

## PATHOLOGICAL PROCESSES OF THE ORAL MUCOSA IN CHRONIC RECURRENT APHTHOUS STOMATITIS ON THE BACKGROUND OF GASTRODUODENAL DISEASES

**KAMILOV KHAYDAR P.**, ORCID:0000-0002-7051-8978; Dr. sc. med., Professor, Head of the Department of Hospital Therapeutic Dentistry, Tashkent State Dental Institute, 103 Taraqiyot str., Yashnabad District, 100047 Tashkent, Uzbekistan; tel.: +99-871-2302073

**IBRAGIMOVA MALIKA Kh.**, ORCID: 0000-0002-4181-9819; Dr. sc. med., Professor at the Department of Hospital Therapeutic Dentistry, Tashkent State Dental Institute, 103 Taraqiyot str., Yashnabad District, 100047 Tashkent, Uzbekistan; tel.: +99-871-2302073

**ERGASHEV NURALI A.**, ORCID:0000-0002-0414-0241; Cand. sc. biol., Head of the Laboratory of Molecular Biophysics, Institute of Biophysics and Biochemistry, Senior Researcher, 174 Talabalar str., Almazar District, 100095 Tashkent, Uzbekistan; tel.: +99-871-2462317

**Abstract. Introduction.** In gastroduodenal diseases, alterations of the oral mucosa (OM) are characterized by various morphological elements, such as erosions, aphthae, ulcers, and pathological processes like acanthosis or atrophy. Chronic inflammation that accompanies this process is a protective body reaction histologically manifested by the development of lymphohistiocytic or round cell infiltrates. **Aim of the study** was to investigate morphological changes in OM in chronic recurrent aphthous stomatitis (CRAS) on the background of chronic gastroduodenitis and to conduct a comparative analysis with clinical findings. **Materials and Methods.** To conduct a histological study, of a total of 114 patients with CRAS, we selected 40 patients, in which it was accompanied by OM lesions, particularly the formation of aphthae, ulcerative and necrotic elements. All patients underwent a complete history collection and clinical examinations. **Results and Discussion.** When analyzing chronic gastroduodenitis by gender in patients with CRAS, we found the pathology equally often in both women and men. Of the total of 114 patients with chronic gastroduodenitis, CRAS was diagnosed in 61 women (53.5%) and in 53 men (46.4%). In terms of age, there was CRAS in patients aged 50 years or older (60.5%) more frequently than in younger patients. **Conclusions.** Analyzing the morphological studies of erosive-ulcerative OM lesions in CRAS patients on the background of chronic gastroduodenitis shows that the most frequent manifestations of the alterations were characterized by the development of the epithelium inflammation and ulceration, formation of ulcerative defects, the surface squamous epithelium hyperplasia, and in some cases, the epithelium atrophy and thinning.

**Keywords:** erosion, aphtha, ulcer, atrophy, acanthosis, hyperplasia, dyskeratosis, dysplasia, infiltration.

**For reference:** Kamilov KhP, Ibragimova MKh, Ergashev NA. Pathological processes of the oral mucosa in chronic recurrent aphthous stomatitis on the background of gastroduodenal diseases. The Bulletin of Contemporary Clinical Medicine. 2023;16(Suppl.2):29-36. DOI:10.20969/VSKM.2023.16(suppl.2).29-36.

## ПАТОЛОГИЧЕСКИЕ ПРОЦЕССЫ СЛИЗИСТОЙ ОБОЛОЧКИ ПОЛОСТИ РТА ПРИ ХРОНИЧЕСКОМ РЕЦИДИВИРУЮЩЕМ АФТНОМ СТОМАТИТЕ НА ФОНЕ ЗАБОЛЕВАНИЙ ГАСТРОДУОДЕНАЛЬНОЙ СИСТЕМЫ

**КАМИЛОВ ХАЙДАР ПОЗИЛОВИЧ**, ORCID:0000-0002-7051-8978; докт. мед. наук, профессор, заведующий кафедрой госпитальной терапевтической стоматологии «Ташкентский государственный стоматологический институт», Узбекистан, 100047, Ташкент, Яшнабадский район, улица Таракиёт, 103, тел. +99-871-2302073

**ИБРАГИМОВА МАЛИКА ХУДАЙБЕРГАНОВНА**, ORCID: 0000-0002-4181-9819; докт. мед. наук, профессор кафедры госпитальной терапевтической стоматологии «Ташкентский государственный стоматологический институт», Узбекистан, 100047, Ташкент, Яшнабадский район, улица Таракиёт, 103, тел. +99-871-2302073

**ЭРГАШЕВ НУРАЛИ АЪЗАМОВИЧ**, ORCID:0000-0002-0414-0241; канд. биол. наук, старший научный сотрудник, заведующий лаборатории «Институт биофизики и биохимии», Узбекистан, 100095, Ташкент, Алмазарский район, улица Талабалар, 174, тел. +99-871-2462317

