



Sivtseva A.I.

### **Clinical and Epidemiological Characteristics of Chronic Bronchitis and its Place in the Structure of COPD**

Chronic obstructive pulmonary disease (COPD) is characterized by poorly reversible respiratory limitation associated with abnormal changes, micro and macro-inflammation of airway. COPD traditionally refers to chronic bronchitis and emphysema. Destruction of alveolar walls is a hallmark of emphysema which may be associated with imbalance of "protease - antiprotease" and such mechanisms as oxidative stress, inflammation of respiratory tract and systemic inflammation [27].

According to the classification made by A. Kokosov [24] chronic bronchitis (CB) is usually divided into two main forms: CB without obstruction of airflow (CNB) and CB with bronchial obstruction (COB). In the structure of COPD prevails notobstructive bronchitis (58-62%), followed by obstructive bronchitis (18-28%), which in the age groups above 50 years is 40-50% [3.19].

Chronic notobstructive bronchitis (CNB) is a diffuse lesion of mucous bronchial tree caused by a long irritation of airways with volatile pollutants of household and industrial nature and by viral or bacterial infection damage with development of inflammation (endobronchitis). This is manifested by constantly or periodically occurring cough with sputum usually not associated with other bronchial processes or involvement of other organs and systems. Not obstructive bronchitis affects mainly large (proximal) bronchi [29].

Chronic obstructive bronchitis (COB) causes great economic loss due to temporary disability, early permanent disability and mortality of patients. Absence of generally accepted ideas about the nature of the disease makes it difficult to modern diagnosis and, therefore, effective treatment [21].

National and international policy documents called consensus were developed for early diagnosis of this steadily progressive disease, conducting adequate therapy and for teaching practitioners. Such consensus for chronic obstructive bronchitis was developed in our country, proposed by A.G. Chuchalin - the president of the Russian Society of Pulmonologists, Academician of the Russian Academy of Medical Sciences (RAMS) and adopted at the 5th National Congress on



Respiratory Diseases in 1995. According to this consensus COB is defined as follows: "Chronic obstructive bronchitis is a disease characterized by diffuse non-allergic inflammation of bronchi of the obstructive type leading to a progressive deterioration of lung ventilation and gas exchange and manifested by cough, shortness of breath and expectoration not associated with damage of other organs and systems". (When diagnosing COB it is important to consider each component of this definition.)

As it is known, COB is characterized by progressive airflow obstruction and intensified bronchoconstriction in response to nonspecific stimuli. Obstruction at COB consists of irreversible and reversible components. Irreversible component, as it will be discussed below, is determined by degradation of elastic collagen base of lungs, fibrosis, shape change and obliteration of bronchioles. Reversible component is formed as a result of inflammation of the bronchial mucosa, spasm of smooth muscle and mucus hypersecretion. It is very important to take into account the existence of a reversible component in COB formation for treatment program with use of bronchodilators. Smooth muscle dysfunction contributes to development of respiratory diseases such as chronic obstructive pulmonary disease and pulmonary hypertension. These diseases can be accompanied by smooth muscles hypertrophy of airways vascular walls and/or proliferation and hyperreactivity, and related processes, such as fibrosis and reconstructions of the extracellular matrix [23].

COPD develops mainly in patients elder than 40 years, with age frequency of COPD cases increases. Thus, according to data of epidemiological study in Irkutsk district COPD was found in 1.5% of urban population aged 30-49 and among those aged over 70 years – in 10.6% [13, 23].

According to A.A. Grigorenko [11] 4 morphological forms of COB were identified: catarrhal chronic bronchitis, catarrhal-sclerotic chronic bronchitis, sclerotic chronic bronchitis, granulating chronic bronchitis. Morphological picture of chronic bronchitis changes depending on duration of the disease. At the initial stages compensatory and protective processes dominated in bronchi manifested by hypertrophy and hyperplasia of mucus-producing structures. In the long duration of bronchitis in its morphological picture of segmental bronchi sclerotic changes are observed indicating the exhaustion of compensatory and protective mechanisms.

The key pathomorphological features of COB are the following: a) changes in the bronchial wall with hyperplasia and hypertrophy of mucus-producing elements (goblet cells, submucosal glands), hypersecretion, abnormality of mucociliary clearance and repeated infection-dependent disease exacerbation, and b) extensive irregular, predominantly centriacinar emphysema, which determines irreversibility of ventilation and hemocirculation disorders [20].

Cellular part of COB morphological changes is based on migration of neutrophils from



bloodstream into airways, increased production of neutrophil elastase and progressive imbalance of proteinase inhibitors with increasing activity of neutrophils, high myeloperoxidase activity and generation of active forms of oxygen, reflecting the imbalance in the system of oxidase-antioxidase. Increased proteolytic activity in inflammatory locus of mucous airway leads to destruction of collagen-elastin relation, proliferation of fibrous tissue, deformation and obliteration of small airways. These are the basic processes at COB development resulted in irreversible airway obstruction. [13]

I.S. Platonov, G.G. Kruglikov et al. [14.18] who studied morphology of respiratory muscles came to the conclusion that at low degree of respiratory failure degenerative and hypertrophic changes dominated, at moderate degree – necrotic changes, at severe degree – change of necrosis to fibrosis and proliferation of fibrous tissue in stroma. The greatest changes occurred in internal intercostal muscle, while the least changes - in diaphragm.

Based on analysis of molecular and cellular changes in the respiratory tract of COB patients four main stages of the disease can be determined [17].

