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ЕЖЕМЕСЯЧНЫЙ НАУЧНЫЙ ЖУРНАЛ

Медицинские новости Грузии

საქართველოს სამედიცინო სიახლენი

GEORGIAN MEDICAL NEWS

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GMN: Georgian Medical News is peer-reviewed, published monthly journal committed to promoting the science and art of medicine and the betterment of public health, published by the GMN Editorial Board since 1994. GMN carries original scientific articles on medicine, biology and pharmacy, which are of experimental, theoretical and practical character; publishes original research, reviews, commentaries, editorials, essays, medical news, and correspondence in English and Russian.

GMN is indexed in MEDLINE, SCOPUS, PubMed and VINITI Russian Academy of Sciences. The full text content is available through EBSCO databases.

GMN: Медицинские новости Грузии - ежемесячный рецензируемый научный журнал, издаётся Редакционной коллегией с 1994 года на русском и английском языках в целях поддержки медицинской науки и улучшения здравоохранения. В журнале публикуются оригинальные научные статьи в области медицины, биологии и фармации, статьи обзорного характера, научные сообщения, новости медицины и здравоохранения. Журнал индексируется в MEDLINE, отражён в базе данных SCOPUS, PubMed и ВИНИТИ РАН. Полнотекстовые статьи журнала доступны через БД EBSCO.

GMN: Georgian Medical News – საქართველოს სამედიცინო სიახლენი – არის ყოველთვიური სამეცნიერო სამედიცინო რეცენზირებადი ჟურნალი, გამოიცემა 1994 წლიდან, წარმოადგენს სარედაქციო კოლეგიისა და აშშ-ის მეცნიერების, განათლების, ინდუსტრიის, ხელოვნებისა და ბუნებისმეტყველების საერთაშორისო აკადემიის ერთობლივ გამოცემას. GMN-ში რუსულ და ინგლისურ ენებზე ქვეყნდება ექსპერიმენტული, თეორიული და პრაქტიკული ხასიათის ორიგინალური სამეცნიერო სტატიები მედიცინის, ბიოლოგიისა და ფარმაციის სფეროში, მიმოხილვითი ხასიათის სტატიები.

ჟურნალი ინდექსირებულია MEDLINE-ის საერთაშორისო სისტემაში, ასახულია SCOPUS-ის, PubMed-ის და ВИНИТИ РАН-ის მონაცემთა ბაზებში. სტატიების სრული ტექსტი ხელმისაწვდომია EBSCO-ს მონაცემთა ბაზებიდან.

WEBSITE

www.geomednews.com

К СВЕДЕНИЮ АВТОРОВ!

При направлении статьи в редакцию необходимо соблюдать следующие правила:

1. Статья должна быть представлена в двух экземплярах, на русском или английском языках, напечатанная через **полтора интервала на одной стороне стандартного листа с шириной левого поля в три сантиметра**. Используемый компьютерный шрифт для текста на русском и английском языках - **Times New Roman** (**Кириллица**), для текста на грузинском языке следует использовать **AcadNusx.** Размер шрифта - **12**. К рукописи, напечатанной на компьютере, должен быть приложен CD со статьей.

2. Размер статьи должен быть не менее десяти и не более двадцати страниц машинописи, включая указатель литературы и резюме на английском, русском и грузинском языках.

3. В статье должны быть освещены актуальность данного материала, методы и результаты исследования и их обсуждение.

При представлении в печать научных экспериментальных работ авторы должны указывать вид и количество экспериментальных животных, применявшиеся методы обезболивания и усыпления (в ходе острых опытов).

4. К статье должны быть приложены краткое (на полстраницы) резюме на английском, русском и грузинском языках (включающее следующие разделы: цель исследования, материал и методы, результаты и заключение) и список ключевых слов (key words).

5. Таблицы необходимо представлять в печатной форме. Фотокопии не принимаются. **Все цифровые, итоговые и процентные данные в таблицах должны соответствовать таковым в тексте статьи**. Таблицы и графики должны быть озаглавлены.

