epithelial cells. In the case of pneumotropic bacteria acting on the lung tissue, the epithelial cells of the mucous membrane of the airways and alveoli, as well as the endothelial cells of small vessels of the inflammation zone, are activated earlier than others [21]. At the same time, epithelial cells, as well as endothelial cells, act as functional analogues of antigen-presenting cells. Cells capable of interactions important for the implementation of immune processes form two rows, representatives of one of which can interact with representatives of the other row. One row consists of macrophages, B-lymphocytes, endothelial and epithelial cells, mast and nerve cells. The second row includes various types of T-lymphocytes.

In the case of infection of rats with virulent pneumotropic bacteria during cold exposure, the totality of the results of light-optical and electron-microscopic studies of the bronchial mucosa showed that already in the early stages an inflammatory process develops with a predominance of infiltrative-exudative changes, structural restructuring of the bronchial mucosa. So, according to the data obtained in our experiments, on the 5th and 10th days from the moment of nasotracheal injection of pneumotropic bacteria in the lung tissue, the picture of microcirculatory disorders in the form of plethora, the presence of a pool of polymorphic nuclear leukocytes in the vascular cavity, swelling of perivascular tissue, and the release of blood cells prevailed. The bronchial epithelial layer basically retains its structural and functional peculiarity; the number of plasma

cells in the bronchial mucous membrane itself increases. The presence of neutrophils, macrophages, and active plasma cells around foci of inflammation indicates the cooperative functioning of all organ systems against the pathological process. In lymphoid follicles, the cooperation of cellular elements is also visible: the macrophage with eosinophil and plasma cells. In their own plate of the bronchial mucosa, destruction centers surrounded by active fibroblasts are also observed [22].

In the subacute period, changes in the integumentary epithelium in the form of damage to the ciliary cells are a consequence of constant antigenic stimulation. In the bronchial epithelium, the process of cell mucus continues, destruction of the cilia and extrusion of cells into the lumen of the bronchus. In the own plate of the bronchial mucosa, along with the presence of cooperations of cellular elements, the connective tissue base is densified in some places, and small foci of microabscesses are noted in some areas. Along the bronchial tree, a large number of lymphoid follicles and lymphoid accumulations are noted.

In a prolonged period, quantitative and qualitative changes in the ciliated epithelial cells dominate in the integumentary epithelium, which are expressed in a quantitative decrease in these cells and damage to the ciliary apparatus. The number of goblet cells throughout the bronchi increases. In the own plate of the bronchial mucosa, a focal increase in the number of connective tissue fibers is noted. In the area of lymphoid infiltration of the lamina propria, clusters of cells are visible, which in some areas are represented by accumulations of B-lymphocytes, in other areas by monocytes with processes that are in contact with plasma cells. In the lung tissue around the foci of destruction, there is an accumulation of metabolically active macrophages, fibroblasts, lymphoid cells, and the appearance of thin collagen fibers is also noted. The mechanisms of the development of the pathological process in the mucous membrane of the bronchi lead to a violation of the regeneration and differentiation of the integumentary epithelium, which are to some extent determined by the state of the stroma and microvasculature. Sclerotic changes in the subepithelial layer of the bronchial

lamina propria and septal zones of the respiratory department lead to a violation of the epithelial-stromal relationship both in the bronchial wall and in the lung tissue.

The defining specific and non-specific barrier-protective function of the border organs is the own plate of the mucous membrane of the respiratory tract, where the cells of loose connective tissue (macrophages, plasma, mast, reticular cells, fibroblasts) and blood (granulocytes, T-, B-lymphocytes and their subpopulations are concentrated) The close integration of the functions of these cells in the mucous membrane of the respiratory tract provides local immune responses, which, in turn, are the trigger for humoral and cellular immune responses that occur at the level of the whole organism. The morphological substrate of this integration is intercellular cooperation, the number and cellular composition varies widely depending on the functional state of the body. Cell cooperation is a response to infection [23].

