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©N. A. Yaskiv

I. Horbachevsky Ternopil National Medical University

e-mail: yasykiv\_nand@tdmu.edu.ua

## The diagnostic process features of recurrent aphthous stomatitis depending on the clinical and morphological form

### ІНФОРМАЦІЯ

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**Key words:** RAS; canker sore; ulcer; stomatitis; mucous membrane of oral cavity; Recurrent Aphthous Stomatitis.

### АНОТАЦІЯ

**Summary.** This article describes the clinical course features of recurrent aphthous stomatitis (RAS) and unifies the clinical criteria for the diagnosis of recurrent aphthous stomatitis, taking into account subjective and objective components. The clinical characteristics of recurrent aphthous stomatitis various forms were carried out in accordance with the WHO classification and systematized in a table.

**The aim of the study** – to unify the clinical criteria for the diagnosis of recurrent aphthous stomatitis based on the analysis of subjective and objective components of the diagnostic process.

**Materials and Methods.** A clinical dental examination was carried out according to generally accepted criteria to achieve the goal, the results were recorded in the outpatient card of the dental patient 0–43/o. 60 patients of both sexes, aged from 18 to 40 years old were screened.

**Results and Discussion.** The minor form (fibrinous, Mikulich's aphtha) accounts for 65 %, major (necrotic, Setton's aphtha) – 18.3 %, herpetiform – 16.7 % in the structure of RAS. Minor form: 2–3 sharply painful aphthae, from 2–3 mm to 1 cm in size, located on an inflammatory background. Localization: the oral mucous is represented by a stratified squamous non-keratinized epithelium (lips, cheeks, transitional folds, lateral surfaces of the tongue). Epithelialization: 7–14 days, without the formation of a scar. Major form: a single intra-connective tissue defect, 1–1.5 cm in size. Localization: the oral mucous is represented by stratified squamous non-keratinized epithelium and is primarily affected with subsequent spread to the keratinized one. Epithelialization: up to 1 month with subsequent scarring and deformations of the oral mucosa. Herpetiform: a large number of small superficial aphthae, located in groups and have a tendency to merge. Localization: this form initially is manifested on oral mucous of the masticatory type with subsequent involvement of all types in the process. Epithelialization: up to 7–10 days, in some cases a permanent course is noted. According to the results of anamnestic data, risk factors should be taken into consideration, namely genetic predisposition, immunological status, diseases of the gastrointestinal tract and ENT organs.

**Conclusions.** A clinical differential table of 3 various forms was designed, including the following characteristics: localization of lesions, duration of the process and appearance of the elements. It helps to distinguish this disease from others and within their forms.

**Introduction.** Recurrent aphthous stomatitis (RAS) still remains one of the most common diseases among the pathologies of the oral mucosa without a clearly defined etiopathogenesis despite a whole array of developments in recent years [1].

The disease is characterized by the presence of painful aphthae on the oral mucosa, mostly occur without a certain pattern and cause pain in patients [2].

There is a large number of modern studies explaining the causes of RAS, but the etiology remains

still unknown. The disease is considered to be a multifactorial. There are many factors that can affect the development of RAS, such as: genetic predisposition, viral and bacterial infection, allergies, vitamins (B6, B12) and trace element (zinc, iron) deficiencies, hormonal disorders, trauma, stress and systemic diseases. RAS can be manifested not only as an independent disease, but also as a clinical sign of a systemic disease (lupus, Behcet's syndrome, HIV infection, inflammatory processes of the digestive tract, celiac disease). More than 30 generalized somatic diseases are accompanied by the formation of aphthous lesions on the oral mucosa [3].

The autoimmune mechanism is the key idea of disease pathogenetic factors. Many scientists agree with the statement that the destruction of the oral mucosa is caused by a T-cell-mediated immune response in RAS. It leads to decrease in the immunoregulatory index, increase in the level of proinflammatory cytokines, tumor necrosis factor and other changes in the immunological status of patients [4].

It should be noted that current views on the etiology, pathogenesis and treatment of RAS are quite ambiguous, as they are changing along with the development of science and the expansion of functional and laboratory diagnostic capabilities.

No data of laboratory tests currently provide a definitive conclusion about the disease. It entails the absence of clinical protocols in health care systems around the world which declare the issue of patients management of RAS [5].

Therefore, works based on the improvement of basic clinical diagnostic methods to objectify the patient's dental status, confirmation and verification of clinical and morphological forms of RAS for further development of additional diagnostic methods algorithms and ensuring a differentiated approach to treatment are of particular relevance [6].