**Реферат. Введение.** Изменения слизистой оболочки полости рта (СОПР) при заболеваниях гастродуоденальной системы характеризуются различными морфологическими элементами, такими как эрозия, афты, язвы, патологическими процессами – акантозом, атрофией. Хроническое воспаление, сопровождающее этот процесс, является защитной реакцией организма и гистологически проявляется развитием лимфогистиоцитарных или круглоклеточных инфильтратов. **Целью** данного исследования явились изучение морфологических изменений СОПР при хроническом рецидивирующем афтозном стоматите (ХРАС) на фоне хронического гастродуоденита и проведение сравнительного анализа с клиническими признаками. **Материалы и методы.** Для проведения гистологического исследования из 114 пациентов с ХРАС мы отобрали 40 пациентов, у которых заболевание сопровождалось повреждением СОПР, в частности образованием афт, с наличием язвенных и некротических элементов. Проводились сбор полного анамнеза и клинические обследования всех пациентов. **Результаты.** При анализе хронического гастродуоденита в разбивке по полу пациентов с ХРАС патология выявлялась одинаково часто как у женщин, так и у мужчин. Из общего числа 114 пациентов с хроническим гастродуоденитом ХРАС наблюдался у 61 женщины (53,5%) и у 53 мужчин (46,4%). В возрастном отношении ХРАС наблюдался у пациентов в возрасте 50 лет и старше (60,5%) чаще, чем у более молодых пациентов. **Заключение.** Анализ проведенных морфологических исследований показывает, что эрозивно-язвенные поражения СОПР при ХРАС

на фоне хронического гастродуоденита представляют собой наиболее частые проявления изменений, характеризующихся развитием воспаления и изъязвления эпителия, образованием язвенных дефектов, гиперплазией плоского эпителия, а в некоторых случаях наблюдается атрофия и истончение эпителия.

**Ключевые слова:** эрозия, афта, язва, атрофия, акантоз, гиперплазия, дискератоз, дисплазия, инфильтрация.

**Для ссылки:** Камиллов Х.П., Ибрагимов М.Х., Эргашев Н.А. Патологические процессы слизистой оболочки полости рта при рецидивирующем афтозном стоматите на фоне заболеваний желудочно-двенадцатиперстной системы // Вестник современной клинической медицины. – 2023. – Т.16, Прил. 2. – С.29-36. DOI: 10.20969/VSKM.2023.16(suppl.2).29-36.

**Introduction.** Gastrointestinal pathologies induce various alterations on the mucous membrane of the oral cavity. There are many reactive changes in OM with various etiology, but chronic with the course of lesions of the gastroduodenal system, characterized by dystrophy, hyperplasia, atrophy, dyskeratosis, and dysplasia. These changes may occur individually or in combination with each other [1,2,3].

Chronic gastroduodenitis is an inflammatory duodenum and gastric disease. It develops due to the formation of gallbladder stones, which leads to cholestasis [3,4]. Periodically arising and passing inflammations lead to a gallbladder wall alteration with the development of chronic gastroduodenitis in it. Along with the general clinical signs of chronic gastroduodenitis, changes develop in oral mucosa [5,6,7].

In most cases of chronic gastroduodenitis, patients feel discomfort on OM caused by swelling, aphthae, erosion, ulceration, and other changes [8,9]. Given the above, to study alterations of the oral mucosa (OM) in case of chronic recurrent aphthous stomatitis (CRAS), we consider it worthwhile to conduct a more in-depth study of morphological changes in patients approaching to the dental clinic and having chronic gastroduodenal disease background [10,11,12].

**Aim of the study** was to investigate morphological changes in OM in CRAS on the background of chronic gastroduodenitis and to conduct a comparative analysis with clinical findings.

**Materials and Methods:** To conduct a histological study, of a total of 114 patients with CRAS, we selected forty patients in which it was accompanied by OM lesions, particularly the formation of aphthae, ulcerative and necrotic elements. For histological examination, the material of the mucous membrane from the affected area was placed in a 4% neutral formalin solution, then it was fixed in alcohol and bathed in paraffin according to the Lloyd method, then it was placed in a thermostat for 24 hours, paraffin blocks were prepared, and sections were stained with hematoxylin and eosin. The cytological research method was conducted by the method of smear OM imprint. The local ethics committee of the center approved the research protocol. Each participant signed a written consent to participate in the study.

We entered all the data obtained in the study into MS Excel PivotTables. Nominal data were described with absolute values and percentages. The comparison of ordinal data was conducted using the criterion  $\chi^2$ . The criterion  $\chi^2$  value was compared with the critical values for  $(r - 1) \times (c - 1)$  the number of degrees of freedom. If the obtained value of  $\chi^2$  exceeded the critical one, it was concluded that there was a statistical relationship

between the studied risk factor and the outcome at the appropriate level of significance.

**Results and Discussion.** CRAS is a chronic OM disease characterized by periodic remissions and exacerbations with a rash of aphthae. According to WHO, this disease affects up to 20% of the population. When analyzing chronic gastroduodenitis by gender of patients with CRAS, pathology was identified equally often in both women and men. Of the total number of patients 114 with chronic gastroduodenitis, there was CRAS observed in 61 women (53.5%), in 53 men (46.4%). In terms of age, there was CRAS in patients aged 50 and more years (60.5%) more often than in younger patients.

Patients with CRAS were divided into 3 representative groups by age and sex: with a mild, moderate to severe and severe course- the main (72) comparison group (42). The number of patients in all groups of patients was equivalent, i.e., in the main groups there were 24, in the comparison groups - 14 patients. The control group consisted of 20 healthy individuals.

Patients of the main group with a mild form of CRAS with chronic gastroduodenitis complained of some aphthous formations on OM, slight discomfort, redness and swelling, dry mouth. The general condition is intact, there are pain and burning when eating. When examining these patients for OM there are 1-3 aphthae, with a hyperemic rim around and slight swelling, the surface of the aphthous elements is coated with a thin fibrinous coating. The diameter of these aphthae ranges from 0.1 to 0.8 mm. The state of regional lymph nodes during palpation without changes. There were 1-2 relapses per year, the duration of relapses from 7-10 days, the duration of remission was 6-7 months.

