



**STUDY OF CHANGES IN PULMONARY ALVEOLAR EPITHELIUM AND AEROGEMATIC BARRIER IN DIABETES MELLITUS**

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**Abstract**

The question of the need to prescribe antibiotic therapy to patients with exacerbation of chronic obstructive pulmonary disease requires justification of the prescription of an antibiotic, taking into account the likelihood of an etiological role of an infectious factor, the possibility of spontaneous remissions, as well as the risk of negative consequences in case of unreasonable prescription (development of microorganism resistance, unwanted side effects, unjustified costs) ... In addition, the large arsenal of modern antibiotics poses the problem of choosing the optimal drug for the doctor. With extreme caution, it is necessary to treat the choice of antibiotic therapy for patients with diabetes mellitus with concomitant chronic obstructive pulmonary disease.

**Keywords** chronic obstructive pulmonary disease, diabetes mellitus, diabetic microangiopathy, microcirculation, lung tissue.

**Introduction**

Currently, there is an increase in the incidence of diabetes mellitus. As a result of insulin treatment, the duration of the illness increased significantly. However, with a prolonged course of diabetes, widespread vascular lesions develop, which are diagnosed in 70-80 / S patients (1). It is known that in diabetes, both the microcirculatory system (diabetic microangiopathy) and large and medium-sized vessels (diabetic macroangiopathy) are affected. ... Damage to the vascular system is a common cause of death in patients, which is 3-4 times higher than the mortality rate in the general population (4). Various metabolic disorders in diabetic patients lead to generalized damage to the microcirculation system. Diabetic microangiopathy has been studied in the skin (2), spleen (5), retina (3), and other



organs of the systemic circulation. At the same time, generalizing studies based on the analysis of morphological vascular lesions in the pulmonary circulation in humans (7), kidneys (8) were not found in the literature.

The study of changes in vessels of both large and small caliber of the lungs in diabetes mellitus is important for elucidating the features of diabetic angiopathy of the lungs and for explaining the essence of morphological and functional disorders in the respiratory organs, and in particular the development of pneumonia in patients with diabetes mellitus (6).

It has been shown that insulin plays an important role in the regulation of carbohydrate and fat metabolism in the lungs (7). Specific receptors for insulin have been found in the lungs (9). Cells carrying these receptors, according to C. PHorreg a1. (2008) are type II pneumocytes. In this regard, it is of undoubted interest to study the early changes in these cells in an experiment on animals with induced diabetes. The study of diabetic microangiopathy in parallel with changes in lung cells - carriers of insulin receptors, will make it possible to more widely represent the pathology of the lungs in diabetes mellitus, to study the features of its pathogenesis and morphogenesis.

Diabetes mellitus (DM) is a common disease. According to the WHO, today there are more than 120 million patients with diabetes mellitus on the planet. Modern treatment technologies make it possible to prolong the life of a patient with diabetes, and this leads to the need for diagnosis and treatment of late disorders in various organs that develop several years after the onset of diabetes mellitus.

Nonspecific lung diseases (NLD) are a common group of diseases, the share of which in the structure of reasons for seeking medical care is more than 60% [4]. About 500 thousand patients with pneumonia are registered annually in the Russian Federation. Moreover, official statistics do not count more than 1 million patients. All this, as well as the severe course of Nonspecific lung diseases in patients with diabetes mellitus, makes it relevant to consider this issue.

Complications diabetes mellitus Teaching about late complications diabetes mellitus is widely covered in modern literature [8] and is based on disorders of carbohydrate metabolism, leading to micro- and macroangiopathies: diabetic nephropathy, retinopathy, gangrene, ischemic heart disease (IHD), which lead to disability and premature death of patients.

### **Nonspecific lung diseases and diabetes mellitus**

Diabetes mellitus contributes to the severe course of pneumonia, chronic obstructive pulmonary disease (COPD), bronchiectasis [10]. The main factor contributing to the severity of nonspecific lung disease in diabetes mellitus is probably a violation of microcirculation. The revealed disorders of nervous regulation, respiration mechanics [7], and vascular permeability [5] have a negative effect on the course of Nonspecific lung diseases in diabetes mellitus. There is evidence of immune dysfunction, but there is no strong scientific evidence for the effect of immunity on angiopathies in diabetes mellitus.