**The aim of the study** – to unify the clinical criteria for the diagnosis of recurrent aphthous stomatitis based on the analysis of subjective and objective components of the diagnostic process.

**Materials and Methods.** A clinical and diagnostic examination of patients was conducted according to generally accepted criteria to achieve the goal, the results were recorded in the outpatient card of the dental patient 0–43/o. 60 patients of both sexes, aged from 18 to 40 years old were screened. Order of the Ministry of Health of Ukraine "On Creation and Implementation of Medical and Technological Documents for Standardization of

Medical Care in the System of the Ministry of Health of Ukraine" of 28.09.2012 No. 751). DMF index, the prevalence of caries, the presence of non-carious cervical lesions (NCCLs), dentoalveolar anomalies and deformations, OHI-S index (J. C. Green, J. R. Wermillion, 1964) were recorded at initial appointment and were taken into account. Periodontal status was objectified on the basis of the PMA index in the modification of C. Parma (1960). The study of various types therapeutic and preventive periodontal care need was performed by using the CPITN index (1982).

Taking into account the data of the history, the patients were noted with diseases of the ENT organs, digestive tract, intake of medication and lactose intolerance at the time of the study. The exclusion criteria were purulent-septic processes, tuberculosis, use of hormonal contraceptive methods, smoking, alcohol and spicy food abuse.

The objective assessment of the lesions was guided by the size and depth (intra-epithelial or intra-connective tissue defects), relative to the types of mucosa location. The number of lesions, duration of epithelialization or scarring were taken into account. Clinical verification was based on the RAS classification proposed by the World Health Organization.

**Results and Discussion.** Minor (fibrinous, Mikulich's aphtha) form of RAS was diagnosed in 39 patients (65.0 %). The main complaints were severe pain, the presence of aphthae and difficulty eating and speaking.

The history of the disease. Recurrences of the disease were noted from 1–2 per year to several within a month, the appearance of lesions was preceded by precursors in the form of paresthesias of the oral mucosa and the presence of a hyperemic spot with prodromal symptoms of burning or tingling from several hours to 1–2 days, followed by the formation of aphthae.

The personal history. RAS patients noted pathology of the digestive tract and ENT organs (frequent sore throats), namely 2–3 times per year.

The objective examination visualized erosions. They were round or oval in shape, 2–3 in the amount, covered with a fibrinous plaque, surrounded by a corolla of hyperemia on the periphery, ranging in size from 3 to 10 mm in diameter. They are localized on the areas of the oral mucosa, represented by a stratified squamous non-keratinized epithelium (the mucosa of the lips, cheeks, closer to the teeth closure lines, the transition zone of the gums movable part to the fixed one and

lateral surfaces of the tongue). The lesions were characterized by sharp pain on palpation (Fig. 1)

Major (necrotic, Setton's aphtha) was diagnosed in 11 patients (18.3 %). Patients complained of severe pain in the oral cavity, ulcers, inability to eat and speak. At the same time they noted a deterioration in their general condition a few days before the next debut of the disease has appeared.

The history of the disease. Patients usually noted the presence of 1–2 lesions. Their appearance was preceded by precursors in the form of focal lump, namely nodules. They are formed due to the inflammatory process in the small salivary glands and the wave-like course of the disease, which initiates the appearance of the oral mucosa deformation.

The personal history. Patients noted a tendency to allergies and pathology of the digestive tract.

During the objective examination, deep intra-connective tissue defects of the oral mucosa (ulcers) were visualized. They measured 1–3 cm in diameter, covered with a fibrinous layer, surrounded by a clear demarcation area of hyperemia along the periphery. These lesions primarily occurred on the mucosa, represented by a stratified squamous non-keratinized epithelium with further spread to the keratinized mucosa, namely the mucous membrane of the lips, cheeks, lateral surfaces of the tongue, soft palate and pharynx (Fig. 2).

Herpetiform was diagnosed in 10 patients (16.7 %). The patients' complaints were intense pain, difficulty eating and speaking. The general condition was not affected.

Anamnestic data. Patients noted hypothermia, a tendency to allergic lesions and stated a permanent course of the disease with frequent relapses.

During the objective examination of the oral mucosa a large number of superficial epithelial defects were revealed. They were small, ranging in size from 1 to 3 mm in diameter, and tended to be grouped and fused. Usually, single lesions are combined into more massive erosive surfaces of irregular shape. Any type of mucosa can be involved, but this form is predominantly manifested in the chewing mucosa with further involvement of immature epithelial cells areas (Fig. 3).

