

# MORPHOFUNCTIONAL POLYMORPHISM OF THE MUCOSA IN CHRONIC LARINGITIS

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## Abstract

Chronic laryngitis, characterized by inflammation of laryngeal tissue, is the most commonly diagnosed organic voice disorder, but treatments targeting putative etiologic factors have shown limited effectiveness. A major obstacle to the development of improved treatments for chronic laryngitis is a fundamental gap in knowledge regarding the pathophysiology of laryngeal inflammation. This article provides a review of the literature on the polymorphism of chronic laryngitis.

**Keywords** Chronic laryngitis, acute laryngitis, PCD, GERD, Reinke-Hajek's edematous polyposis laryngitis, CD differentiation cluster.

## INTRODUCTION

Chronic laryngitis, characterized by inflammation of laryngeal tissue, is the most commonly diagnosed organic voice disorder, but treatments targeting putative etiologic factors have shown limited effectiveness. A major obstacle to the development of improved treatments for chronic laryngitis is a fundamental gap in knowledge regarding the pathophysiology of laryngeal inflammation. Diseases of the larynx occupy a leading place in the general structure of pathology of the upper respiratory tract. Chronic laryngitis, according to various authors, accounts for up to 34% of inflammatory pathology of the larynx.

Chronic laryngitis is the most commonly diagnosed organic voice disorder, with almost 10% of all cases of dysphonia classified as such [12,13]. Laryngitis is an inflammation of the tissues of the larynx caused by infectious (for example, viral, bacterial, fungal) and mechanical agents. Depending on the nature of the course of the disease, there are: acute form of laryngitis (has a sudden development, accompanied by vivid manifestations); chronic form (alternating with phases of exacerbation and remissions).

Acute laryngitis. Most cases of laryngitis are temporary and resolve once the underlying cause is addressed. Causes of acute laryngitis include

viral infections similar to those that cause the common cold, vocal tension caused by shouting or excessive use of the voice, and bacterial infections, although these are less common [6].

Chronic laryngitis. Laryngitis that lasts more than three weeks is known as chronic laryngitis. This type of laryngitis is usually caused by prolonged exposure to irritants. There are the following forms of chronic laryngitis:

- Catarrhal chronic laryngitis
- Atrophic chronic laryngitis
- Hyperplastic

Chronic laryngitis can cause vocal cord stretching, injury, or growths (polyps or nodules). Chronic laryngitis develops gradually, with major signs and symptoms waxing and waning over very long periods of time. The disease is characterized by a variety of symptoms, including a hoarse voice, difficulty speaking, sore throat, coughing and coughing. Examination of the larynx is variable but usually reveals diffuse supraglottic and glottal erythema and edema in addition to excessive mucus thickness [9].

Although chronic inflammatory diseases of the larynx are quite common, their therapy has so far been carried out without taking into account the cause of the disease, which significantly reduces the effectiveness of therapeutic treatment. Pathogenetically based effective treatment of exacerbation of chronic laryngitis allows you to quickly not only restore voice function, but also detect malignant neoplasms if they are present. New ideas about the etiology and pathogenesis of chronic laryngitis require the development of pathogenetically based methods of its treatment. In the last decade, gastroesophageal reflux disease (GERD) has attracted increased attention from doctors, as it plays an important role in the development of diseases of the ENT organs. According to Toohill et al. in 4 - 10% of cases, the cause of ENT pathology is gastroesophageal reflux disease. According to new ideas about the etiology of the disease, a clear understanding of the acid-forming function of the stomach is also of great importance for the correct choice of treatment

method. The question of the role of microbial factors in the development of chronic inflammatory diseases of the larynx remains controversial. A number of authors do not consider microbial flora to be the leading cause in the genesis of chronic laryngitis or completely deny the bacterial etiology of the disease. According to Feigin G. A. (2003), in chronic laryngopharyngitis or pharyngolaryngotracheobronchitis, persistent changes in the mucous membrane of the larynx are associated with the action of viruses, which subsequently contribute to an increase in bacterial contamination of the respiratory tract.

Chronic polyposis-edematous laryngitis Reinke-Hajek (Reinke's edema, or smoker's laryngitis) is one of the forms of chronic hyperplastic laryngitis. This disease is classified as tumor-like along with vocal fold nodules, polyps, cysts and nonspecific granulomas. The incidence of benign diseases of the larynx is 55–70% among productive processes of the upper respiratory tract, in particular polyps make up 39–68%, papillomas – 24–59%, Reinke's edema – 5.5%, cysts – 5%, nonspecific granulomas – 3 –4%, amyloidosis – less than 1% [5]. For effective treatment of this disease, it is necessary to take into account the etiological factors and its pathogenesis. The development of Reinke's edema is associated with smoking and is more common in women (80%) between 40 and 60 years of age [10]. Reinke-Hajek edematous-polyposis laryngitis is characterized by a specific zone of neoplasm formation, namely the membranous part of the vocal folds. Ulcerative changes, granulations, and scars may be present, as well as benign vocal fold pathology such as polypoid changes or Reinke's edema. Signs of chronic inflammation are present in the form of diffusely located connective tissue cords infiltrated by inflammatory cells, with foci of fibrosis and partial sclerosis. [2]. Regardless of clinical and morphological affiliation, in all cases there is a violation of microcirculation in the area of Reinke's space, with phenomena of hyperpermeability of the capillary bed and the formation of tissue interstitial edema. Lymphatic drainage of the larynx is complex, which reflects the different embryological origin of the supraglottis, but it can be assumed that lymphoid

