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## **STATUS OF ORAL MUCOSA MICROBIOTOPE IN PATIENTS WITH GASTROESOPHAGEAL REFLUX DISEASE**

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*In recent years, the issues of "extraesophageal manifestations" of gastroesophageal reflux disease has been receiving more attention from researchers and clinicians that can be explained by the complexity in diagnosis and treatment of the disease, and the necessity in collaboration between medical professional of different specialties as extra-esophageal manifestations can come to the fore imitating diseases of other organs. In the oral cavity there is a favourable environment for the development of beneficial, pathogenic and opportunistic microorganisms. The aim of this study is to investigate the state of oral mucosa microbiotope in patients with gastroesophageal reflux disease. The study included 90 individuals aged from 25 to 55 years, the two test groups involved 30 people in each who had clinically and laboratory confirmed diagnosis of gastroesophageal reflux disease with hyperacidity and hypoacidity; control group consisted of 30 healthy individuals. The study has demonstrated that the number of microorganisms in the oral cavity differs significantly in sick and healthy people. The most significant changes have been found on the tongue (presence of a large number of opportunistic microorganisms and pathogens) and observed in patients with gastroesophageal reflux disease, especially with high gastric juice acidity. Changes in the micro-biotope on the tongue can be used for confirming diagnosis of gastrointestinal disorders (chronic gastritis, peptic ulcer disease, duodenitis), and gastroesophageal reflux disease in particular.*

Key words: gastroesophageal reflux disease, oral mucosa, salivation, erosive lesions, tongue, cheeks, microorganisms.

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### **Introduction**

In the recent years, the problem of extra-esophageal manifestations in gastroesophageal reflux disease (GERD) has been receiving more attention from scientists and clinicians [1, 2] that can be explained by the complexity in diagnosis and treatment of the disease, and the necessity in collaboration between medical professional of different specialties as extra-oesophageal manifestations can come to the fore imitating diseases of other organs [3, 4]. There is a connection between the status of the oral cavity and other parts of the gastrointestinal tract (GIT) that is quite clear as the oral cavity is an initial division, an upper part of the gastrointestinal tract (GIT), and the state of latter has a significant impact on oral microecology [5, 6].

The oral mucosa provides a normal functioning level of the local immune system at the expense of the immune synergy of other mucous membranes [7, 11]. Data about the oral mucosa colonization are taken into account when determining pathological changes in the body: distorted resistance mechanisms of the oral mucosa can indicate alterations in the general health status [8, 12].

Bacterial populations are known to possess different adhesion abilities to epithelial cells in the oral mucosa. The connection between somatic diseases and the state of oral organs can result from distorted haemodynamics, metabolism, and immunological changes in the body.

In the oral cavity, there is a favourable environment for various microorganisms, including beneficial, opportunistic, and pathogenic ones. Pathogenic microorganisms when entering the

body come in contact with oral mucosa first, and under certain conditions they can multiply quickly causing harm to the whole body. An increasing number of beneficial microbes in the oral mucosa, on the other hand, contribute to the formation of local immunity. Colonization resistance is one of the most important functions of normal oral microbiota that enables to prevent colonization with non-characteristic microflora for this biotope [6, 8, 11-13].

The aim of this study is to investigate the state of oral mucosa microbiotope in patients with gastroesophageal reflux disease.

### **Materials and methods**

The series of experiments were conducted at the Department of Dentistry, NNIPO, Center of Clinical Medicine, University Clinic of Ivano-Frankivsk National Medical University, clinical and biochemical laboratory of the University Clinic (Prof. Semotyuk M.M., Head of Physician Assoc.), Ivano-Frankivsk National Medical University.