6. Фотографии должны быть контрастными, фотокопии с рентгенограмм - в позитивном изображении. Рисунки, чертежи и диаграммы следует озаглавить, пронумеровать и вставить в соответствующее место текста **в tiff формате**.

В подписях к микрофотографиям следует указывать степень увеличения через окуляр или объектив и метод окраски или импрегнации срезов.

7. Фамилии отечественных авторов приводятся в оригинальной транскрипции.

8. При оформлении и направлении статей в журнал МНГ просим авторов соблюдать правила, изложенные в «Единых требованиях к рукописям, представляемым в биомедицинские журналы», принятых Международным комитетом редакторов медицинских журналов - http://www.spinesurgery.ru/files/publish.pdf и http://www.nlm.nih.gov/bsd/uniform_requirements.html
В конце каждой оригинальной статьи приводится библиографический список. В список литературы включаются все материалы, на которые имеются ссылки в тексте. Список составляется в алфавитном порядке и нумеруется. Литературный источник приводится на языке оригинала. В списке литературы сначала приводятся работы, написанные знаками грузинского алфавита, затем кириллицей и латиницей. Ссылки на цитируемые работы в тексте статьи даются в квадратных скобках в виде номера, соответствующего номеру данной работы в списке литературы. Большинство цитированных источников должны быть за последние 5-7 лет.

9. Для получения права на публикацию статья должна иметь от руководителя работы или учреждения визу и сопроводительное отношение, написанные или напечатанные на бланке и заверенные подписью и печатью.

10. В конце статьи должны быть подписи всех авторов, полностью приведены их фамилии, имена и отчества, указаны служебный и домашний номера телефонов и адреса или иные координаты. Количество авторов (соавторов) не должно превышать пяти человек.

11. Редакция оставляет за собой право сокращать и исправлять статьи. Корректура авторам не высылается, вся работа и сверка проводится по авторскому оригиналу.

12. Недопустимо направление в редакцию работ, представленных к печати в иных издательствах или опубликованных в других изданиях.

При нарушении указанных правил статьи не рассматриваются.

REQUIREMENTS

Please note, materials submitted to the Editorial Office Staff are supposed to meet the following requirements:

1. Articles must be provided with a double copy, in English or Russian languages and typed or compu-ter-printed on a single side of standard typing paper, with the left margin of **3** centimeters width, and **1.5** spacing between the lines, typeface - **Times New Roman** (**Cyrillic**), print size - **12** (referring to Georgian and Russian materials). With computer-printed texts please enclose a CD carrying the same file titled with Latin symbols.

2. Size of the article, including index and resume in English, Russian and Georgian languages must be at least 10 pages and not exceed the limit of 20 pages of typed or computer-printed text.

3. Submitted material must include a coverage of a topical subject, research methods, results, and review.

Authors of the scientific-research works must indicate the number of experimental biological species drawn in, list the employed methods of anesthetization and soporific means used during acute tests.

4. Articles must have a short (half page) abstract in English, Russian and Georgian (including the following sections: aim of study, material and methods, results and conclusions) and a list of key words.

5. Tables must be presented in an original typed or computer-printed form, instead of a photocopied version. **Numbers, totals, percentile data on the tables must coincide with those in the texts of the articles.** Tables and graphs must be headed.

6. Photographs are required to be contrasted and must be submitted with doubles. Please number each photograph with a pencil on its back, indicate author's name, title of the article (short version), and mark out its top and bottom parts. Drawings must be accurate, drafts and diagrams drawn in Indian ink (or black ink). Photocopies of the X-ray photographs must be presented in a positive image in **tiff format**.

Accurately numbered subtitles for each illustration must be listed on a separate sheet of paper. In the subtitles for the microphotographs please indicate the ocular and objective lens magnification power, method of coloring or impregnation of the microscopic sections (preparations).

7. Please indicate last names, first and middle initials of the native authors, present names and initials of the foreign authors in the transcription of the original language, enclose in parenthesis corresponding number under which the author is listed in the reference materials.