The development of a picture of catarrhal bronchitis, focal pneumonia, increased secretory processes and macrophage reactions are the primary signs of lung tissue response to the damaging factor of a foreign antigen. The condition of the vascular bed, bronchial tree and interstitial tissue of the respiratory department in the early stages indicate an active inflammatory process. In this (acute) period of the development of inflammation, non-specific and specific defense mechanisms are mobilized in the form of enhanced secretion of mucus in the bronchi - the secretory stage, diapedesis of blood cells from the lumen of the vessel into the perivascular tissue and into the lumen of the bronchi and alveoli - leukocyte stage. Neutrophilic leukocytes, in contact with a foreign agent, are activated and produce active substances, which in turn trigger a macrophage response - the macrophage stage. Macrophages contribute to the elimination and elimination of them from the body, stimulate immunocompetent cells, other blood cells and fibroblasts. As a result, more and more defense cells are involved in the lesion. Depending on the virulence of the microorganisms, the state of the macroorganism, the inflammation ends successfully without complications, and under adverse conditions (secondary immunological deficiency, hypofunction of actively secreting cells, bronchial

obstruction, maladaptation processes, hypoxia, etc.), it necessarily goes to the stage of the purulent process or in a protracted course.

At the stage of the purulent process, tissue edema of a perivascular and peribronchial nature is pronounced, abscess formation foci or large areas of the necrotic-purulent process are clearly localized or diffusely scattered. In the same period, not pronounced sclerosis begins to form. Changes in the airborne barrier with impaired function (hypoxia) are characteristic. It was during these periods of development of experimental inflammation that we noted a high lethal outcome of experimental animals (up to 50%), as well as a large percentage of bacteria seeding from lung tissue. The purulent-destructive process destroys the lung tissue and depletes the protective mechanisms of the macroorganism, as a result of which the dissemination by bacteria and their toxins of the whole organism occurs with the development of sepsis.

At the late stages of experimental inflammation, destruction of epithelial cells is still preserved. The development of focal pneumosclerosis (the stage of sclerosis) comes to the fore. Complete involution of lung tissue is rare, usually there are areas of atrophy and sclerotic changes, which in turn are the entrance gate for repeated infections. The chronicity of the process is indicated by the detection of multiple lymphatic clusters in the walls of the bronchi, in the peribronchial zones and in the thickened interalveolar septa, containing cells of different functional activity.

Thus, a single intratracheal administration of a virulent culture of staphylococcus, streptococcus and Klebsiella on the background of hypothermia led to the formation of an active inflammatory process in the lungs. In our case, the transition of the acute stage (5-10 days) to subacute (or prolonged) fluctuated between 15 and 21 days of the experiment. It was during these periods that extensive destruction of the pulmonary parenchyma (period of destruction of the lung tissue) occurred. In subsequent periods, the process took a protracted form with a predominance of atrophic and sclerotic changes, both in the airways and in the respiratory department of the lung tissue.

CONCLUSION

1. A study of the dynamics of structural and functional changes in lung tissue during experimental inflammation revealed that the development of the process up to 10 days is characterized by acute, from 10 to 21 days - subacute, and in periods of more than 30 days a prolonged stage of the course.

2. Violations of epithelial stromal relationships in the process of development of inflammation in the lung cause destructive, atrophic and sclerotic processes.

3. The disproportion between epithelial and immunocompetent cells in the process of inflammation leads to profound changes in the system of nonspecific and specific defense mechanisms, to a decrease in the functional state of alveolar epithelial cells, which determine the protracted course of the process.

4. Under the influence of virulent strains of pneumotropic bacteria, inflammation and destruction with extensive destruction of both the epithelial cover and interstitium prevail in the lung tissue. In the later stages of the experiment, the processes of pneumosclerosis prevail.

Figures:

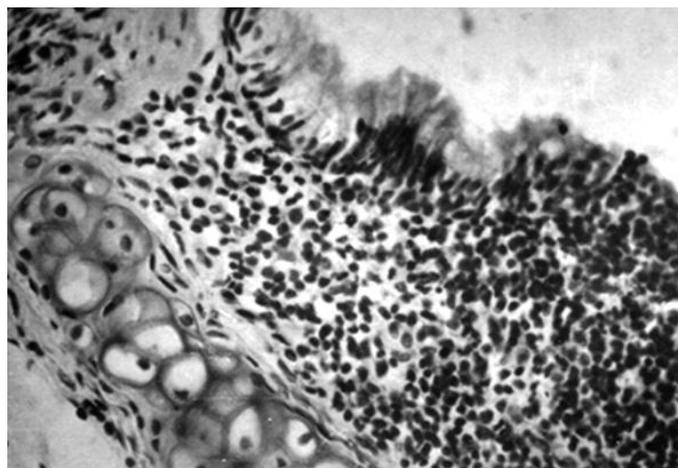


Figure 1. 5th day of the experiment. Fragment of the middle bronchus. Lymphoid follicle. Hematoxylin and eosin stain. Increase x200.