**Stage of aseptic inflammation.** It is caused by excessive production of ROS and nitric oxide in the respiratory tract. Its major clinical manifestation is productive cough. Important biomarkers of this stage of COB are: increased chemiluminescence in blood leukocytes and bronchial-alveolar lavage of smoking patients and increased concentration of nitric oxide in expiration of non-smoking patients. For correction of inflammation intake of water-soluble antioxidants is needed: N-acetyl cysteine, ascorbic acid, etc. Intake of active metabolites of Krebs cycle - monosodium glutamate, malate and, to less extent, succinic acid are useful. These metabolites increase resistance of phagocytes to pathogenic factors.

**Stage of obstructive changes.** The cause of this stage is some relative lack of  $\alpha_1$ -antitrypsin because of imbalance of proteolytic enzymes activity and their inhibitors in lung tissue. As criteria serve decreased rate of expiratory airflow and increased content of oxyprilin in urine of COB patients. Increased content of hydrogen peroxide in expiration of COB patients was also revealed. Basic therapy of chronic obstructive pulmonary syndrome includes bronchodilators, preferably of anticholinergic nature. Such treatment reduces severity of main clinical symptoms of the disease, the rate of progression of pathological process and significantly improves the quality of life. Regenerations of elastic base of lungs can contribute to inhalation of natural inhibitors of protease or synthetic  $\alpha_1$ -antitrypsin.

**Stage of reduction of bactericidal protection.** This stage is the result of blockade of oxygen-dependent bactericidal system of alveolar macrophages and neutrophils on the background



of atrophic changes of bronchial mucosa. Methodology of assessment of the degree of suppression of lung antibacterial protection requires improvements. It seems that for this purpose assessment of the degree of myeloperoxidase oppression in blood neutrophils, in bronchial-alveolar lavage or the degree of suppression of ROS production by neutrophils and macrophages can be used. Clinical feature of this stage is appearance of purulent sputum. At this only stage of the disease appears need for antibiotic therapy, often in combination with immunostimulators (polyoxydony). Antibiotics should be prescribed immediately and in doses sufficient to suppress purulent process. Use of specific vaccines and trial of oxygen therapy as a means of restoring of alveolar macrophages stimulation is also proved.

**Stage of severe respiratory failure.** The final stage of chronic obstructive bronchitis development is caused by two factors: decrease of the total respiratory alveolar surface caused by emphysema, and collapse of bronchiole at expiration caused by atrophy of elastic fibers and smooth muscles of the walls. Hypoxemia is the main feature of this stage of disease. Intensive but little effective work of the external breathing is also characteristic. At this stage bronchodilators lose their therapeutic value. To reduce respiratory failure prolonged oxygen therapy is required both in hospital and at home.

Currently the death rate from chronic bronchitis is equal to mortality from lung cancer that indicates the high social impact of the disease. In Europe COPD mortality rate ranges from 10.5 per 100,000 of population in France to 61.4 per 100,000 of population in the UK. In Germany mortality rate from complications of chronic bronchitis is the fourth behind heart diseases, cancer and neurological diseases and equals 63.7 per 100,000 of population [25, 27, 28].

COB is the cause of 80% of death cases and over 50% of disability among all bronchopulmonary system diseases [16].

In the structure of CNPD identified during mass studies of population CB proportion ranges from 62.3% to 90% [1, 27, 12, 22].

In recent decades CB as the cause of primary disability made 42% in the structure of CNPD and to one third of these patients was given II degree of invalidism [10, 15].

Moreover, in Russia according to appeal for medical aid CB morbidity made 10% in total and it prevails in men population.

Single studies conducted in different years showed high prevalence of CNPD in the structure of internal organs pathology in Yakutia and Magadan district [4, 6]. High prevalence of CNPD was also found in population of Taimyr Autonomous District (14.8%) and chronic bronchitis took the leading place in the structure of CNPD - 86.9% that was significantly higher than the Russian



average rate [5].

Until now, relatively more investigated is the prevalence of chronic bronchitis among the organized population employed in the mining industry of the Republic of Sakha (Yakutia). Thus, it varies from 183.0 to 219.0 per 1,000 workers [8]. And there are only some reports concerning CONP prevalence in rural residents of Yakutia [9].

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#### **Information about the authors:**

1. Sivtseva Anna Innokentievna - MD, Head of Respiratory Disease Research Group, Institute of Health NEFU named after M.K. Ammosov, 677000, Yakutsk, Vinokourov str. 21, apt. 24, c / ph.: 89141036523, e-mail: sannai@inbox.ru

2. Neustroeva Tatyana Semenovna - PhD, Senior Researcher of Respiratory disease Group, Institute of Health NEFU named after M.K. Ammosov, 677009, Yakutsk, Dzerzhinsky str. 36/1, apt. 22, c / ph.: 89141064537, e-mail: sannai@inbox.ru

3. Ivanova Mariana Adolfovna - Junior Researcher, Respiratory Disease Research Group, Institute of Health NEFU named after M.K. Ammosov, 677005, Yakutsk, Lermontov str. 58, apt. 32, c / ph.: 89241704624, e-mail: mariv.81 @ mail.ru

4. Petrova Yevgenia Robertovna - Junior Researcher, Respiratory Disease Research Group,





Institute of Health NEFU named after M.K. Ammosov, 677000, Yakutsk, Sergelyakhskoe sh. 4 km.

2C, c / ph.: 89241712395, e-mail: mariv.81 @ mail.ru