Patients of the main group, with an average CRAS degree, mainly complained of a violation of the general condition of the body, which was expressed in moderate headaches. Pain and burning were manifested when eating ordinary food, and eating spicy foods was accompanied by discomfort. On examination of such patients, hyperemia and edema in the area of aphthous rash, covered with fibrinous plaque, were observed. The number of aphthae did not exceed 4-6, but the diameter increased and was in the range of 1.0-1.2 mm (*figure 1*). When analyzing the state of the edges of erosion, inflammatory infiltrate is observed. The number of relapses in these patients was 2-3 times a year, the duration of relapses is 10-13 days, the duration of remission is 4-6 months.

Patients of the main group of people with severe CRAS complained of disorders of the general condition of the body which are most expressed by constant headache, severe pain and burning of the erosive surface, not associated with food intake. During

examination of patients with severe CRAS, significant hyperemia and edema with inflammatory infiltrate were noted within the lesion elements – aphthae and erosion covered with fibro-necrotic plaque (*figure 2*), regional lymph nodes were enlarged and painful (*figure 3*). According to patients, aphthae and erosion ulcerated, a putrid odor from the mouth appeared, the healing of such elements took place within 2-3 weeks. The number of relapses in the severe course of CRAS was 4-5 times a year, the duration of remission was 2-3 months (*figures 4,5*).

Patients with mild CRAS of the comparison group without somatic pathology usually denied violations of the general condition of the body, only with spicy food they felt a slight burning sensation and pain. Appetite and sleep were not disturbed. During the examination, the mucous membrane of the mouth was pale pink, without hyperemia and edema (*figures 6,7*).

Patients with the average CRAS degree sometimes felt isolated aphthae on OM, the fast-passing pain and

burning sensation that appeared during meals. On examination the mucous membrane of the mouth is of the usual color, with the exception of the location of the aphthae, where hyperemia and slight edema were observed, sometimes inflammatory infiltration (*figures 8,9*).

Patients with severe CRAS of the comparison group complained of the presence of several aphthous formations on OM, pain and burning when eating. During the examination hyperemia, edema and inflammatory infiltration at the site of aphthous-erosive formation, discomfort were noted (*figure 10*). Regional lymph nodes are slightly dilated and painful (*figure 11*).

As can be seen from *table 1*, the cheek and upper lip were affected in 45.6% of cases, the lower lip was 41.2%, the sublingual region was 7.0%, and the tip of the tongue was 6.1%. Other OM parts, such as hard palate, gums, and transitional folds, were rarely affected.

Table 1

**CRAS localizations on OM**

Таблица 1

**Локализации ХРАС на СОПР**

Localization of aphtha	Cheek, upper lip		Lower lip		Sublingual region		Tip of the tongue	
	abs	%	abs	%	abs	%	abs	%
Number of patients	52	45,6	47	41,2	8	7,0	7	6,1

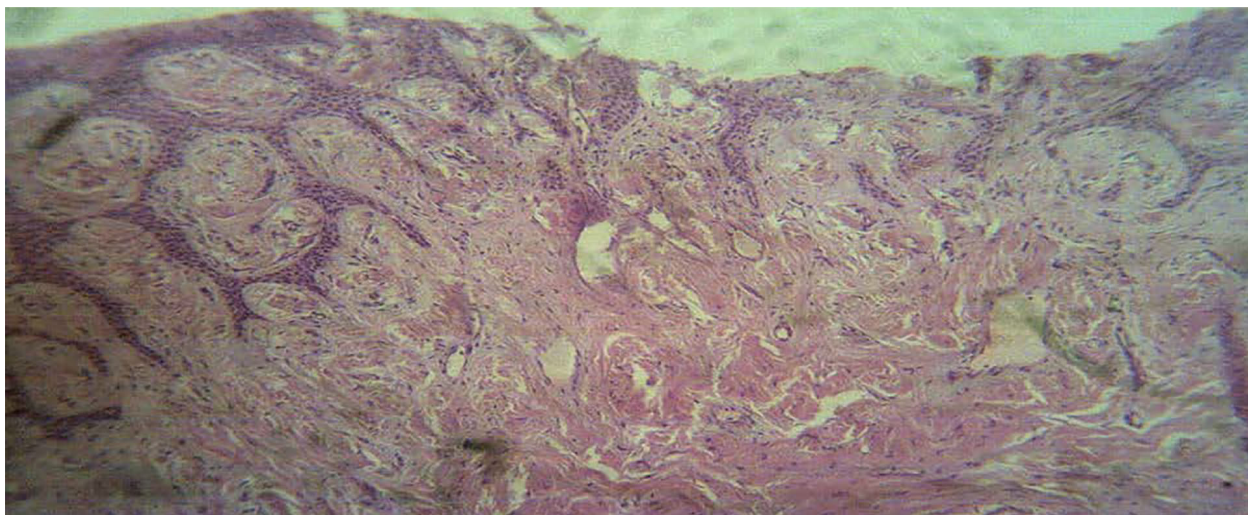


Fig. 1. Thinning of the surface squamous epithelium with ulcerous regions and with the ingrowth of basal-layer epithelial papillae into the deeper stroma layers of the mucous membrane of the lateral surface of the tongue.

Coloring with hematoxylin and eosin. V.incr. × 4.