The study included 90 individuals aged from 25 to 55 years: 30 of them were diagnosed as having GERD with hyperacidity, and the same number of the patients was diagnosed as having GERD with hypoacidity. The control group consisted of 30 healthy individuals of the same age with healthy oral cavity, who presented no gastrointestinal complaints. The diagnosis was established by a gastroenterologist according to generally accepted criteria considering clinical symptoms (eructation, nausea, heartburn, chest pain) and findings obtained by fibrogastroscopy, pH monitoring, and oesophageal ultrasound scan.

All patients underwent oral examination to

assess oral health condition and find any pathological changes in hard dental tissues, periodontium, or oral mucosa.

Sample collections from the oral cavity were taken by scraping with a sterile spatula from different parts of the oral mucosa from fasting participants in the morning. The samples were stained according to the LDF 200 Biolatest method; preparations were studied by using the PrimoStar Zeiss Plan-Achromat microscope (1000 magnification).

All manipulations were carried out in accordance with the Convention for the Protection of Human Rights and Dignity with regard to the Application of Biology and Medicine: Convention on Human Rights and Biomedicine.

**Results and discussion**

Gastroesophageal reflux disease is accompanied by oral manifestations, and most patients often present them. The manifestations typically include high prevalence of dental caries and non-cariou lesions, inflammatory and inflammatory-dystrophic conditions of periodontal tissues, subjective and objective changes in the tongue and lips.

The necessity of in-depth GERD study is due to the fact that its oral manifestations may often be found in a patient without pronounced subjective symptoms, and there may be no gastrointestinal complaints from patients. However, during the oral examination, dentists can assume the presence of this disease by assessing the clinical presentations, which are often associated with the disease and then refer a patient to consult a gastroenterologist.

The study of oral GERD-associated changes is

determined by several reasons. First, these manifestations are not well known to dentists, who may mistakenly regard non-cariou dental lesions (enamel erosion, hard tissue necrosis) as a reaction of dental tissues to the action of exogenous factors (mechanical damage to enamel, consumption of acidic food and drinks, etc.). Secondly, during the teeth restoration, the physicochemical properties of the oral fluid are usually not taken into account, therefore, it is difficult to forecast the further course of non-cariou dental lesions (erosion, necrosis of hard tissues) following the filling. Third, only the joint actions of a gastroenterologist and a dentist can guarantee successful treatment outcomes and further prevention of GERD oral manifestations.

Patients with gastroesophageal reflux disease present besides catarrhal mucosa changes, isolated erosive lesions on the tongue and cheeks, hypertrophied filiform papillae usually due to high gastric juice acidity, while areas of papillary atrophy are resulted from low gastric acidity. Thus, there is a reverse effect of pathologic processes in internal organs on the oral cavity [8].

Infections are known to play a leading role in oral mucosa changes [9]. Saprophytic and opportunistic intestinal flora gets virulent properties and causes pathological processes in the gastrointestinal tract, starting with the oral cavity. A significant number of bacteria go from the oral cavity down to the gastrointestinal tract causing pathological processes in the lower divisions of the gastrointestinal channel [10-13].

Microscopic findings obtained from tongue swabs (base, lateral borders, tip), gums, and cheeks are represented in the table 1.

Table 1. Structure of oral microorganisms in the study groups

Survey groups	Main group						Control group, n		
	High acidity, n (relatively, %)			Low acidity, n (relatively, %)			Tongue	Cheeks	Gums
	Tongue	Cheeks	Gums	Tongue	Cheeks	Gums			
Leukocytes	++++	++	++++	++	+/-	+	-	-	-
Fusobacteria	+++	+/-	++	+	+/-	+	-	-	-
Oral trichomonas	++	++	+/-	+/-	+	+	+/-	-	-
Fungi	++++	+/-	++++	++	+	+	+	-	+/-
Streptococci, staphylococci	++++	++	+++	++	++	+	+	-	+/-

*slight +, moderate ++, significant +++, large +++++, single microorganisms +/-*

Oral microbiota, in particular, at the back of the tongue, its lateral surfaces and the tip, demonstrate a wide range of microorganisms. The patients with gastroesophageal reflux disease with high acidity and increased salivation have been found out to have a large number (30-60) of coccal flora, leukocytes, fungi in the field of view, a moderate amount of oral Trichomonas (2-9 in the field of view) and a significant amount (10-40) fusobacteria.

