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PATHOPHYSIOLOGICAL MECHANISMS OF MORPHOFUNCTIONAL POLYMORPHISM OF THE LARYNGEAL MUCOSA IN CHRONIC LARYNGITIS

Baxranova Malika Shavkatovna
PhD student, Samarkand State Medical University

Abstract: Chronic laryngeal diseases are accompanied by diverse structural and functional alterations of the laryngeal mucosa, referred to as morphofunctional polymorphism. These changes include epithelial hyperplasia, squamous metaplasia, subepithelial fibrosis, glandular hypertrophy, and vascular remodeling, which are closely associated with impaired mucosal elasticity and vocal fold function. Environmental and lifestyle factors, such as smoking, occupational irritants, and gastroesophageal reflux, significantly contribute to the development of chronic laryngeal pathology. Immune responses, oxidative stress, and neurogenic mechanisms play a critical role in the persistence and progression of these alterations. Understanding the pathophysiological mechanisms underlying morphofunctional polymorphism is essential for accurate diagnosis, prediction of disease progression, and the development of targeted preventive and therapeutic strategies. This article provides a comprehensive analysis of current literature on chronic laryngeal diseases, emphasizing the cellular, molecular, and functional mechanisms that determine the diversity of mucosal changes.

Key words: Chronic laryngitis, laryngeal mucosa, morpho functional polymorphism, epithelial hyperplasia, subepithelial fibrosis, glandular hypertrophy, vascular remodeling, oxidative stress, neurogenic inflammation, vocal fold dysfunction.

Introduction. Chronic diseases of the larynx represent a significant and growing problem in modern clinical medicine, particularly within the fields of otorhinolaryngology, pathology, and clinical immunology. The larynx plays a critical role not only in phonation and respiration, but also in airway protection and immune defense. Its mucosal lining is constantly exposed to a wide range of physical, chemical, and biological irritants, including environmental pollutants, tobacco smoke, occupational hazards, infectious agents, and gastroesophageal reflux. Prolonged or repeated exposure to such factors can lead to persistent inflammatory processes, structural remodeling, and functional impairment of the laryngeal mucosa. In this context, the study of pathophysiological mechanisms underlying morpho functional polymorphism of the laryngeal mucosa in chronic conditions is of considerable scientific and practical importance. Morpho functional polymorphism of the laryngeal mucosa refers to the diversity of structural and functional alterations that develop in response to chronic pathological stimuli. These changes may include epithelial hyperplasia or atrophy, metaplasia, dysplasia, subepithelial fibrosis, glandular hypertrophy, vascular remodeling, and alterations in local immune responses. Such variability reflects the complex interplay between damaging factors and adaptive-compensatory mechanisms of the mucosa. Understanding these mechanisms is essential for explaining the heterogeneity of clinical manifestations observed in chronic laryngeal diseases, ranging from mild dysphonia to severe airway obstruction and precancerous lesions.

Chronic inflammatory conditions of the larynx, including chronic laryngitis of various etiologies, are among the most common disorders affecting voice professionals and individuals exposed to adverse environmental conditions. Despite their high prevalence, the pathogenesis of these conditions remains insufficiently elucidated, particularly with regard to the cellular and

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molecular mechanisms that drive long-term mucosal remodeling. Chronic inflammation is known to disrupt normal epithelial differentiation, impair mucociliary clearance, and alter the balance between pro-inflammatory and anti-inflammatory mediators. Over time, these processes may lead to irreversible morpho functional changes, significantly reducing the regenerative capacity of the laryngeal mucosa. At the cellular level, persistent inflammatory stimulation activates a wide range of immune and non-immune cells, including macrophages, lymphocytes, mast cells, fibroblasts, and endothelial cells. These cells produce cytokines, chemokines, growth factors, and matrix metalloproteinases that modulate tissue repair and extracellular matrix turnover. Dysregulation of these signaling pathways contributes to pathological remodeling, fibrosis, and angiogenesis. Moreover, repeated epithelial injury and regeneration increase the risk of abnormal cellular differentiation, creating conditions favorable for the development of epithelial dysplasia and malignant transformation.

