

DOI: 10.18481/2077-7566-20-16-2-5-10  
УДК: 616.31-02:616.34

## СОВРЕМЕННЫЕ АСПЕКТЫ ЭТИОПАТОГЕНЕЗА, КЛИНИКИ И ЛЕЧЕНИЯ ПАТОЛОГИИ СЛИЗИСТОЙ ОБОЛОЧКИ РТА У ПАЦИЕНТОВ С ЗАБОЛЕВАНИЯМИ ЖЕЛУДОЧНО-КИШЕЧНОГО ТРАКТА

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### Аннотация

**Предмет.** Несмотря на множество патогенетических звеньев поражений желудочно-кишечного тракта и слизистой оболочки рта, остаются нерешенными вопросы, связанные с их этиопатогенезом, диагностикой и проведением качественных лечебно-профилактических мероприятий. Среди различных патологических процессов, проявляющихся на слизистой оболочке рта, рецидивирующий афтозный стоматит представляет собой хроническое заболевание, для которого характерно появление вторичных патоморфологических элементов (афт) в ответ на развитие острого пролиферативного воспаления.

**Цель** — анализ и систематизация литературных данных по проблеме поражения слизистой оболочки рта при кислотозависимых заболеваниях желудочно-кишечного тракта.

**Методология.** Рецидивирующие афты полости рта относятся к хронической патологии слизистой оболочки рта, характеризуются длительным течением и периодическими рецидивами, которые чаще всего связаны с состоянием соматического статуса, в том числе и наличием кислотозависимых заболеваний желудочно-кишечного тракта.

**Результаты.** Основной патоморфологический элемент, свойственный данной патологии, — афта. Ее локализация — слизистая оболочка преддверия полости рта, щек и боковой поверхности языка, визуальна овальной или округлой формы, покрыта грязно-белым фибринозным налетом. Лечение рецидивирующих афт полости рта включает комплекс, состоящий из общей системной терапии основного заболевания. Местное лечение включает применение препаратов антигистаминного ряда, иммунокоррекции, средств, повышающих неспецифическую гипосенсибилизацию, нормализацию клеточного метаболизма и стимулирующих механизмы неспецифической защиты, витаминотерапии и методов физиотерапии.

**Выводы.** Данное лечение в итоге должно быть направлено на устранение не только болевых ощущений, но и на повышение факторов местного иммунитета, борьбу с патогенной микрофлорой и способствовать эпителизации патологических процессов на слизистой оболочке рта. Важное значение при лечении и профилактике рецидивирующих афт имеет комплексное обследование пациента с целью выявления факторов риска.

**Ключевые слова:** слизистая оболочка рта, рецидивирующие афты, заболевания желудочно-кишечного тракта, факторы риска, качество жизни

Авторы заявили об отсутствии конфликта интересов.

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Гурьевская О. А., Ишмухаметова А. Н., Сарвалиева А. Ф.  
СОВРЕМЕННЫЕ АСПЕКТЫ ЭТИОПАТОГЕНЕЗА, КЛИНИКИ  
И ЛЕЧЕНИЯ ПАТОЛОГИИ СЛИЗИСТОЙ ОБОЛОЧКИ РТА У ПАЦИЕНТОВ  
С ЗАБОЛЕВАНИЯМИ ЖЕЛУДОЧНО-КИШЕЧНОГО ТРАКТА  
Проблемы стоматологии, 2020, т. 16, № 2, стр. 5—10  
© Галимова И. А. и др. 2020  
DOI: 10.18481/2077-7566-20-16-2-5-10

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### For citation:

Galimova I. A., Usmanova I. N., Khismatullina Z. R., Granot Yigal,  
Guryevskaya O. A., Ishmukhametova A. N., Sarvalieva A. F.  
MODERN ASPECTS OF ETIOPATHOGENESIS, CLINICS AND  
TREATMENT OF PATHOLOGY MUCOUS MEMBRANE OF MOUTH  
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Actual problems in dentistry, 2020, vol. 16, № 2, pp. 5—10  
© Galimova I. A. et al. 2020  
DOI: 10.18481/2077-7566-20-16-2-5-10