Рис. 1. Истончение покровного плоского эпителия с участками язвенного дефекта и вращанием эпителиальных сосочков базального слоя в глубжележащие слои стромы слизистой оболочки боковой поверхности языка.

Окраска гематоксилином и эозином. Увел. об. × 4.

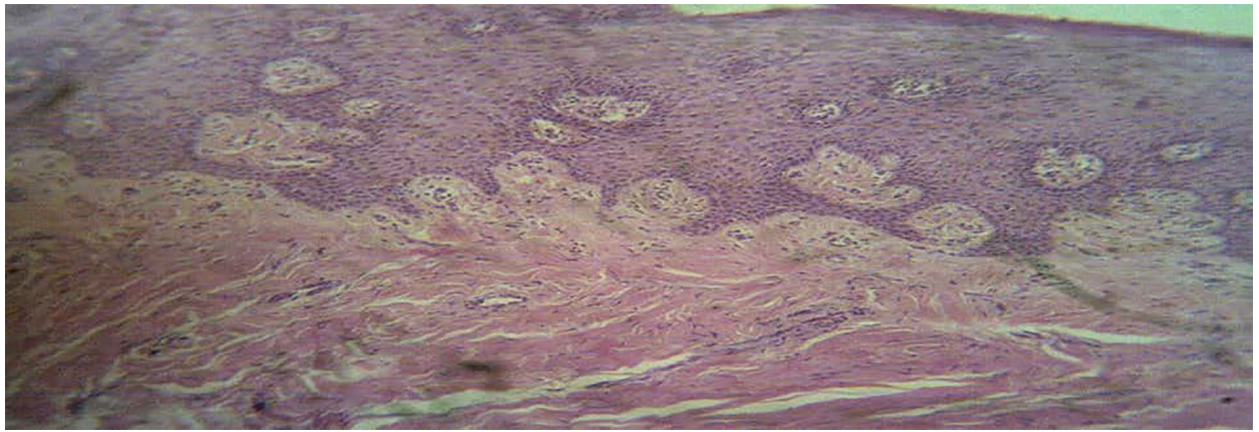


Fig. 2. Hyperplasia of the multilayered flat epithelium of the sublingual mucosa, acanthosis with an uneven arrangement of the cells of the basal layer, the number of layers is increased, the penetration of the epithelial papillae to different depths of the connective tissue. Hematoxylin and eosin coloring. V.incr.  $\times 10$ .

Рис. 2. Гиперплазия многослойного плоского эпителия, акантоз с неравномерным расположением клеток базального слоя, число слоев увеличено, отмечается проникновение эпителиальных сосочков соединительной ткани на различную глубину. Окраска гематоксилином и эозином. Ув.об.  $\times 10$ .

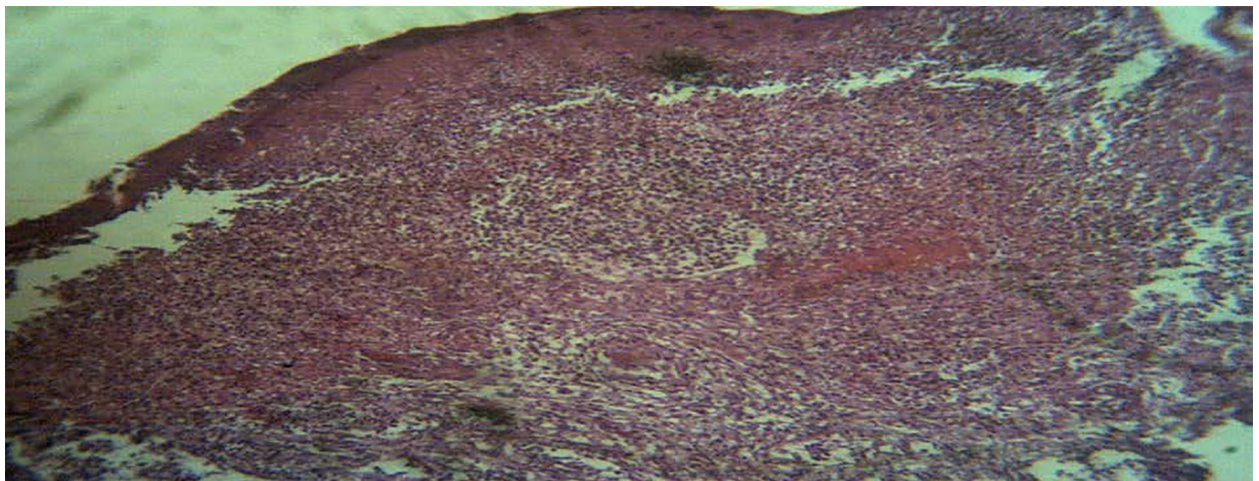


Fig. 3. Thinning and atrophy of the multilayered flat epithelium of the mucosa of the buccal region on the right, the underlying connective tissue is densely infiltrated by inflammatory cells. Hematoxylin and eosin coloring. V.incr.  $\times 10.0$

Рис. 3. Истончение и атрофия многослойного плоского эпителия, подлежащая соединительная ткань густо инфильтрирована клетками воспаления. Окраска гематоксилином и эозином. Ув.об.  $\times 10.0$ .



Figure 4. Subepithelial vesicle and focal squamous inflammatory infiltration of the stroma under an epithelial defect. Hematoxylin and eosin coloring. V.incr.  $\times 4.0$

Рис. 4. Субэпителиальный пузырек и очаговая круглоклеточная воспалительная инфильтрация стромы под дефектом эпителия. Окраска гематоксилином и эозином. Ув.  $\times 4.0$ .