Taking into account the variety of clinical and morphologic forms of RAS, this differentiation is important for planning the most appropriate diagnostic assessment and therapy (Table).

Thus, the minor (fibrinous, Mikulich's aphtha) form accounts for 65 %, major (necrotic, Setton's aphtha) – 18.3 %, herpetiform – 16.7 % in the struc-



*Fig. 1.* Minor (fibrinous, Mikulich's aphtha) form of RAS.



*Fig. 2.* Major (necrotic, Setton's aphtha) form of RAS.



*Fig. 3.* Herpetiform RAS.

ture of RAS, that is consistent with the developments in this area over the past decades [7].

After integrating the results of the clinical examination, it is concluded that it is advisable to focus



**Table.** Clinical features differential table of three forms of recurrent aphthous stomatitis

WHO classification	Localization of lesions	Duration of the oral mucous process	Appearance of lesions
Minor (fibrinous, Mikulich's aphtha)	The mucous membrane is represented by a stratified squamous non-keratinized epithelium (lips, cheeks, transitional folds, lateral surfaces of the tongue).	7–14 days, epitalization occurs without scarring.	2–3 sharply painful aphthae, from 2-3 mm to 1 cm in size, located on an inflammatory background.
Major (necrotic, Setton's aphtha)	The oral mucous is represented by stratified squamous non-keratinized epithelium and is primarily affected with subsequent spread to the keratinized one.	Up to 1 month with subsequent scarring and deformations of the oral mucous.	A single intra-connective tissue defect, 1–1.5 cm in size.
Herpetiform	This form initially is manifested on oral mucous of the masticatory type with subsequent involvement of all types in the process.	Up to 7–10 days, a permanent course is noted in some cases.	A large number of small superficial aphthae, located in groups and have a tendency to merge.

on the WHO systematization, included 3 forms of RAS: minor – fibrinous (Mikulich's aphtha), major – necrotic (Setton's aphtha) and herpetiforme [8].

While studying recurrent aphthous stomatitis modern domestic scientists distinguish the following forms of RAS: classical aphthae (fibrinous) and Seton's stomatitis (necrotic); by severity – mild, moderate and severe. Rabinovich I.M. (1998) distinguishes the following forms: fibrinous, necrotic, glandular, deforming.

The disadvantage of all these classifications is the selection of forms that are clinically indistinguishable from each other. Therefore, the results of clinical observations make it possible to recommend the WHO classification.

Based on the results of anamnestic data, risk factors should be taken into account (Figs. 4, 5).

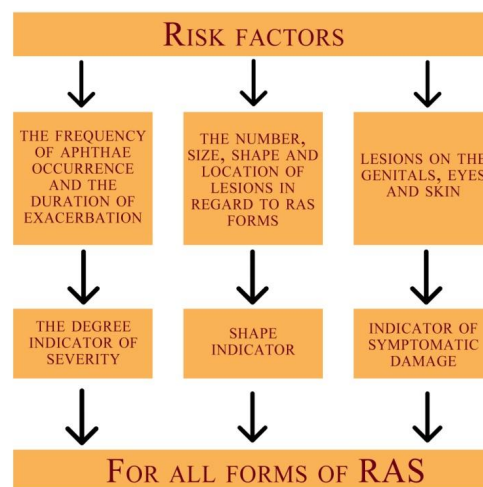
Due to the lack of clear etiologic or diagnostic criteria for RAS, the identification of this disease in clinical practice is often determined by a combination of the above risk factors, history, and clinical signs. We propose a structure of diagnostic clinical criteria for all forms of RAS, the aim is to distinguish this disease from others and within clinical and morphologic form.

The clinical guidelines will help focus the practitioner on the key points in the diagnosis for further development of a comprehensive treatment plan, namely the frequency of aphthae and the duration of exacerbation; the number, size, shape and location of lesions; the presence of aphthae not only in the oral cavity, that may be an indicator of symptomatic RAS.

It will be important to develop a system of additional diagnostic methods before using these data



**Fig. 4.** Characterization of recurrent aphthous stomatitis risk factors.



**Fig. 5.** Risk factors and clinical guidelines for the diagnosis of recurrent aphthous stomatitis.

to confirm the disease as idiopathic and to differentiate it from the manifestation of other systemic diseases (Behçet's disease, Crohn's disease) [9].