### **Pneumonia and diabetes mellitus**

The data on the course of pneumonia in diabetes mellitus are presented most fully today. Modern recommendations for pneumonia highlight diabetes mellitus as an important risk factor for its severe



course [9]. The frequency of pneumonia is higher in patients with diabetes mellitus. In the United States, diabetic patients who died between the ages of 25 and 64 were more likely to develop pneumonia than non-diabetic patients. In intensive care units in patients with diabetes mellitus, the incidence of pneumonia is higher than in those without diabetes - 13.1% versus 3.2% [7]. According to T.A. Goncharova et al. [6] and other literature data, in patients with diabetes mellitus pneumonia had a severe course in 31% of cases and extremely severe - in 17% of patients, as well as a prolonged, complicated course. Thus, 25% of diabetics with pneumonia developed its protracted course, 18% were diagnosed with pleurisy, and 10.3% with abscess formation [1]. RM Severinenko et al. [13] note that pneumonia against the background of diabetes mellitus proceeds with severe intoxication, respiratory failure, and often bilateral lung damage.

Diabetes mellitus determines the death rate of patients with pneumonia. According to the National Mortality Followback Survey, 10.3% of deaths from pneumonia and influenza in the USA in 2006 suffered from diabetes mellitus, which increases the risk of postoperative pulmonary infectious complications after coronary artery bypass grafting [10].

### **Morphological changes in the lungs in diabetes mellitus**

Morphological changes in the lungs have been studied in detail in animals with diabetes mellitus. D. Popov et al. [3] revealed specific changes in streptozotocin diabetes in hamsters and mice. 6 weeks after the development of diabetes, animals showed significant narrowing of 28-35% of capillaries and 25-30% of alveoli, hyperplasia of the extracellular matrix and collagen fibers. In the capillaries, the adherence of macrophages was determined, which indicated inflammation. The capillary endothelium was characterized by a well-developed synthetic apparatus (endoplasmic reticulum and Golgi complex). The venule endothelium was rich in Weibel-Palade bodies.

In patients with diabetes mellitus, the thickness of the basement membrane of the bronchial epithelium of the cell was greater than in individuals without diabetes mellitus [2]. Thickening of the basement membrane of the alveolar epithelium and capillary endothelium was observed along with thickening of the basement membrane of the glomerular capillary endothelium and renal tubules, and the thickening of the basement membrane did not depend on the type of diabetes mellitus. D.K. Najmutdinova et al. [3] found neutrophilic infiltration and decreased macrophage and lung function in experimental diabetes. The results of these studies indicate the development of specific morphological changes in the lungs in diabetes mellitus.

### **Oxidative stress**

Non-enzymatic autooxidative glycosylation and oxidative stress caused by impaired carbohydrate metabolism, along with genetic predisposition, are now considered an important link in the pathogenesis of vascular complications diabetes mellitus [3]. The presence of markers of oxidative stress (N (epsilon) - carboxymethyl) lysine) in the lungs confirms the involvement of pulmonary vessels in this process in diabetes mellitus [6].



Oxidative stress underlies endothelial dysfunction, which is characterized by an imbalance in the balance of factors involved in the regulation of vascular tone, thrombogenesis, and muscle cell growth [8]. Pulmonary endothelial dysfunction, identified by S. Nagamachi et al, depended on the severity of diabetes mellitus.

Iodine-123-MIBG is considered a biochemical marker of pulmonary endothelial dysfunction. An increase in its content presumably indicates pulmonary endothelial dysfunction and ischemia in diabetes.

R.D.Russ and B.W. Tobin revealed changes in pulmonary hemodynamics in rats with streptozotocin diabetes. In diabetic rats, the total pulmonary vascular resistance was higher than in the control. The increase in resistance occurred at the level of the small pulmonary veins. In addition, vascular resistance has moved from arterioles to venules. Development of neuropathy in the lungs and respiratory mechanics in diabetes mellitus.