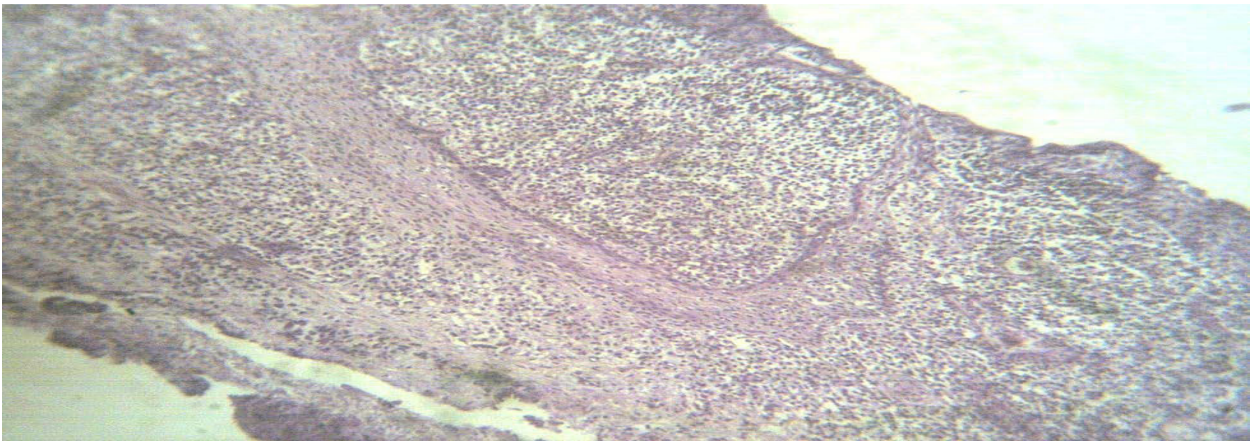


Fig. 5. Among the dense lymphohistiocytic inflammatory infiltration of the stroma, epithelial cords of the mucous membrane of the palate in the form of a collar are determined. Hematoxylin and eosin coloring. Inscr.  $\times 4.0$ .

Рис. 5. Среди густой лимфо-гистиоцитарной воспалительной инфильтрации стромы выделяются эпителиальные тяжи слизистой оболочки в виде воротничка. Окраска гематоксилином и эозином. Ув.  $\times 4.0$ .

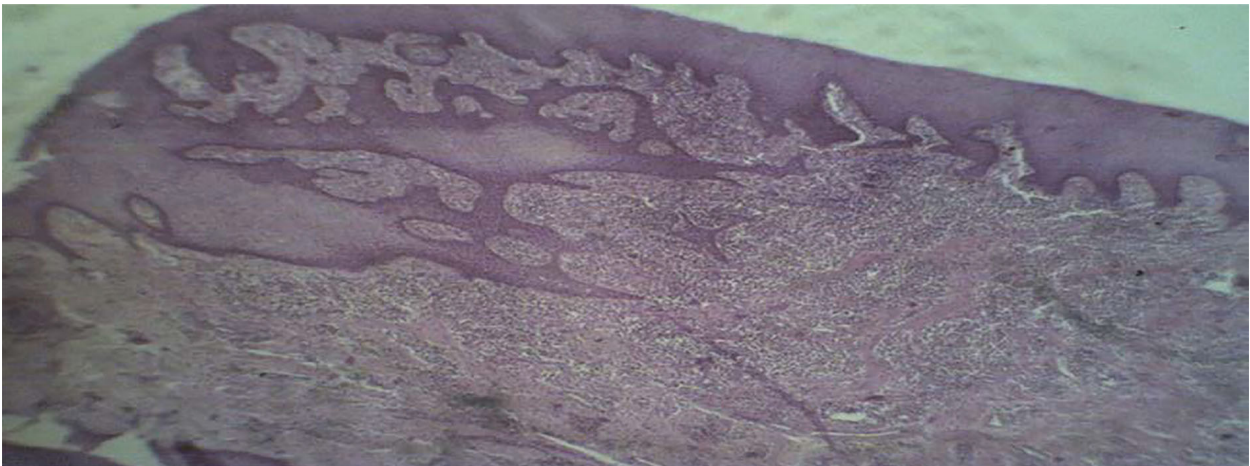


Fig. 6. Uneven thickening of the layers of the flat non-keratinized epithelium of the mucous membrane of the cheek, hypertrophy of the basal layer with the growth of epithelial outgrowths. Stroma with severe lymphocytic inflammatory cell infiltration. Hematoxylin and eosin coloring. Inscr.  $\times 4.0$ .

Рис. 6. Неравномерное утолщение слоев плоского неороговевающего эпителия, гипертрофия базального слоя с разрастанием эпителиальных выростов. Строма с выраженной лимфоцитарной воспалительно-клеточной инфильтрацией. Окраска гематоксилином и эозином. Ув.  $\times 4.0$ .