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## MODERN ASPECTS OF ETIOPATHOGENESIS, CLINICS AND TREATMENT OF PATHOLOGY MUCOUS MEMBRANE OF MOUTH IN PATIONS WITH GASTROINTESTINAL TRACT DISEASES

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### Annotation

**Subject.** Despite the many pathogenetic links in the lesions of the gastrointestinal tract and oral mucosa, unresolved issues related to their etiopathogenesis, diagnosis and high-quality therapeutic and preventive measures. Among the various pathological processes manifesting on the oral mucosa, recurrent aphthous stomatitis is a chronic disease characterized by the appearance of secondary pathomorphological elements (aphthae) in response to the development of acute proliferative inflammation.

**The goal** is the analysis and systematization of literature data on the problem of damage to the oral mucosa in acid-dependent diseases of the gastrointestinal tract.

**Methodology.** Recurrent aphthae of the oral cavity belong to the chronic pathology of the oral mucosa, are characterized by a prolonged course and periodic relapses, which are most often associated with the state of somatic status, including the presence of acid-dependent diseases of the gastrointestinal tract.

**Results.** The main pathomorphological element inherent in this pathology is aphtha. Its localization is the mucous membrane of the vestibule of the oral cavity, cheeks, and lateral surface of the tongue, visually oval or round, covered with a dirty white fibrinous coating. Treatment of recurrent aphthae of the oral cavity includes a complex consisting of general systemic therapy of the underlying disease. Local treatment includes the use of antihistamines, immunocorrection, drugs that increase nonspecific hypersensitivity, normalization of cellular metabolism and stimulate nonspecific defense mechanisms, vitamin therapy and physiotherapy methods.

**Conclusions.** This treatment should ultimately be aimed at eliminating not only pain, but also at increasing local immunity factors, combating pathogenic microflora and promoting the epithelization of pathological processes on the oral mucosa. Of great importance in the treatment and prevention of recurrent aphthae is a comprehensive examination of the patient in order to identify risk factors.

**Keywords:** oral mucosa, recurrent aphthosis, gastrointestinal tract diseases, risk factors, quality of life

**The authors declare no conflict of interest.**

### Introduction

Among the various pathological processes manifesting on the oral mucosa - recurrent aphthosis is a chronic disease with unclear etiopathogenesis, which is characterized by the appearance of secondary pathomorphological elements - aphthae in response to the development of proliferative inflammation. The frequency of manifestations of recurrent aphthae of the oral cavity in the general population varies on average from 10 to 20 % of cases, however, with diseases of the gastrointestinal tract, there is a tendency to increase them from 60 to 87.8 % of examinations [16]. The age of most patients with mucosal pathology ranges from 20 to 40 years with a predominance in women [1, 14, 19—21, 32, 36, 37, 39]. Numerous researchers have proven the relationship between the oral cavity and the gastrointestinal tract within the framework of a single morphofunctional system with the reflection of various pathological processes affecting the quality of life of patients [5—9, 12, 16, 17]. An undoubted role in their development is assigned to other factors, in

particular, a certain role is given to trauma of the oral mucosa, allergic reaction, genetic factors, and stress [14, 16, 38].

**The aim of the study** was the theoretical justification for determining the severity of significant etiopathogenetic and therapeutic measures in patients with recurrent aphthosis of the oral cavity against the background of the gastrointestinal tract diseases.

### Materials and methods

We studied issues by using a systematic review of number of literature domestic and foreign sources. Inclusion criteria: publications registered in PubMed, Medline, Cochrane, Elibrari, described studies of the clinical manifestations of aphthous stomatitis from 2000 to 2019. Exclusion criteria: experimental animal studies and clinical case descriptions.

This situation determines the relevance of studying the causes and mechanisms of the development of pathology of the oral mucosa against the background

of the presence of various diseases of the gastrointestinal tract, including acid-dependent diseases.