According to researchers [10], who studied the correlation between the appearance of lesions, the severity of the disease and micronutrient deficiencies in the blood, a significant decrease in vitamin D, B12, folic acid and iron levels in the blood of patients with RAS compared to healthy were found. No relationship was found between blood deficiencies and disease severity, assessed by ulcer diameter, number and frequency. However, logistic regression showed a significant association between the number of ulcers (single or multiple) and vitamin D deficiency.

Analyzing these data, we can conclude that further study of the issue is needed. Finding a correlation between the lack of iron, vitamin D, B12, folic acid and the course of RAS has been chosen as one of the areas for our future research.

**Conclusions.** By studying the above forms of RAS, we were able to unify the clinical criteria for

the diagnosis of recurrent aphthous stomatitis, taking into account the analysis of subjective and objective components of the diagnostic process and the WHO classification.

Visualized differences in the clinical forms of RAS should be considered at the stage of applying the main clinical methods, taking into account the morphological features of the mucous membrane structure at the time of the lesions verification by the dentist.

The absence of clear etiologic or diagnostic criteria for RAS makes it difficult to diagnose the disease in clinical practice, so a combination of risk factors, history and clinical signs improves this process. We propose a structure of diagnostic clinical criteria for all forms of RAS, the aim is to distinguish the disease from others and within clinical and morphologic form.

Taking into account the variety of clinical and morphological forms of RAS, a differential table of three forms was created to improve the diagnostic process of practicing physicians.

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Тернопільський національний медичний університет імені І. Я. Горбачевського МОЗ України

## Особливості діагностичного процесу рецидивного афтозного стоматиту залежно від клініко-морфологічної форми

**Резюме.** У даній статті описано особливості клінічного перебігу рецидивного афтозного стоматиту (РАС) та проведено уніфікацію клінічних критеріїв діагностики рецидивного афтозного стоматиту, беручи до уваги суб'єктивні та об'єктивні складові. Клінічну характеристику різних форм рецидивного афтозного стоматиту здійснили відповідно до класифікації ВООЗ та систематизували у таблицю.

**Мета дослідження** – уніфікація клінічних критеріїв діагностики рецидивного афтозного стоматиту, виходячи з аналізу суб'єктивних та об'єктивних складових діагностичного процесу.

**Матеріали і методи.** Для досягнення поставленої мети проведено клінічне стоматологічне обстеження 60 осіб обох статей віком від 18 до 40 років за загальноприйнятими критеріями, результати занесли в амбулаторні карти стоматологічного хворого 0–43/0.

**Результати досліджень та їх обговорення.** У структурі РАС фібринозна форма (афта Мікуліча, мала афта) складає 65 %, некротична (афта Сеттона, велика афта) – 18,3 %, герпетиформна – 16,7 %. Фібринозна форма: 2–3 афти різко болючі, розміром від 2–3 мм до 1 см, розташовані на запальному тлі, різко болючі при пальпації. Локалізація: слизова оболонка представлена багат шаровим плоским неороговілим епітелієм (губ, щік, перехідних складок, бічних поверхонь язика). Епітелізація: 7–14 днів, без утворення рубця. Некротична форма: поодинокий внутрішній сполучнотканинний дефект розміром 1–1,5 см. Епітелізація: до 1 місяця, із подальшим рубцюванням та деформаціями слизової. Локалізація: первинно вражається слизова оболонка, яка представлена багат шаровим плоским неороговілим епітелієм із подальшим розповсюдженням на ороговілий. Герпетиформна: велика кількість дрібних поверхневих афт, які розташовані групами і мають тенденцію до злиття. Епітелізація: до 7–10 днів, у деяких випадках відмічають перманентний перебіг. Локалізація: первинно маніфестує із слизової оболонки жувального типу, подальше залучення у процес усіх типів. Згідно з результатами анамнестичних даних, необхідно брати до уваги фактори ризику, а саме: генетичну схильність, імунологічний статус, захворювання ШКТ та ЛОР-органів.

**Висновки.** Було розроблено диференційну таблицю клінічних ознак трьох різних форм РАС, що включають у себе такі характеристики: локалізацію уражень, тривалість процесу та зовнішній вигляд елементів. Це допомагає відрізнити дане захворювання від інших та в межах клініко-морфологічних форм.

**Ключові слова:** РАС; афта; виразка; стоматит; слизова оболонка порожнини рота; рецидивний афтозний стоматит.

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