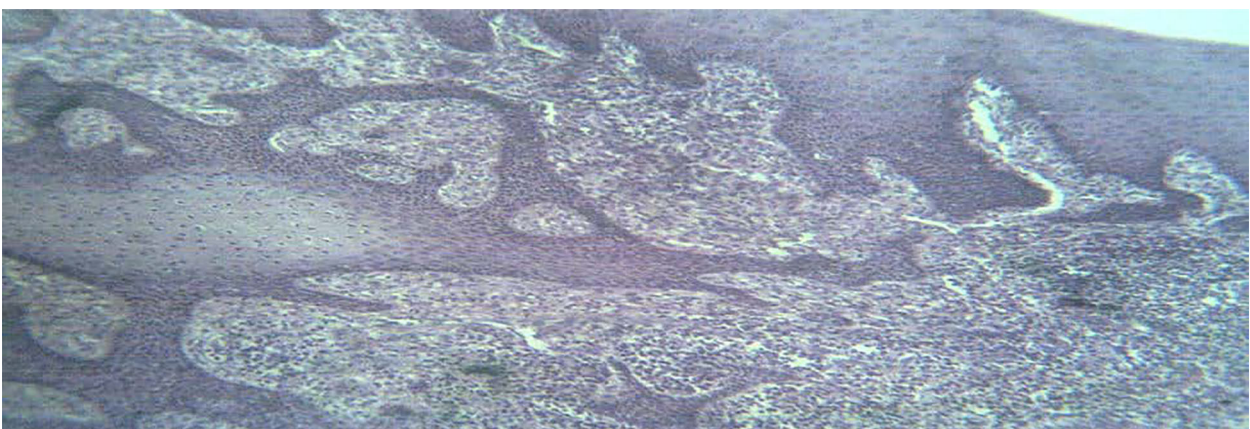


Fig. 7. Expressed acanthosis and flat epithelium dysplasia of mild degree and thick inflammatory stromal infiltration. (the same picture). Hematoxylin and eosin coloring. Inscr.  $\times 10.0$ .

Рис. 7. Выраженный акантоз и дисплазия плоского эпителия легкой степени и густая воспалительная инфильтрация стромы. Окраска гематоксилином и эозином. Ув.  $\times 10.0$ .

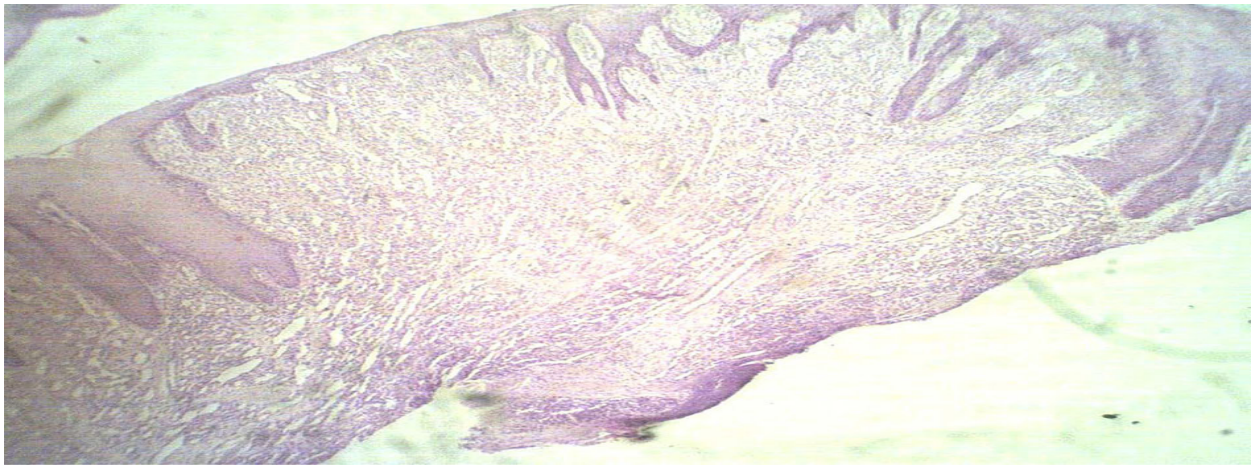


Fig. 8. Uneven hyperplasia of the basal layer of the integumentary flat epithelium of the mucous membrane, alternation of atrophy of the epithelium. In the stroma, an increase in the number of thin-walled and slit-like vessels. Hematoxylin and eosin coloring. Inscr.  $\times 4.0$ .

Рис. 8. Неравномерная гиперплазия базального слоя покровного плоского эпителия слизистой оболочки. В строме увеличение числа тонкостенных и щелевидных сосудов. Окраска гематоксилином и эозином. Ув.  $\times 4.0$ .