### Results and discussion

Literary sources indicate numerous trigger factors that cause the appearance of pathology of the oral mucosa in the form of recurrent aphthous stomatitis, dermatitis, leukoplakia, candidiasis.

The clinical manifestations and course of recurrent aphthosis of the oral cavity depends on gastrointestinal tract diseases, endocrine diseases, as well as the relationship of other risk factors causing this disease [21].

Anisimova I. V. (2017) revealed various pathologies of the oral mucosa in patients with somatic diseases, including in 6 % recurrent aphthosis of the oral cavity, in 23 % of tongue lesions, in 6 % of cheilitis, in 22 % of traumatic lesions, dermatoses and candidiasis in 15 % and in 25 % of cases of periodontal disease examinations.

A number of domestic and foreign researchers have proven a close anatomical and functional relationship between the occurrence of pathology of the oral mucosa, as well as inflammatory periodontal diseases in diseases of the gastrointestinal tract [2, 5—9, 12, 16, 17, 33, 38].

When conducting a therapeutic examination of patients with concomitant diseases of the digestive system — chronic gastritis, cholecystitis, inflammatory bowel diseases in 96.1 % of cases, gingivitis and periodontitis, recurring oral aphthae, cheilitis and glossitis [8, 9, 12].

Gazhva S. I. (2013, 2016) after studying the condition of the oral mucosa in 80 % of patients with various diffuse liver lesions, the prevalence of recurrent aphthous stomatitis (9.5 %), lichen planus (40.5 %), candidiasis (30.8 %), leukoplakia and cheilitis, in inflammatory periodontal diseases (70.5 %).

In patients diagnosed with duodenal ulcer (ULC), erosive-ulcerative lesions in the form of recurrent aphthae, but also manifestations of an erosive-ulcerative form of lichen planus, predominate on the mucous membrane of the mouth [7]. Severe recurrent course of inflammatory bowel disease creates favorable conditions for the development of stomatitis, gingivitis, hyperplasia [8, 16, 17].

The leading role in pathogenesis of oral cavity recurrent aphthae is given to the state of the immune system — T and B cell and humoral immunity, which reduce the activity of anti-inflammatory cytokines IL-1-IL-1p, IL-4, IL-10, phagocytic activity of neutrophils, and antioxidant systems, content of C3, C4, and the expression of heat shock protein HSP27, increase the activity of pro-inflammatory cytokines — IL-2, IL-6, IL-8, interferon- $\gamma$ , lipid peroxidation activity, complement level C5, which ultimately contributes to the active development inflammatory reaction of delayed-type hypersensitivity (mediated by Th1 cells) [5, 6, 8, 14, 19—21, 26].

In the development of an acute inflammatory reaction, the role of tumor necrosis factor-TNF- $\alpha$ , interleukin-1 $\beta$

(IL-1 $\beta$ ) is important, since they, having a pronounced chemotactic effect against neutrophils, lead to mucosal epithelial cell damage by cytotoxic T cells, and  $\gamma\delta$ T lymphocytes in The response is actively produced by a large number of inflammatory cytokines. The increase in serum  $\gamma\delta$ T cells, the ratio of CD8+ T-lymphocytes with a decrease in CD4+/CD8+score, CD4+/CD25+ (high) T-regulatory cells leads to the development of a T-cell-mediated cytotoxic reaction. An increase in the level of IgA, IgG, IgM and IgE in the blood serum indicates immunocomplex destruction of keratinocytes, an increase in IgG, IgM in the composition of fibrous exudate aphtha leads to destruction of the capillary wall [4—6, 8, 9, 14, 16, 24, 26, 29, 31, 32].