cells from the larynx migrate to the deep cervical chain of lymph nodes [10]. A feature of the lymphatic drainage system of the connective tissue of the Reinke space is the insufficiency of the lymphocapillary system and the almost complete absence of collector formations. Lymphoid fluid must overcome a number of obstacles on the way to the collector systems of the larynx, dense tissue of the vocal cord and vocal muscle, tissue of the thyroid cartilage, sub- and supraglottic sections of the mucous membrane of the larynx. Similar studies of the lymphatic drainage pathway have been investigated using the determination of the marker molecule of endothelial cells CD34+, which makes it possible to determine the outlines of lymphatic vessels, with the presence of lymphostasis phenomena. At the same time, the authors clearly show the difference between lymphostatic formations and the presence of interstitial edema, as a result of disorganization of the structures of the connective tissue matrix. The laryngeal epithelium is a covering tissue that is in direct contact with actively or passively arriving antigens, irritants and triggers that trigger the first line of defense in the form of activation of innate immune cells, determining the generation of pro-inflammatory cytokines through Toll-like receptors and their signaling pathways, mediating inflammatory reactions. In turn, epithelial cells expressing the CD80 molecule, initiate recognition and presentation of antigens, mediating the activity of effector reactions of adaptive immunity. A number of studies have shown the informativeness of the expression of markers p53, Ki67, CD138 as criteria for the risk of developing a malignant process in various chronic inflammatory pathologies of the larynx [15,16]. Involvement in the implementation of reparative processes at the stages of chronic inflammation of matrix metalloproteinases, activated by a change in the cytokine repertoire at the site of inflammation, is accompanied, on the one hand, by disorganization and disintegration of the intercellular matrix, including basement membranes; on the other hand, activation of fibroblasts leads to increased expression of endogenous inducers of vasculogenesis and repair

[15]. However, it cannot be ruled out that the tissue interstitial edema observed in polyposis with scant leukocyte content is a consequence of a reduction in the synthesis of pro-inflammatory cytokines under the influence of matrix metalloproteinases.

Infectious and inflammatory diseases of the respiratory tract are characterized by a variety of clinical and morphological manifestations, which is associated with the specific structure of the respiratory tract and a large number of etiological factors affecting the respiratory tract. Therefore, the creation of experimental models for an objective assessment of the condition of the laryngeal mucosa and their specific pharmacological activity is one of the pressing issues of registration of new pharmacological substances and drugs used in the treatment of chronic laryngitis. Chronic laryngitis occurs under the influence of a number of exogenous factors: prolonged exposure to cold or hot air, smoking, alcohol, contact with dust, shavings, toxic substances in the air, prolonged voice strain, etc. Some researchers note that chronic laryngitis usually develops gradually, and the main signs and symptoms may wax and wane over long periods of time, while chronic laryngitis is rarely considered an infectious process [7,8].

Some researchers note the frequent combination of chronic laryngitis with the presence of metabolic syndrome, with a predominance of the female population in the association of metabolic syndrome and chronic laryngitis, however, the reason for the gender difference is not entirely clear. The larynx, located at the junction of the respiratory and gastrointestinal tracts, is the primary site of exposure to pathogens and irritants. Not the last place in the implementation of this pathology is occupied by constitutional features and hormonal levels [6]. According to modern concepts, vocal fold polyps are classified as benign exudative neoplasms [11,17]. A separate subgroup includes edematous polyposis laryngitis, or Reinke-Hajek disease, which is morphologically located on the membranous part of the vocal folds. The formation of edema in the area of Reinke's space is a consequence of a deficiency of lymphatic

drainage supply to the membranous part of the vocal folds. The anatomical characteristics of Reinke's space also play a role. Literature data indicate the presence of a single pathomorphosis of changes that are realized in the form of microthrombosis, plasmorrhagia, fibrin deposits, interstitial edema and activation of neoangiogenesis processes, the intensity of which is reflected in the formation of histologically different morphotypes of polyps: myxomatous, angiomatous or mixed.

According to a number of authors, benign laryngeal formations account for about 60% of all laryngeal diseases. Benign diseases of the larynx often lead to dysfunction of the respiratory and phoniatic functions. A large percentage of benign neoplasms of the larynx are associated with functional loads on this organ, which experiences mechanical and other types of impact. Precancerous diseases of the larynx (PCD) belong to the category of head and neck diseases that combine fundamental aspects of molecular genetic processes that carry the potential for malignancy of laryngeal epithelial cells, a fairly wide prevalence and great practical significance. The lack of prognostic criteria for the likelihood of malignancy of laryngeal cells, which have specificity and sensitivity values acceptable in the practical work of a doctor, does not allow the development of a unified algorithm for the management, treatment and follow-up of patients with this pathology. Currently, analysis of the pathomorphology of surgical and biopsy material with verification of the degree of dysplasia/hyperplasia of the laryngeal epithelium is the only methodological approach used in practice for screening patients by risk groups [1,3]. Taking material for histological examination is associated with objective difficulties associated with the anatomical and physiological characteristics of the larynx, and also different interpretation of drugs unnecessarily delays diagnosis, which cannot but affect the results of treatment and prognosis of the disease. The ambiguity in the interpretation of the pathomorphology of the epithelial lining of the larynx often raises questions among attending physicians.

## CONCLUSIONS

Thus, chronic laryngitis, characterized by inflammation of laryngeal tissue, is the most commonly diagnosed voice disorder, but treatments targeting putative etiologic factors have shown limited effectiveness. A major obstacle to the development of improved treatments for chronic laryngitis is a fundamental gap in knowledge regarding the pathophysiology of laryngeal inflammation. Likewise, the role of resident and pathogenic bacteria in the formation of laryngeal immune responses has not been established. Basic research examining the specific biological mechanisms underlying laryngeal inflammation is urgently needed to improve the treatment of chronic laryngitis.

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