



**PATHOGENESIS AND PATHOMORPHOSIS OF CHRONIC OBSTRUCTIVE
PULMONARY DISEASE AT THE PRESENT STAGE**

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Abstract: Chronic obstructive pulmonary disease (COPD) remains a leading cause of morbidity and mortality worldwide. Traditionally viewed as a disease caused by exposure to harmful particles and gases (primarily tobacco smoke) and characterized by incompletely reversible bronchial obstruction, COPD is currently understood as a complex, heterogeneous, and systemic pathology. This review article highlights current understanding of COPD pathogenesis, focusing on key mechanisms: chronic inflammation, oxidative stress, protease and antiprotease imbalance, and autoimmune processes. Particular attention is paid to the concept of COPD pathomorphosis—the historical change in the clinical and morphological manifestations of the disease under the influence of environmental factors, new treatments, and changing pathomorphological profiles of patients. The shift from the classical dichotomy of chronic bronchitis/emphysema to an understanding of multiple phenotypes and endotypes of the disease is emphasized, opening the way to personalized therapy.

Keywords: COPD, pathogenesis, pathomorphosis, systemic inflammation, oxidative stress, phenotypes, airway remodeling.

Introduction. Chronic obstructive pulmonary disease (COPD) is a global medical and social problem. According to the WHO, COPD is the third leading cause of death worldwide [1]. The historically established model of pathogenesis, which associates the disease primarily with smoking and manifests itself as either chronic bronchitis or emphysema, has undergone significant evolution. Modern research demonstrates that COPD is a disease with a complex, multicomponent pathogenesis that extends far beyond the lungs, and with marked heterogeneity of clinical manifestations. The relevance of this topic is determined by the need to rethink old paradigms in light of new data on the mechanisms of disease development, which is dictated by both the changing patient profile (increasing number of non-smokers, the influence of new pollutants) and the insufficient effectiveness of existing standard therapy in a significant proportion of patients. The purpose of this review is to integrate current data on the key pathogenetic mechanisms of COPD and analyze the phenomenon of its pathomorphosis.

1. Modern aspects of COPD pathogenesis

The pathogenesis of COPD is a cascade of interrelated processes initiated by chronic exposure to pathogenic particles and gases.

1.1 Chronic inflammation: the cornerstone of pathogenesis

Inhalation of toxic agents (cigarette smoke, industrial dust) activates innate and adaptive immunity in the respiratory tract and lung parenchyma. The key effector cells are:

Neutrophils: Infiltrate the airways, releasing proteases (neutrophil elastase, matrix metalloproteinases (MMPs) and generating reactive oxygen species (ROS), which leads to the destruction of elastin and damage to the epithelium.

Macrophages: They are the main source of proinflammatory cytokines (FNO - α , IL-1 β , IL-6), chemokines (IL-8) and proteases (MMP-9, MMP-12). Their quantity in the lungs and sputum directly correlates with the severity of the disease [2].



Lymphocytes: An increase in the number of CD8+ cytotoxic T lymphocytes and CD4+ T helper type 1 (Th1) cells is observed. CD8+ lymphocytes are capable of inducing apoptosis. alveolar and epithelial cells, aggravating the damage. Recently, the role of Th17 lymphocytes and their associated IL-17 in maintaining neutrophilic inflammation has been discussed [3].

1.2. Imbalance in the protease- antiprotease and oxidant -antioxidant systems

The classical hypothesis proposed to explain the development of emphysema remains relevant, but has been significantly expanded.

Proteolytic cascade: Activated inflammatory cells release excess serine proteases (neutrophil elastase) and MMPs (MMP-9, -12), which destroy the structural proteins of the extracellular matrix (elastin, collagen) of the alveolar walls. A decrease in the activity of inhibitors (α 1-antitrypsin, TIMP) aggravates this process.

Oxidative stress: Tobacco smoke and activated leukocytes themselves generate massive amounts of ROS. Oxidative stress leads to direct damage to lipids, proteins, and cellular DNA, inactivation antiproteases , activation of proinflammatory transcription factors (NF- κ B), which enhances the inflammatory response, and induction of apoptosis [4].