A significant role in the development of recurrent aphthosis of the oral cavity is given to the state of the microbiome of the gastrointestinal tract. This biotope is the presence of various microorganisms, while it is most often detected in 61.1 % of staphylococcus, in 55.5 % of streptococcus, in 50 % of lactobacillum, H. pylori is present in 44 % of cases, and in 22,2 % — fungi of the genus Candida, as well as bacteroids, corynebacteria, micrococci [22]. Oral cavity being the initial section of the digestive tract Aerobic and facultative aerobic microorganisms predominate in the oral cavity. In samples of the oral fluid, the activity of the anti-inflammatory factor — lysozyme — decreases, the content of histamine and urea, lysosomal hydrolases, mucin, C-reactive protein increase, which is convincing evidence of the suppression of nonspecific factors of local immunity in diseases of the gastrointestinal tract [3, 5, 7, 9, 12, 14].

During recurrent aphthosis of the oral cavity, several stages of the inflammatory process are pathomorphologically distinguished. In the first stage, a depigmented and erythematous lesion appears on the oral mucosa, which gradually passes into the second stage — the erosive-ulcerative and the third stage are characterized by a healing process [14, 21].

When diagnosing and making clinical diagnosis, recurrent aphthous stomatitis is the most acceptable classification adopted on the recommendation of the WHO and according to which several clinical forms are distinguished — the fibrinous form represented by the classic Mikulich aphthae, the second form cicatricial proceeds with a persistent course and the duration of the Setton aft, the third form-deforming even harder clinically.

Diagnostic criteria for recurrent aphthosis are the sum of the data obtained during the collection of anamnesis, visible clinical manifestations and the results of additional diagnostic methods. Nevertheless, there is a similarity in the clinical picture of recurrent aphthae of the oral cavity with manifestations of recurrent herpes, with Behcet's disease, large Touraine aphthosis, traumatic lesions of the oral mucosa and various papular rashes.

The clinical picture of the fibrous form of recurrent aphthous stomatitis begins classically with the appearance of a hyperemic and painful lesion (diameter up to 1 cm) of a round or oval shape, which after a few hours rises slightly above the surrounding mucous membrane, against the background of the development of acute inflammation, erosion occurs. Upon objective examination, the aphthae is covered with a fibrinous grayish-white coating, along the periphery of which there is a thin hyperemic rim. With the influence of risk factors, congestive hyperemia appears at the base of the aphthous element, and the focus is infiltrated by grayish-white necrotic masses. Rashes are often localized on the mucous membrane of the cheeks, lips, and lateral surfaces of the tongue [7, 17, 21, 31, 35, 38].

Modern approaches to the treatment and preventive measures of recurrent aphthous stomatitis involves the use of certain algorithms and complexes consisting of antihistamine drugs, immunocorrection drugs that increase non-specific hypersensitivity, normalization of cellular metabolism, stimulation of non-specific defense mechanisms, and vitamin therapy [2, 4, 8, 9, 11, 12, 15, 17–19, 21, 23, 24, 27, 30, 33, 35].

In the complex of therapeutic and preventive measures, the application of various physiotherapy methods is especially relevant — darsonvalization, ultraviolet radiation, HBO therapy, laser therapy, nitric oxide therapy,

aeroionic massage, the use of low temperatures, reflexology, magnetic laser therapy [4, 10, 13, 17, 25, 28].

In the planning of complex treatment, the successive participation of doctors of various profiles (dentists, therapists, gastroenterologists, urologists, dermatologists) is relevant [4, 8, 9, 17].

### Conclusions and recommendations

Thus, despite the large amount of literature data on etiopathogenesis, clinical features, and methods of treating recurrent aphthae of the oral cavity, there are many unresolved issues and additional studies in patients with acid-dependent diseases of the gastrointestinal tract.

Currently, there is no universally accepted method for the treatment of recurrent aphthosis of the oral cavity in patients with acid-dependent diseases of the gastrointestinal tract, and the existing complex treatment methods reduce the severity of clinical manifestations express a reduction in the epithelization time of pathological elements, but there are no methods of effective complex therapy with the ability to achieve more persistent results, which remains an urgent task and requires further research.

The development of a system for medical examination of patients with acid-dependent diseases of the gastrointestinal tract diseases will allow to actively identify pathology of the oral mucosa, to conduct therapeutic and preventive measures aimed at their systematic observation, which will lead to an increase in their quality of life.

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