8. Please follow guidance offered to authors by The International Committee of Medical Journal Editors guidance in its Uniform Requirements for Manuscripts Submitted to Biomedical Journals publication available online at: http://www.nlm.nih.gov/bsd/uniform_requirements.html
http://www.icmje.org/urm_full.pdf
In GMN style for each work cited in the text, a bibliographic reference is given, and this is located at the end of the article under the title "References". All references cited in the text must be listed. The list of references should be arranged alphabetically and then numbered. References are numbered in the text [numbers in square brackets] and in the reference list and numbers are repeated throughout the text as needed. The bibliographic description is given in the language of publication (citations in Georgian script are followed by Cyrillic and Latin).

9. To obtain the rights of publication articles must be accompanied by a visa from the project instructor or the establishment, where the work has been performed, and a reference letter, both written or typed on a special signed form, certified by a stamp or a seal.

10. Articles must be signed by all of the authors at the end, and they must be provided with a list of full names, office and home phone numbers and addresses or other non-office locations where the authors could be reached. The number of the authors (co-authors) must not exceed the limit of 5 people.

11. Editorial Staff reserves the rights to cut down in size and correct the articles. Proof-sheets are not sent out to the authors. The entire editorial and collation work is performed according to the author's original text.

12. Sending in the works that have already been assigned to the press by other Editorial Staffs or have been printed by other publishers is not permissible.

Articles that Fail to Meet the Aforementioned Requirements are not Assigned to be Reviewed.

ავტორთა საყურადღებოდ!

რედაქციაში სტატიის წარმოდგენისას საჭიროა დავიცვათ შემდეგი წესები:

1. სტატია უნდა წარმოადგინოთ 2 ცალად, რუსულ ან ინგლისურ ენებზე,დაბეჭდილი სტანდარტული ფურცლის 1 გვერდზე, 3 სმ სიგანის მარცხენა ველისა და სტრიქონებს შორის 1,5 ინტერვალის დაცვით. გამოყენებული კომპიუტერული შრიფტი რუსულ და ინგლისურენოვან ტექსტებში - **Times New Roman (Кириллица)**, ხოლო ქართულენოვან ტექსტში საჭიროა გამოვიყენოთ **AcadNusx.** შრიფტის ზომა – 12. სტატიას თან უნდა ახლდეს CD სტატიით.

2. სტატიის მოცულობა არ უნდა შეადგენდეს 10 გვერდზე ნაკლებს და 20 გვერდზე მეტს ლიტერატურის სიის და რეზიუმეების (ინგლისურ, რუსულ და ქართულ ენებზე) ჩათვლით.

3. სტატიაში საჭიროა გაშუქდეს: საკითხის აქტუალობა; კვლევის მიზანი; საკვლევი მასალა და გამოყენებული მეთოდები; მიღებული შედეგები და მათი განსჯა. ექსპერიმენტული ხასიათის სტატიების წარმოდგენისას ავტორებმა უნდა მიუთითონ საექსპერიმენტო ცხოველების სახეობა და რაოდენობა; გაუტკივარებისა და დაძინების მეთოდები (მწვავე ცდების პირობებში).

4. სტატიას თან უნდა ახლდეს რეზიუმე ინგლისურ, რუსულ და ქართულ ენებზე არანაკლებ ნახევარი გვერდის მოცულობისა (სათაურის, ავტორების, დაწესებულების მითითებით და უნდა შეიცავდეს შემდეგ განყოფილებებს: მიზანი, მასალა და მეთოდები, შედეგები და დასკვნები; ტექსტუალური ნაწილი არ უნდა იყოს 15 სტრიქონზე ნაკლები) და საკვანძო სიტყვების ჩამონათვალი (key words).

5. ცხრილები საჭიროა წარმოადგინოთ ნაბეჭდი სახით. ყველა ციფრული, შემაჯამებელი და პროცენტული მონაცემები უნდა შეესაბამებოდეს ტექსტში მოყვანილს.