The development of neuropathy in the lungs in diabetes mellitus is indicated by an increase in the activity of muscarinic receptors in rats, which, with distal electrical stimulation, leads to the development of bronchoconstriction and hyperinflation [6]. M. Mancini et al. [2], studying the mechanics of respiration, the function of respiratory muscles and ventilation control in patients with type 1 diabetes mellitus, revealed normal or slightly reduced lung volumes and diffusion capacity of the lungs, decreased dynamic compliance, high central respiratory drive and neuroventilation dissociation. There was no association with changes in the peripheral airways.

Other studies have found a decrease in blood oxygen saturation in patients with chronic hyperglycemia, significant restrictive disorders, and a decrease in diffusion capacity. Patients with glucose levels close to normal were less susceptible to these changes [13]. It was revealed that the change in the diffusion capacity of the lungs is associated with the appearance of proteinuria. The authors conclude that the development of renal and pulmonary complications has similar microcirculation disorders [17].

### **Vascular permeability**

The development of microangiopathy in diabetes mellitus is associated with increased permeability and plasma impregnation of blood vessels. Y.Kim et al. [5] revealed an increase in endothelial growth factor with an increase in endothelial permeability against the background of diabetes mellitus and respiratory distress syndrome in adults.

### **Immunity**

Immunological aspects also play a role in the pathogenesis of diabetic angiopathies [5]. So, the composition of immune complexes that damage the vascular wall includes IgG, (3-lipoproteins, complement. molecules on leukocytes, endothelial cells and platelets [10]. In patients with pulmonary and myocardial complications after coronary artery bypass grafting, an increase in neutrophilic endothelial cell adhesion was found. with diabetes mellitus.





### **Diabetes mellitus and bronchial asthma**

A special position when considering the issue of diabetes - lungs, is occupied by bronchial asthma (BA). Patients suffering from bronchial asthma suffer from type 2 diabetes mellitus or steroid diabetes. On the other hand, diabetics suffer from bronchial asthma no less frequently than in the general population [2]. J.Clck and B. Rogala [4] conducted a retrospective analysis for 1988-1997. in two Polish clinics and identified 18 patients (0.3% of hospitalized patients) who suffered simultaneously from bronchial asthma and type 2 diabetes mellitus. In the majority of patients, bronchial asthma was detected several years earlier than diabetes mellitus, i.e. the development of type 2 diabetes mellitus was not associated with the intake of glucocorticosteroids.

The administration of insulin to diabetic rats promotes the development of bronchial hyperreactivity [17]. Children with type 1 diabetes who receive insulin have asthma symptoms, i.e. against the background of a decrease in the level of insulin, a decrease in the reactivity of the bronchi is observed, and with its introduction, hyperreactivity appears. The hyporeactivity of the bronchi can contribute to the development of a severe course of pulmonary diseases in diabetes mellitus.

### **Conclusion**

So, diabetes mellitus has a negative impact on the course of NZD. Microcirculation disorders with morphological confirmation and, possibly, nervous regulation lead to changes in the mechanics of respiration, pulmonary hemodynamics, immune response and hyporeactivity of the bronchi. Pulmonary changes occur in parallel with the development of diabetic nephropathy. This suggests, by analogy with diabetic nephropathy, retinopathy, the development of diabetic pneumopathy in the lungs in diabetes mellitus. Its clinical manifestation is a severe course of nonspecific lung diseases, and above all pneumonia, as in the case of a lesion of the foot - gangrene. A small number of studies, the difficulties of a direct study of the microcirculation of the lungs leave unresolved theoretical and practical issues of this problem. However, the prevalence of diabetes mellitus and nonspecific lung diseases, their mutual influence on mortality, and the economic costs of treating severe NZL make it relevant to consider the problem of diabetic pneumopathy.

Thus, the study of the patterns of impairment of pulmonary functions, primarily microcirculation, will help create a new approach to the prevention and treatment of non-specific lung diseases in diabetes mellitus.

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