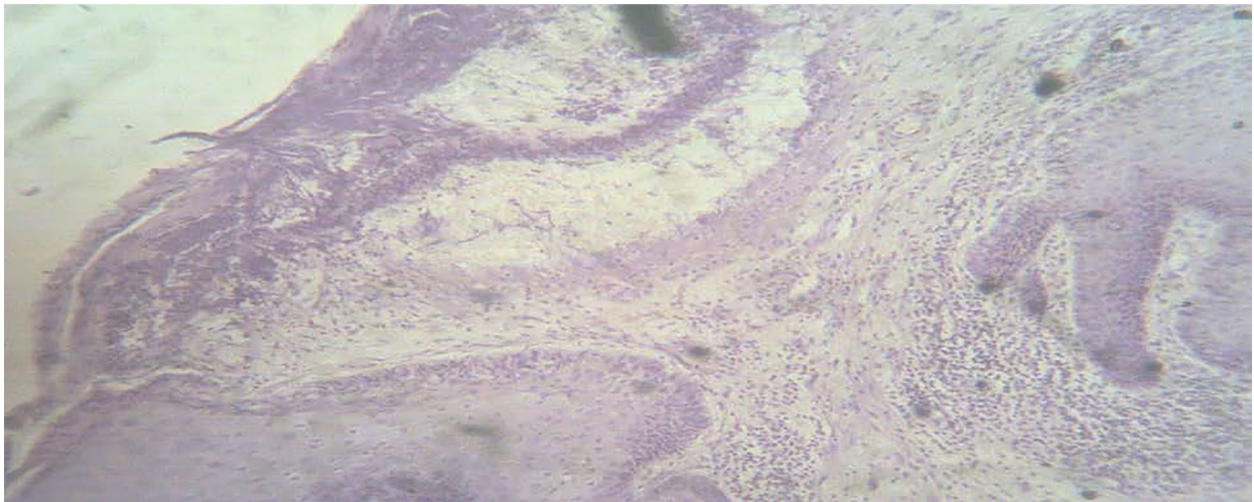


Fig. 9. Desquamation of the integumentary epithelium with the formation of a large subepithelial vesicle with transparent contents, swelling of the surrounding tissue, diffuse lymphocytic infiltration and uneven hyperplasia of the flat epithelium of the mucous membrane of the sublingual region. Hematoxylin and eosin colouring. Inscr.  $\times 10$ .

Рис. 9. Десквамация покровного эпителия с образованием крупного субэпителиального пузырька с прозрачным содержимым, отеком окружающей ткани, диффузной лимфоцитарной инфильтрацией и неравномерной гиперплазией плоского эпителия слизистой оболочки. Окраска гематоксилином и эозином. Ув.  $\times 10$ .

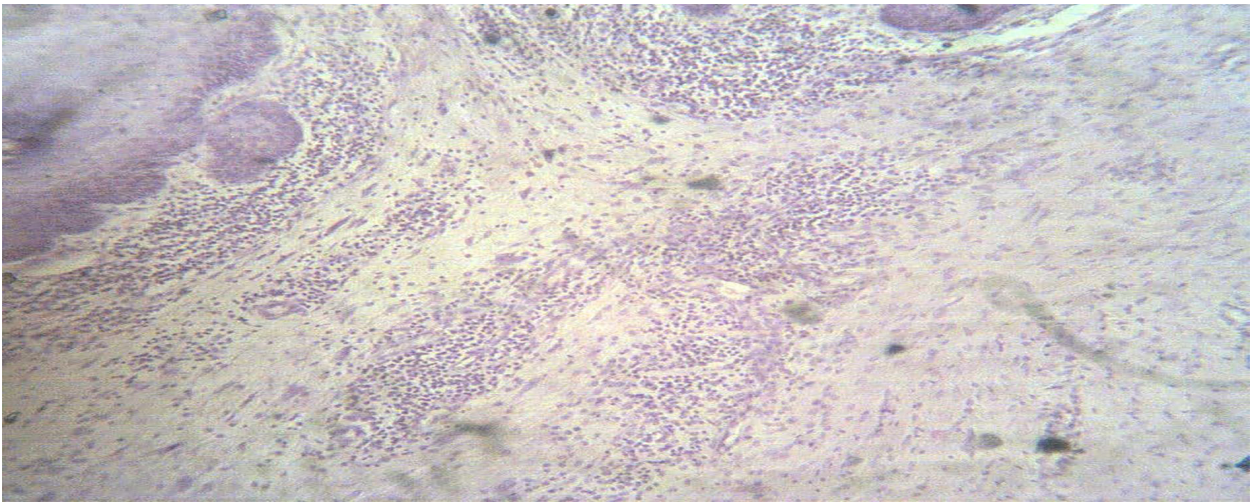


Fig. 10. Focal round cell inflammatory infiltration of stroma in the area of damage to the epithelium of the inner surface of the gums. Hematoxylin and eosin coloring. Inset.  $\times 4.0$ .

Рис.10. Очаговая круглоклеточная воспалительная инфильтрация стромы в области поражения эпителия. Окраска гематоксилином и эозином. Ув.  $\times 4.0$ .

