PROGRESSIVE STRUCTURAL REORGANIZATION AND FIBROTIC-EMPHYSEMATOUS REMODELING OF THE LUNGS UNDER CHRONIC EXPOSURE TO NICOTINE-CONTAINING PRODUCTS

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Abstract. *This article presents the results of an experimental study investigating progressive structural reorganization and the development of fibrotic-emphysematous remodeling of lung tissue under prolonged exposure to nicotine-containing products. The study was performed on white outbred rats with a model of chronic nicotine intoxication lasting 9 and 12 months. It was established that long-term nicotine exposure induces pronounced remodeling of the bronchopulmonary system, characterized by thickening of bronchial walls, hypertrophy of smooth muscle elements, hypersecretory transformation of the epithelium, and progression of perivascular fibrosis. In the alveolar compartment, destructive changes were observed, including the formation of emphysematous spaces (up to 50%), as well as features of chronic inflammation. The findings reflect the transition from compensatory alterations to a stage of stable fibrotic-destructive remodeling of lung tissue, forming the morphological basis of irreversible bronchopulmonary dysfunction.*

Keywords: *nicotine intoxication, lungs, remodeling, emphysema, fibrosis, inflammation, experiment.*

Introduction. Chronic nicotine intoxication is currently considered not only a factor in functional impairment but also a cause of profound structural transformation of lung tissue. Long-term exposure to nicotine-containing products is accompanied by the development of persistent morphological changes that form the morphological basis for irreversible damage to the bronchopulmonary system (1,8).

The key stage of the pathological process is the transition from initial adaptive-compensatory responses to the stage of progressive remodeling, including fibrotic remodeling of the interstitium, vascular changes, and destruction of the alveolar apparatus. It is at this stage that emphysematous changes and sclerotic processes develop, determining the irreversibility of morphological abnormalities and a decrease in the functional reserve of the lungs (2, 3, 5).

Of particular importance is the study of the complex nature of remodeling, which simultaneously involves the bronchial tree, vascular bed, and alveolar tissue. The combination of fibrotic and destructive processes, accompanied by chronic inflammation and activation of immune systems, forms a persistent pathological continuum, which has not been adequately reflected in experimental studies (4, 6, 7).

In this regard, identifying patterns of progressive structural reorganization of the lungs during long-term exposure to nicotine-containing products represents a pressing scientific task aimed at clarifying the mechanisms of formation of fibro-emphysematous remodeling and morphological criteria of irreversible damage to the bronchopulmonary system.

The aim of the study is to identify patterns of progressive remodeling of lung tissue during long-term exposure to nicotine-containing products in an experiment with morphologicalverification of fibro-emphysematous changes.

Material and methods of research. The work was carried out in an experimental series on

white mongrel rats of both sexes weighing 220–240 g. The animals were kept under standard vivarium conditions with free access to water and food, in compliance with generally accepted standards for keeping laboratory animals.

Animals were divided into control and experimental groups. In the experimental groups, chronic exposure to nicotine-containing products for oral consumption was simulated. The exposure duration was 9 and 12 months, respectively, allowing for an assessment of the progression of morphological changes in lung tissue in the late stages of chronic nicotine intoxication. The control group was maintained under similar conditions without exposure to nicotine-containing substances.

During the experimental period, dynamic observation of the animals was carried out with an assessment of their general condition, motor activity, food and water consumption, as well as changes in body weight.

At the end of the experimental period, the animals were withdrawn from the study in accordance with bioethical principles, after which lung tissue was collected. The tissue was fixed in 10% neutral formalin, processed using standard histological procedures, and then embedded in paraffin. Serial sections of 5–7 μm thickness were cut from the resulting blocks.

Histological examination was performed using hematoxylin and eosin staining, as well as van Gieson staining to assess the degree of fibrotic transformation of the connective tissue. Microscopic analysis was performed to assess structural changes in the bronchopulmonary system, including the condition of the bronchial tree, vascular bed, and alveolar apparatus.

The morphometric study included an assessment of the severity of fibrotic changes, the degree of bronchial wall remodeling, the thickness of the vascular wall, the density of the alveoli and the proportion of emphysematous areas.

The obtained morphometric data were subjected to statistical processing using methods of variation statistics with the calculation of mean values (M) and standard error of the mean (m).

Research results. Microscopic examination of the lung tissue of animals exposed to long-term exposure to nicotine-containing products revealed a pronounced progressive structural reorganization of the bronchopulmonary system with the formation of persistent fibrotic-destructive changes.

At the level of the serous membrane, significant thickening was observed, with compaction of the submesothelial layer due to the proliferation of coarse fibrous connective tissue. Mesothelial cells acquired a cuboidal shape, with signs of nuclear hyperchromia and cytoplasmic granularity. In some areas, foci of hyalinosis and perivascular sclerosis were detected, indicating the development of fibro-dystrophic processes.

The bronchi and bronchioles demonstrated marked wall remodeling. The thickness of the connective tissue lamellae increased to 69.5–72.0 μm, accompanied by disorganization of collagen and elastic fibers. The epithelial layer was unevenly thinned, locally desquamated, with marked cell deformation. The number of goblet cells increased to 15.5–17%, reflecting persistent hypersecretory remodeling of the mucosa (Fig. 1).

The basement membrane was thickened and had an uneven, wavy contour. The smooth muscle elements of the bronchial wall were markedly hypertrophied, with signs of fragmentation of muscle bundles and thickening of the intermuscular stroma. These changes indicate the development of persistent airway remodeling.