1.3. Autoimmune mechanisms

One of the most significant modern discoveries is the role of autoimmunity in the persistence of inflammation in COPD even after smoking cessation. Destruction of lung tissue by proteases and oxidants leads to the exposure of previously hidden autoantigens (e.g., elastin, collagen). This can trigger the production of autoantibodies and the activation of autoreactive T lymphocytes, perpetuating chronic inflammation regardless of the initial damaging factor [5].

1.4 Systemic effects

Chronic inflammation in COPD is not limited to the lungs. Inflammatory mediators (such as IL-6, FNO - α , and C-reactive protein) enter the systemic circulation, causing systemic manifestations such as cachexia, muscle dysfunction, osteoporosis, cardiovascular disease, anemia, and neurocognitive impairment. This confirms COPD's status as a systemic disease.

2. Pathomorphosis of COPD at the present stage

Pathomorphism is the historical change in the clinical and morphological manifestations of a disease. For COPD, this manifests itself in several key aspects.

2.1. Change in the etiological portrait

Although tobacco smoking remains the main risk factor, there is an increase in the importance of other causes:

Air pollution: Particulate matter (PM_{2.5}, PM₁₀) and nitrogen dioxide are recognized as independent risk factors for the development and exacerbation of COPD [6].

Occupational hazards: The contribution of industrial dust, fumes and vapors to the development of COPD in non-smokers is becoming increasingly evident.

Biomass: Using fossil fuels for cooking and heating in poorly Ventilated indoor air is the leading cause of COPD in women in developing countries.

2.2. Evolution of pathomorphological characteristics

"Classic" panacinar emphysema associated with α 1-antitrypsin deficiency is becoming a relatively rare phenomenon.

Predominance of centriacinar Emphysema in smokers remains, however, modern studies using HRCT reveal greater heterogeneity: a combination of emphysematous and bronchitis changes in one patient, and a predominance of the "air trap" phenomenon over emphysema itself in the early stages.



Small airway remodeling (<2 mm in diameter) is recognized as a key pathological substrate of airway obstruction in COPD. It includes airway wall fibrosis, goblet cell hyperplasia, epithelial metaplasia, and accumulation of inflammatory exudate (obstructive follicular bronchiolitis).

2.3. Clinical pathomorphosis : from dichotomy to phenotypes

The strict division into "emphysematous" (the "pink puffer " type) and " bronchitis " (the "blue edema " type) is becoming a thing of the past. Modern medicine operates with the concept of COPD phenotypes—stable characteristics that allow one to predict the course of the disease and the response to therapy [7]. The following are distinguished:

Emphysematous phenotype.

Bronchitis (chronic bronchitis) phenotype.

Phenotype with frequent exacerbations.

Phenotype with overlap syndrome (COPD + bronchial asthma).

Phenotype with a predominance of extrapulmonary manifestations (cachexia, muscle dysfunction).

The phenotypic approach is being replaced by the search for endotypes - subtypes of the disease determined by specific biological mechanisms (for example, eosinophilic vs. neutrophilic endotype), which is the basis for targeted therapy.

2.4. Effect of therapy on pathomorphism

The widespread use of inhaled corticosteroids (ICS) and long-acting bronchodilators has altered the natural history of the disease: exacerbation rates have decreased, progression has slowed, and quality of life has improved. However, long-term ICS therapy, especially in elderly patients with comorbidities , is associated with new clinical challenges , such as an increased risk of pneumonia and the development of steroid-induced complications.

Conclusion

The current understanding of COPD pathogenesis has evolved from a simplified model based on protease imbalance and inflammation to a comprehensive concept that incorporates the role of oxidative stress, autoimmune processes, and systemic effects. The pathomorphosis of COPD is manifested by changing etiologies, a "mixing" of classic pathomorphological features, the dominance of small airway remodeling , and a shift toward a phenotypic and endotypic classification of the disease. These changes reflect the influence of new environmental threats, diagnostic advances (HRCT), and the widespread use of pharmacotherapy. Further research should focus on identifying biomarkers for precise endotype determination , which will enable a transition from a uniform treatment approach to truly personalized medicine targeting key pathogenetic links in individual patients.

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