Functional alterations of the laryngeal mucosa are closely linked to its structural changes. The viscoelastic properties of the mucosa, which are essential for normal vocal fold vibration, are highly sensitive to inflammatory edema, fibrosis, and changes in glandular secretion. Even subtle morphologic disturbances can result in significant voice disorders, negatively affecting quality of life and professional performance. Therefore, a comprehensive analysis of morpho functional polymorphism is necessary not only from a theoretical standpoint but also for improving diagnostic accuracy and therapeutic strategies. Recent advances in histopathology, immunohistochemistry, and molecular biology have provided new insights into the mechanisms of chronic mucosal inflammation and remodeling. Studies have demonstrated the involvement of oxidative stress, epithelial barrier dysfunction, microbiome alterations, and neurogenic inflammation in the pathophysiology of chronic laryngeal diseases. However, existing data are often fragmented and lack a unified conceptual framework that explains the diversity of morpho functional changes observed in clinical practice. This underscores the need for integrative, analytical research focused on the pathophysiological basis of mucosal polymorphism. Furthermore, the growing incidence of chronic laryngeal disorders associated with lifestyle factors, such as smoking, alcohol consumption, and vocal overuse, as well as systemic diseases and aging, highlights the relevance of this research topic. Age-related changes in tissue regeneration, immune response, and microcirculation may significantly modify the course of chronic inflammation and contribute to distinct morpho functional phenotypes of the laryngeal mucosa.

In light of the above considerations, an in-depth analysis of the pathophysiological mechanisms responsible for morpho functional polymorphism of the laryngeal mucosa in chronic conditions is both timely and necessary. Elucidating these mechanisms will enhance understanding of disease progression, facilitate early identification of high-risk morphological patterns, and support the development of targeted preventive and therapeutic interventions. This scientific analytical article aims to synthesize current knowledge on the structural and functional alterations of the laryngeal mucosa in chronic pathology, emphasizing the underlying pathophysiological processes that determine their diversity and clinical significance.

Literature review. The problem of chronic diseases of the larynx and the associated morpho functional changes of the laryngeal mucosa has been widely discussed in scientific literature over the past decades. Numerous experimental and clinical studies have focused on the structural remodeling of the mucosa, mechanisms of chronic inflammation, and functional disturbances of the vocal folds. However, despite the abundance of research, the issue of morpho functional polymorphism of the laryngeal mucosa in chronic pathological conditions remains

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insufficiently systematized, and many aspects of its pathophysiology continue to be debated. Early morphological studies of the laryngeal mucosa emphasized the role of chronic inflammation as a key etiological factor leading to epithelial and subepithelial alterations. Classical histological investigations described epithelial hyperplasia, squamous metaplasia, thickening of the basement membrane, and infiltration of inflammatory cells as characteristic features of chronic laryngitis. These studies laid the foundation for understanding that prolonged inflammatory exposure results not only in reversible changes but also in persistent structural remodeling that affects mucosal function.

Subsequent research expanded the focus to include ultrastructural and immunohistochemical analyses. Investigations using electron microscopy revealed damage to ciliated epithelial cells, disruption of intercellular junctions, and degeneration of mucous-secreting glands. Immunohistochemical studies demonstrated increased expression of pro-inflammatory cytokines, such as interleukin-1β, tumor necrosis factor-α, and interleukin-6, as well as growth factors involved in tissue repair and fibrosis. These findings confirmed that chronic inflammation of the laryngeal mucosa is a dynamic process involving continuous interaction between immune responses and tissue regeneration mechanisms. A significant body of literature has addressed the role of environmental and lifestyle factors in the development of chronic laryngeal pathology. Smoking has been consistently identified as a major contributor to mucosal damage, inducing oxidative stress, epithelial dysplasia, and vascular changes. Studies have shown that tobacco smoke alters mucous secretion, impairs local immunity, and promotes chronic inflammatory infiltration, thereby enhancing morpho functional heterogeneity of the laryngeal mucosa. Similarly, exposure to industrial pollutants and occupational irritants has been associated with increased prevalence of chronic laryngeal disorders and distinct morphological patterns. Another extensively studied factor is laryngopharyngeal reflux, which has been recognized as an important cause of chronic laryngeal inflammation. Numerous authors have reported that prolonged exposure of the laryngeal mucosa to gastric acid and pepsin leads to epithelial erosion, edema, and inflammatory infiltration. Reflux-related laryngeal pathology is characterized by specific morpho functional features, including increased epithelial permeability, altered glandular secretion, and heightened sensitivity of sensory nerve endings. These studies highlight the multifactorial nature of chronic laryngeal diseases and the diversity of mucosal responses to different pathological stimuli.