The vascular bed was characterized by pronounced reorganization. Arteriolar wall thickening to 10.8–11.5 μm was noted, with the development of perivascular fibrosis and the formation of dense collagen ridges. In some areas, signs of hyalinosis of the vascular wall and narrowing of the vascular lumen were detected. Intravascular congestion was pronounced, with stasis and aggregation of blood cells, indicating impaired microcirculation.

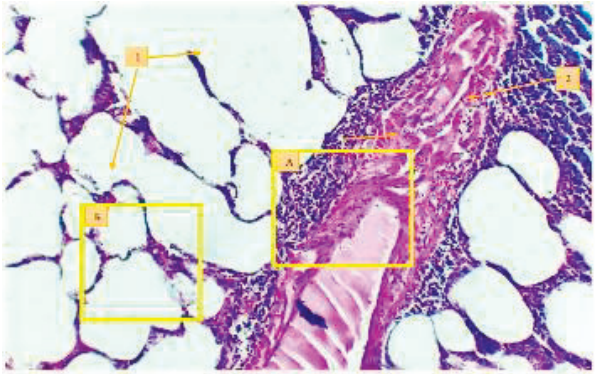


Fig. 1. Microscopic image of the lung tissue of a 9-month-old white mongrel rat with chronic poisoning with nicotine-containing products for oral consumption. 1-emphysematous alveolar sacs; 2-hypertrophy of the muscular layer of the blood vessel wall and the formation of intermuscular ruptures. Stained with hematoxylin and eosin. 10x magnification. 20 mm

The alveolar apparatus underwent the most pronounced destructive changes. A significant decrease in alveolar density (to 5.0–5.4 per 1 mm²) and a decrease in their number per visual field were noted. The interalveolar septa were thickened, fragmented in places, or completely destroyed, leading to the fusion of alveoli and the formation of large air pockets. The proportion of emphysematous changes reached 42–50%, indicating a marked progression of the destructive process.

The interstitial tissue was characterized by an increase in fibrous content, with an increase in connective tissue content and the appearance of areas of sclerosis. Clusters of fibroblasts, lymphocytes, and macrophages were detected in the interalveolar septa, reflecting a chronic inflammatory-proliferative process (Fig. 2).

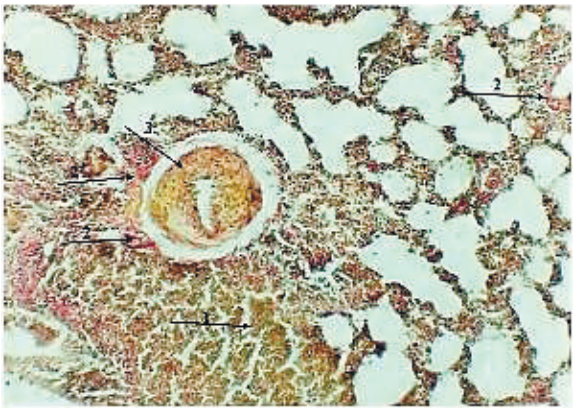


Fig. 2. Microscopic image of lung tissue of a 12-month-old white mongrel rat with chronic poisoning with nicotine-containing products for oral consumption. 1 - a strong infiltrative process was observed around the venous vessel; 2 - purple collagen fibers indicating the fibrosis process; 3 - hypertrophy of the lamina propria of the vascular wall. Van Gieson staining. Ok.10x Ob.20

The cellular composition of the lung tissue also underwent significant changes. The number of alveolar macrophages increased to 7–8 per field of view, most of which contained pigment inclusions. Macrophages were located in groups within the lumens of the alveoli and bronchioles, forming foci of cellular infiltration. Marked hyperplasia of the bronchi-associated lymphoid tissue was noted, accompanied by peribronchial and perivascular lymphocytic infiltrates.

A comparative analysis showed that with increasing duration of exposure to nicotine-containing products, a transition occurs from relatively compensatory changes to a stage of persistent fibrotic-destructive restructuring of lung tissue. In contrast to earlier stages,These changes are characterized by stability, severity and signs of irreversibility.

Discussion. The results indicate that prolonged exposure to nicotine-containing products leads to progressive structural changes in lung tissue that go beyond compensatory responses. The identified changes reflect the transition of the pathological process to a stage of persistent remodeling.

Remodeling of the bronchial tree is characterized by thickening of the walls, hypertrophy of smooth muscle elements and hypersecretory restructuring of the epithelium, which creates the preconditions for impaired ventilation function.Simultaneously increasing interstitial and perivascular fibrosis indicates a profound restructuring of the connective tissue framework of the lung.

Changes in the vascular bed, including thickening of arteriolar walls and stasis, indicate impaired microcirculation and the development of chronic hypoxia, which intensifies fibrotic processes. Destruction of the interalveolar septa and an increase in the proportion of emphysematous areas reflect the progressive loss of lung tissue architecture.

Activation of the macrophage-lymphocyte system and hyperplasia of bronchial-associated lymphoid tissue indicate chronic inflammation. Taken together, these changes form a fibro-emphysematous type of remodeling, characterized by stability and signs of irreversibility.

Conclusion. Long-term exposure to nicotine-containing products leads to the formation of progressive structural reorganization of lung tissue with the development of pronounced remodeling of the bronchopulmonary system.

It has been established that the pathological process is characterized by a combination of fibrous and destructive changes, including interstitial and perivascular fibrosis, remodeling of the vascular bed and the formation of emphysematous areas.

The identified changes reflect the transition of compensatory reactions to the stage of stable fibro-emphysematous transformation, accompanied by a violation of the architecture of the lung tissue and a decrease in its functional potential.

Thus, the formed morphological complex of changes can be considered as the structural basis of irreversible disorders of the bronchopulmonary system in chronic nicotine intoxication.

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