The obtained data point out the necessity for further in-depth study of oral changes in patients with gastroesophageal reflux disease taking into account physicochemical properties of oral fluid in order to develop effective primary and secondary prevention of dental and oral disease.

Moderate (2-9) leukocytes, oral Trichomonas, a single number of fungi and fusobacteria (5-8 in the field of view), and a significant number of streptococci and staphylococci were observed in smears from the buccal mucosa. There is a large number (30-60) of leukocytes and fungi on the gums, a significant moderate number (2-9) of fusobacteria and single (2-5) oral Trichomonas. With low acidity, there is a decrease in salivation, therefore, we can observe a moderate number (2-10) of leukocytes, fungi, streptococci and staphylococci, a small number (2-9) of fusobacteria and single (2-10) oral Trichomonas on the tongue. Buccal mucosa contained single (2-8) leukocytes and fusobacteria, a slight presence of fungi and

Trichomonas and a moderate number (1-5) of streptococci and staphylococci.

The microscopic picture of smears taken from healthy individuals differed significantly from the GEARD participants: the presence of single microorganisms (2-9) of oral Trichomonas, fungi of the genus Candida, a small and moderate amount of coccal-staphylococcal flora. Fast accumulation and spread of pathogens (especially streptococci) promote infectious (inflammatory) processes, autoimmune processes, and diseases of different organs and systems. Besides this, pathogens produce toxins and enzymes, which seep into lower tissues and damage them, go down to lower GIT parts, thus, causing pathologic changes.

Given our results and literature data, further work needs to be done to study the features of other manifestations of GERD mucosal changes, to develop specialized questionnaires for effective and timely diagnosis, as well as to improve the therapy of this disease, especially in the elderly patients.

**Conclusion.** The number of microorganisms in the oral cavity differs significantly in sick and healthy people. The most significant changes are found on the tongue (presence of a large number of opportunistic microorganisms and pathogens) and observed in patients with gastroesophageal reflux disease, especially with high gastric juice acidity.

Changes in the micro-biotope on the tongue can be used for confirming diagnosis of gastrointestinal disorders (chronic gastritis, peptic ulcer disease, duodenitis), and gastroesophageal reflux disease in particular.

We have established that the connection between the oral microorganism colonization and the course of gastroesophageal reflux disease that creates a need to perform an in-depth study to determine the role of some microorganisms in pathologic changes in the oral cavity and

prevention of extra-oesophageal manifestations of gastroesophageal reflux disease.

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### Реферат

СТАН МІКРОБІОТОПУ СЛИЗОВОЇ ОБОЛОНКИ РОТОВОЇ ПОРОЖНИНИ У ХВОРИХ ІЗ ГАСТРОЕЗОФАГЕАЛЬНОЮ РЕФЛЮКСНОЮ ХВОРОБОЮ

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Ключові слова: слизової оболонки, слиновиділення, ерозивні ураження, язик, щоки, слиновиділення, мікроорганізми.