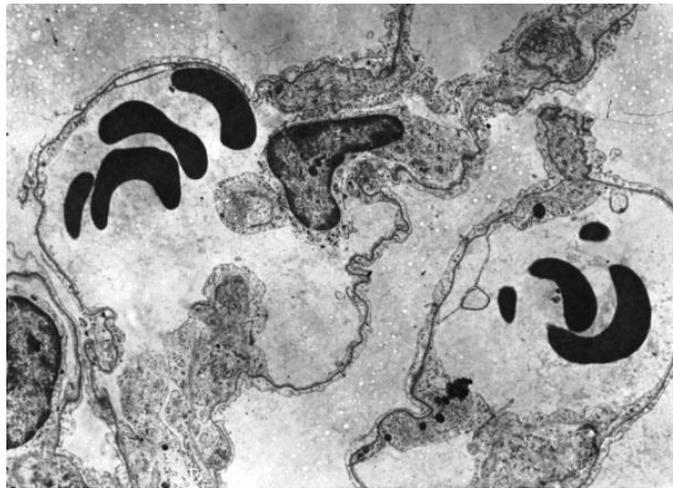


Figure 2. 10 days. Expanded capillaries of the respiratory part of the lung tissue. Electron microscopic pattern. Increase x3000.

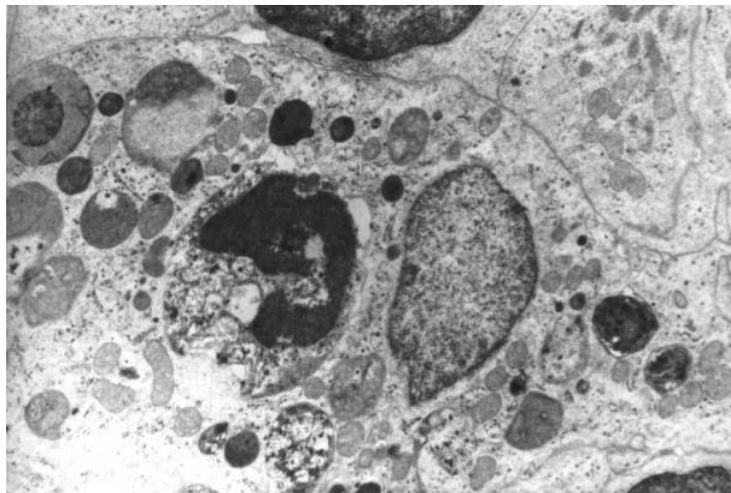


Figure 3. 15 days. Lymph node. Macrophage. Electron microscopic pattern. X5000 magnification.

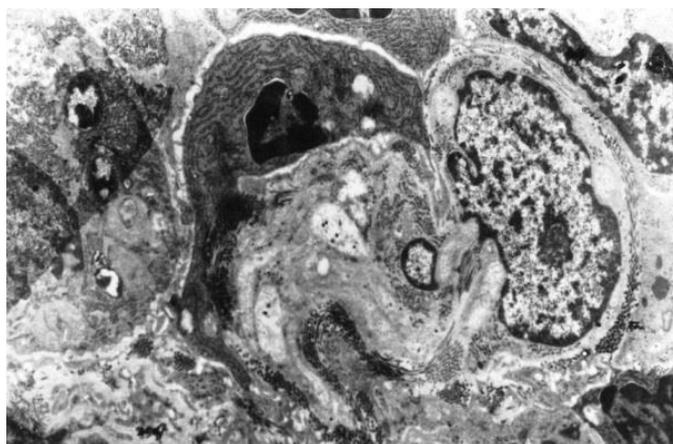


Figure 4. 15 days. Plasma cell and fibroblast in the own plate of the bronchial mucosa. Electron microscopic pattern. Increase X5000.