In recent years, attention has increasingly shifted toward the molecular and cellular mechanisms underlying chronic mucosal remodeling. Research has demonstrated the involvement of fibroblasts and myofibroblasts in subepithelial fibrosis and extracellular matrix accumulation. The dysregulation of matrix metalloproteinases and their inhibitors has been implicated in abnormal tissue remodeling, contributing to changes in mucosal elasticity and vocal fold vibration. Additionally, angiogenesis and microcirculatory disturbances have been identified as important components of chronic inflammatory processes, influencing tissue oxygenation and metabolic balance. The role of local immune defense and mucosal barrier function has also been extensively explored. Several studies have shown that chronic inflammation disrupts the integrity of the epithelial barrier, leading to increased permeability and susceptibility to secondary infections. Alterations in the composition of the local microbiota have been reported, suggesting a potential contribution of microbial dysbiosis to persistent inflammation and morpho functional polymorphism. Moreover, neurogenic inflammation mediated by sensory nerve fibers and neuropeptides has been proposed as an additional mechanism influencing vascular tone, glandular activity, and inflammatory responses. From a

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functional perspective, numerous clinical investigations have examined the relationship between morphological changes of the laryngeal mucosa and voice disorders. Researchers have demonstrated that edema, fibrosis, and epithelial thickening significantly affect the viscoelastic properties of the vocal folds, resulting in dysphonia of varying severity. Voice analysis and stroboscopic studies have provided evidence that even minor structural abnormalities can lead to pronounced functional impairment, emphasizing the clinical relevance of morpho functional diversity. Despite substantial progress, the literature reveals several unresolved issues. Many studies focus on isolated aspects of laryngeal pathology, such as inflammation, reflux, or smoking-related changes, without considering their combined effects on mucosal polymorphism. In addition, there is a lack of standardized morphological criteria for classifying chronic changes of the laryngeal mucosa, which complicates comparative analysis and clinical interpretation. Furthermore, limited attention has been given to the adaptive and compensatory mechanisms that may underlie different morpho functional phenotypes in chronic conditions.

Overall, the analysis of existing literature indicates that morpho functional polymorphism of the laryngeal mucosa in chronic diseases is the result of complex, multifactorial pathophysiological processes. While significant data have been accumulated on individual mechanisms, there remains a clear need for integrative analytical studies that synthesize morphological, functional, immunological, and molecular findings. Such an approach is essential for advancing the understanding of chronic laryngeal pathology and for developing more effective diagnostic and therapeutic strategies.

Research discussion. The analysis of existing studies on chronic laryngeal diseases and morpho functional polymorphism of the laryngeal mucosa demonstrates the complexity and multifactorial nature of these conditions. Chronic inflammatory processes are not merely localized epithelial reactions but involve intricate interactions between structural, cellular, and molecular mechanisms. Morpho functional changes, such as epithelial hyperplasia, squamous metaplasia, subepithelial fibrosis, and glandular hypertrophy, represent adaptive responses of the mucosa to persistent pathological stimuli. However, while these changes may initially be protective, prolonged or excessive remodeling can lead to functional impairment, decreased regenerative potential, and increased risk of precancerous transformations. One key aspect of the discussion is the role of environmental and lifestyle factors. Tobacco smoke, occupational irritants, and gastroesophageal reflux contribute significantly to mucosal injury and polymorphic remodeling. The literature shows that the type and intensity of exposure often determine the specific morpho functional phenotype of the laryngeal mucosa. For example, tobacco-induced oxidative stress primarily affects epithelial integrity and vascular structures, while reflux-induced chemical irritation leads to edema, glandular dysfunction, and heightened sensitivity of sensory nerve endings. These findings highlight the necessity of considering individual etiological factors when evaluating mucosal polymorphism in chronic laryngeal pathology.