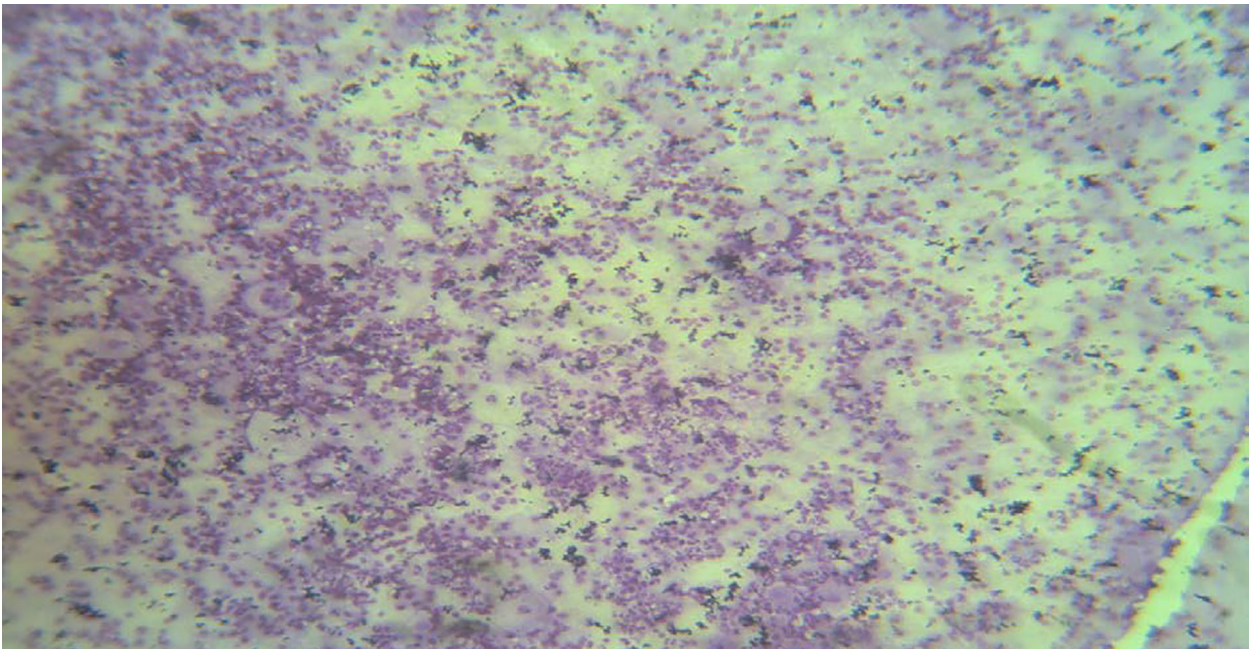


Fig. 11. Diffuse inflammatory cell infiltration with epithelial cells and desquamated cells. Hematoxylin and eosin coloring. Inset.  $\times 4.0$ .

Рис. 11. Диффузная лимфоцитарная инфильтрация с примесью единичных слущенных эпителиальных клеток. Окраска гематоксилином и эозином. Ув.  $\times 10$ .

During cytological studies of smears of typos from the affected OM surface, the following changes were found, presented below in microphotographs.

**Conclusion.** As a result of a morphological study of CRAS-related erosive-ulcerative OM lesions on the background of chronic gastroduodenitis, the most frequent manifestations were characterized by the development of the epithelium inflammation and ulceration, formation of ulcerative defects, hyperplasia of the surface squamous epithelium, and in some cases, atrophy and thinning of epithelium. The above indicated CRAS-related morphological changes in OM correlate

with the clinical data of patients with somatic pathology, namely in combination with chronic gastroduodenitis.

**Прозрачность исследования.** Исследование не имело спонсорской поддержки. Автор несет полную ответственность за предоставление окончательной версии рукописи в печать.

**Декларация о финансовых и других взаимоотношениях.** Все авторы принимали участие в разработке концепции, дизайна исследования и в написании рукописи. Окончательная версия рукописи была одобрена всеми авторами. Авторы не получали гонорар за исследование.

## ЛИТЕРАТУРА/ REFERENCES

1. Daminova ShB. Prediction, treatment and prevention of diseases of the oral cavity in children with chronic hepatitis B. *J Clinical density*. 2018; 12: 63.
2. Edgar NR, Saleh D, Miller RA. Recurrent aphthous stomatitis: A review. *J Clin Aesthet Dermatol*. 2017; 10(3): 26-36. DOI: 10.4103/0973-029X.86669
3. Ibragimova MK. Features diagnostics of periodontal diseases in patients with chronic cholecystitis. *European research: innovation in science, education and technology*, 2023; 3: 75-77.
4. Ibragimova MKh, Kamilova SR. Tactics of diagnosis and treatment of chronic recurrent aphthous stomatitis in chronic calculous cholecystitis. *Medical Journal of Uzbekistan*. 2019; 3: 65-68.
5. Natalie Rose Edgar, Dahlia Saleh, Richard A. Miller. Recurrent Aphthous Stomatitis: A Review. *J Clin Aesthet Dermatol*. 2017; 10(3): 26–36. DOI:10.4103/0973-029X.86669
6. Kamilov KhP, Ibragimova MKh. Evaluation of the effectiveness of complex treatment of patients with chronic recurrent aphthous stomatitis. *Medical Journal of Uzbekistan*. 2016; 2-4.
7. Karman B. Lankarani, Gholam Reza Sivandzadeh, Shima Hassanpour. Oral manifestation in inflammatory bowel disease: A review. 2013; 19(46): 8571 – 8579. DOI: 10.3748/wjg.v19.i46.8571
8. Hamed Mortazavi, Yaser Safi, Maryam Baharvand, Somayeh Rahmani. Diagnostic features of common oral ulcerative lesions: an updated decision tree. *Journal of Dentistry Volume*. 2016; 14. DOI: 10.1155/2016/7278925
9. Feleshtynska OY, Dyadyk OO. Substantiation of diagnosis and treatment of chronic recurrent aphthous stomatitis in crohn's disease. *J Wiadomosci Lekarskie*. 2020; 3.
10. Rabinovich OF, Abramova ES, Umarova KV, Rabinovich IM. Aspects of the etiology and pathogenesis of recurrent aphthous stomatitis. *Clinical dentistry*. 2015; 4: C.8-13; DOI: 10.1007/s00005-013-0261-y
11. Stephen Porter, Anne Hegarty, Fotini Kaliakatsou, Hodgson A, Crispian Scully. Recurrent Aphthous Stomatitis. *Clinics in Dermatology*. 2000; 18: 569 –578. DOI: 10.1016/s0738-081x(00)00147-4
12. Trukhan DI, Sulimov AF, Lebedev OI, Trukhan LYu. Changes in the skin, oral mucosa and organ of vision in diseases of the hepatobiliary system and pancreas. *Handbook of a polyclinic physician*. 2018; 2: 17-23. DOI: 10.26739/ 2181-0966-2020-2-1