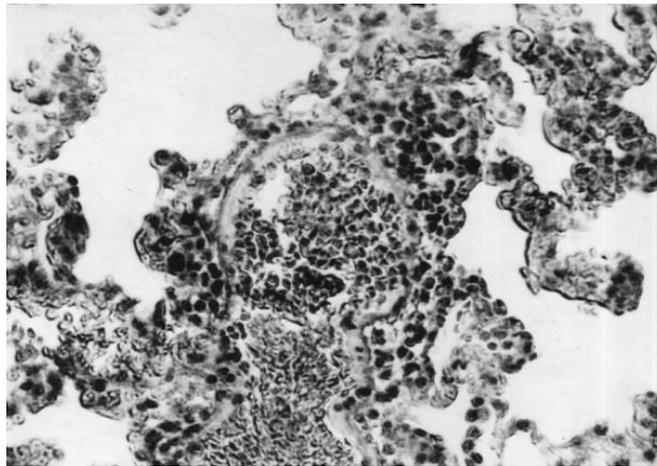


Figure 5. 21 days of the experiment. Expansion and plethora of the vessels of the respiratory department of the lung tissue. Perivascular lymphoid infiltration. Van Gieson stain. Increase x200.

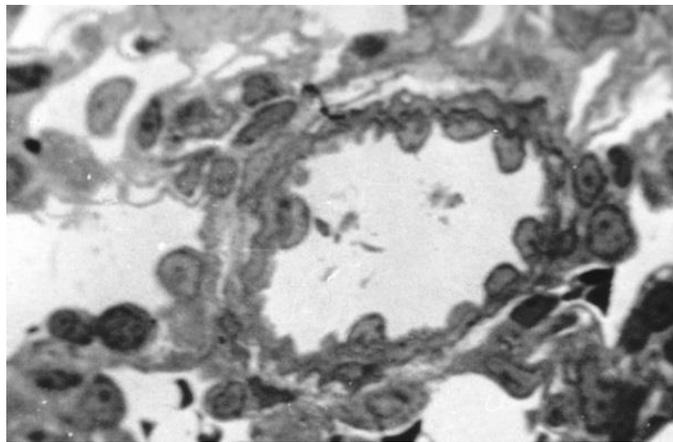


Figure 6. Small vessel of the respiratory part of the lung tissue. Semi-thin section. Increase X400.

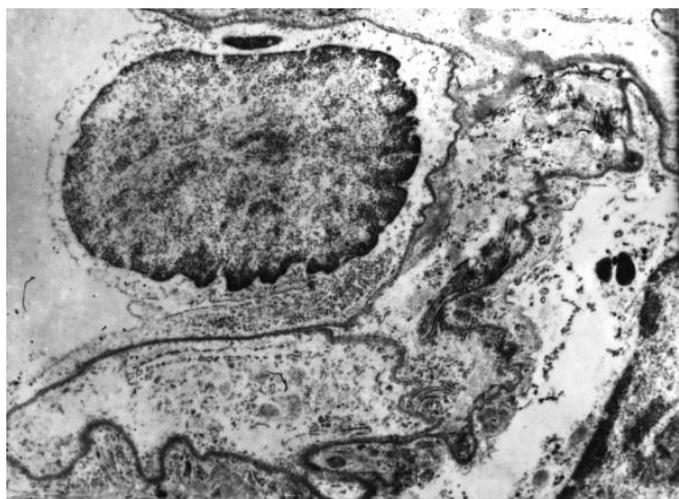


Figure 7. 60 days. AE type I. Thickening of the blood-air barrier. Electron microscopic pattern. Increase X15000.

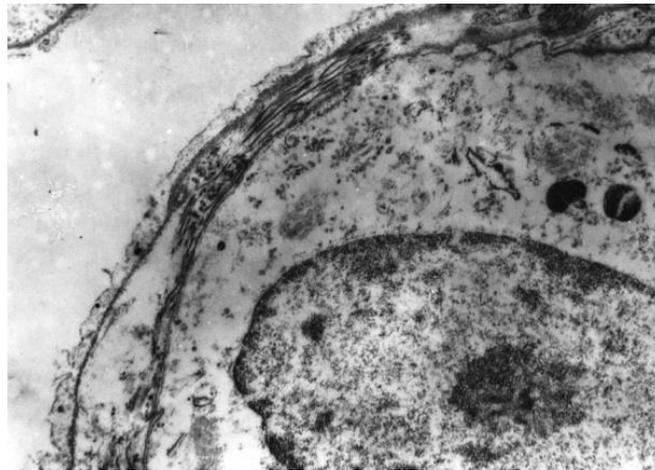


Figure 8. 90 days. Collagen fibers in the inter-basal space. Electron microscopic pattern. Increase x15000.

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