Immunological and cellular mechanisms are equally important. Persistent inflammation activates a broad range of immune and non-immune cells, which release cytokines, growth factors, and enzymes that regulate tissue repair and remodeling. Dysregulation of these pathways can exacerbate fibrosis, angiogenesis, and extracellular matrix accumulation, resulting in alterations of the viscoelastic properties of the mucosa and impaired vocal fold function. Neurogenic inflammation has also been proposed as a significant contributor, modulating both vascular tone and glandular activity, thereby influencing local tissue homeostasis. Recent molecular studies have provided insights into oxidative stress, epithelial barrier dysfunction, and microbial dysbiosis as underlying contributors to mucosal polymorphism. Disruption of the

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epithelial barrier increases susceptibility to secondary infections and perpetuates inflammatory signaling. Alterations in the local microbiota can further exacerbate chronic inflammation, suggesting that morpho functional variability is influenced not only by external irritants but also by intrinsic changes in the mucosal microenvironment.

Clinically, the functional consequences of morpho functional polymorphism are substantial. Edema, fibrosis, and epithelial thickening can compromise the vibratory properties of the vocal folds, leading to dysphonia, reduced vocal endurance, and in severe cases, airway obstruction. Stroboscopic and acoustic analyses confirm that even minor structural changes can significantly impair voice quality, highlighting the importance of early detection and preventive management strategies. Despite substantial progress in understanding these processes, the discussion reveals several limitations in current research. Most studies focus on individual pathogenic factors or isolated morphological changes, lacking integrative approaches that correlate histological, molecular, and functional findings. Furthermore, there is no universally accepted classification of chronic laryngeal mucosal changes, which complicates comparison of results across studies and limits the applicability of findings in clinical practice. Adaptive and compensatory mechanisms, which may explain variability in morpho functional phenotypes among patients with similar exposures, remain poorly investigated.

The discussion underscores that morpho functional polymorphism of the laryngeal mucosa in chronic diseases is the outcome of complex interactions between environmental exposures, cellular responses, immunological activity, and molecular signaling pathways. Understanding these interactions is critical for accurate diagnosis, prediction of disease progression, and development of targeted therapeutic interventions. Future research should focus on integrative studies that combine morphological, functional, and molecular analyses, as well as longitudinal investigations that assess the dynamics of mucosal remodeling in response to chronic pathological stimuli. Such an approach will provide a more comprehensive understanding of chronic laryngeal diseases and inform strategies for prevention, treatment, and rehabilitation of affected individuals.

Conclusion. Chronic diseases of the larynx are characterized by pronounced morpho functional polymorphism of the laryngeal mucosa, which reflects the complex interplay of structural, cellular, and molecular mechanisms in response to prolonged pathological stimuli. Morphological changes, including epithelial hyperplasia, squamous metaplasia, subepithelial fibrosis, glandular hypertrophy, and vascular remodeling, are closely associated with functional impairments such as dysphonia, reduced mucosal elasticity, and impaired vocal fold vibration. Environmental and lifestyle factors, including smoking, occupational irritants, and gastroesophageal reflux, significantly influence the type and severity of mucosal alterations, while immune and inflammatory responses, oxidative stress, and neurogenic mechanisms contribute to the persistence and progression of these changes.

The literature highlights the multifactorial nature of chronic laryngeal pathology and emphasizes the need for integrative approaches that combine morphological, functional, and molecular analyses. Despite advances in understanding individual mechanisms, standardized criteria for classifying morpho functional polymorphism are lacking, and adaptive compensatory processes remain underexplored. Addressing these gaps is essential for improving diagnostic accuracy, predicting disease progression, and developing targeted preventive and therapeutic strategies.

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