В останні роки проблема “позастравохідних проявів” гастроєзофагеальної рефлюксної хвороби привертає до себе все більше увагу вчених. Увага до цієї проблеми зумовлена тяжкістю діагностики та її лікування, співпрацею лікарів різного фаху, тому що на перший план можуть виступати тільки “позастравохідні” прояви, імітуючи захворювання інших органів. У ротовій порожнині існує сприятливе середовище для розвитку корисних, патогенних і умовно-патогенних мікроорганізмів. Патогенні мікроорганізми при проникненні в організм в першу чергу контактують зі слизовою оболонкою ротової порожнини, де за певних умов вони швидко розмножуються і чинять негативний вплив на весь організм. А збільшення на слизовій оболонці ротової порожнини корисних мікроорганізмів забезпечує формування місцевого імунітету. Колонізаційна резистентність є однією з найважливіших функцій нормальної мікрофлори ротової порожнини і перешкоджає заселенню та розмноженню нехарактерної для даного біотопу мікрофлори. Встановлення діагнозу проводилось лікарем-гастроентерологом за загальноприйнятими критеріями з урахуванням клінічних симптомів (відрижка, нудота, печія, біль за грудиною) та даних фіброгастроскопії, рН моніторингу, ультразвукове дослідження стравоходу. Так у хворих на гастроєзофагеальну рефлюксну хворобу відмічалось окрім катаральних змін слизової оболонки, були наявні поодинокі ерозивні ураження на язичку і щоках, гіпертрофію ниткоподібних сосочків, посилене слиновиділення особливо при підвищеній кислотності шлункового соку, при пониженой кислотності шлунка наявні ділянки атрофії сосочків, язик обкладений, сухість губ зменшення слиновиділення. То-

му, існує зворотній вплив патологічних процесів внутрішніх органів на ротову порожнину. Виявлений взаємозв'язок між колонізацією мікроорганізмів у ротовій порожнині та перебігом гастроєзофагеальної рефлюксної хвороби створює необхідність проведення поглибленого дослідження для визначення ролі певних мікроорганізмів у формуванні патологічних змін у ротовій порожнині та профілактиці позастравохідних проявів гастроєзофагеальної рефлюксної хвороби.

#### **Реферат**

СОСТОЯНИЕ МИКРОБИОТОПА СЛИЗОВОЙ ОБОЛОЧКИ РОТОВОЙ ПОРОЖНИКИ У БОЛЬНЫХ С ГАСТРОЭЗОФАГЕАЛЬНОЙ РЕФЛЮКСНОЙ БОЛЕЗНЬЮ

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Ключевые слова: слизистая, слюноотделение, эрозивные поражения, язык, щеки, слюноотделение, микроорганизмы.

В последние годы проблема "внепищеводных проявлений" гастроэзофагеальной рефлюксной болезни привлекает к себе все большее внимание ученых. Внимание к этой проблеме обусловлено тяжестью диагностики и ее лечения, сотрудничеством врачей разной профессии, потому что на первый план могут выступать только "внепищеводные" проявления, имитируя заболевания других органов. В полости рта существует благоприятная среда для развития полезных, патогенных и условно-патогенных микроорганизмов. Патогенные микроорганизмы при проникновении в организм в первую очередь контактируют со слизистой ротовой полости, где при определенных условиях они быстро размножаются и оказывают негативное влияние на весь организм. А увеличение на слизистой оболочке полости рта полезных микроорганизмов обеспечивает формирование местного иммунитета. Колонизационная резистентность является одной из важнейших функций нормальной микрофлоры полости рта и препятствует заселению и размножению нехарактерной для данного биотопа микрофлоры. Установление диагноза проводилось врачом-гастроэнтерологом по общепринятым критериям с учетом клинических симптомов (отрыжка, тошнота, изжога, боль за грудиной) и данных фиброгастроскопии, рН мониторинга, ультразвуковое исследование пищевода. Так у больных гастроэзофагеальной рефлюксной болезнью отмечалось кроме катаральных изменений слизистой оболочки, имелись единичные эрозивные поражения на языке и щеках, гипертрофию нитевидных сосочков, усиленное слюноотделение особенно при повышенной кислотности желудочного сока. губ уменьшение слюноотделения. Поэтому существует обратное влияние патологических процессов внутренних органов на полость рта. Выявленная взаимосвязь между колонизацией микроорганизмов в полости рта и течением гастроэзофагеальной рефлюксной болезни создает необходимость проведения углубленного исследования для определения роли определенных микроорганизмов в формировании патологических изменений в полости рта и профилактике внепищеводных проявлений гастроэзофагеальной рефлюксной болезни.