6. ფოტოსურათები უნდა იყოს კონტრასტული; სურათები, ნახაზები, დიაგრამები - დასათაურებული, დანომრილი და სათანადო ადგილას ჩასმული. რენტგენოგრამების ფოტოასლები წარმოადგინეთ პოზიტიური გამოსახულებით **tiff** ფორმატში. მიკროფოტოსურათების წარწერებში საჭიროა მიუთითოთ ოკულარის ან ობიექტივის საშუალებით გადიდების ხარისხი, ანათალების შეღებვის ან იმპრეგნაციის მეთოდი და აღნიშნოთ სურათის ზედა და ქვედა ნაწილები.

7. სამამულო ავტორების გვარები სტატიაში აღინიშნება ინიციალების თანდართვით, უცხოურისა – უცხოური ტრანსკრიპციით.

8. სტატიას თან უნდა ახლდეს ავტორის მიერ გამოყენებული სამამულო და უცხოური შრომების ბიბლიოგრაფიული სია (ბოლო 5-8 წლის სიღრმით). ანბანური წყობით წარმოდგენილ ბიბლიოგრაფიულ სიაში მიუთითეთ ჯერ სამამულო, შემდეგ უცხოელი ავტორები (გვარი, ინიციალები, სტატიის სათაური, ჟურნალის დასახელება, გამოცემის ადგილი, წელი, ჟურნალის №, პირველი და ბოლო გვერდები). მონოგრაფიის შემთხვევაში მიუთითეთ გამოცემის წელი, ადგილი და გვერდების საერთო რაოდენობა. ტექსტში კვადრატულ ფჩხილებში უნდა მიუთითოთ ავტორის შესაბამისი N ლიტერატურის სიის მიხედვით. მიზანშეწონილია, რომ ციტირებული წყაროების უმეტესი ნაწილი იყოს 5-6 წლის სიღრმის.

9. სტატიას თან უნდა ახლდეს: ა) დაწესებულების ან სამეცნიერო ხელმძღვანელის წარდგინება, დამოწმებული ხელმოწერითა და ბეჭდით; ბ) დარგის სპეციალისტის დამოწმებული რეცენზია, რომელშიც მითითებული იქნება საკითხის აქტუალობა, მასალის საკმაობა, მეთოდის სანდოობა, შედეგების სამეცნიერო-პრაქტიკული მნიშვნელობა.

10. სტატიის ბოლოს საჭიროა ყველა ავტორის ხელმოწერა, რომელთა რაოდენობა არ უნდა აღემატებოდეს 5-ს.

11. რედაქცია იტოვებს უფლებას შეასწოროს სტატია. ტექსტზე მუშაობა და შეჯერება ხდება საავტორო ორიგინალის მიხედვით.

12. დაუშვებელია რედაქციაში ისეთი სტატიის წარდგენა, რომელიც დასაბეჭდად წარდგენილი იყო სხვა რედაქციაში ან გამოქვეყნებული იყო სხვა გამოცემებში.

აღნიშნული წესების დარღვევის შემთხვევაში სტატიები არ განიხილება.

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ORAL MANIFESTATIONS IN JUVENILE SCLERODERMA: CLINICAL PRESENTATIONS AND HISTOPATHOLOGICAL CHARACTERISTICS

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Abstract.

Juvenile scleroderma (JS) is a rare chronic connective tissue disorder characterized by stiffening of the skin and soft tissues, including the oral cavity and perioral tissues, leading to fibrosis and a large spectrum of internal organs involvement, cosmetic defects, and early infant disability.

The aim of this study was to investigate the histomorphological features of lesions of oral mucosa tissues in children with juvenile scleroderma (JS).

39 JS patients (9 with juvenile systemic sclerosis – JSS and 20 with juvenile scleroderma of head-JSH aged from 5 to 17 years were observed with dental examination and morphological investigation of the oral mucosa. Signs of damage of the mucous membrane of the oral cavity, was detected in 100% of JS patients observed. Lesions of mucosa appear at the earliest stages of the disease and are associated with the development of dystrophic and atrophic processes, and abnormal vascularization.C3 deposition of the complement component and IgM and IgG containing immune complexes were found in the vessel walls of the oral cavity in 72.63% of patients. Vasculitis of the oral cavity was detected among 1/3 of patients, and vasculopathy was found among 52,63 % of those examined. Mucosal, dystrophic, and vascular abnormalities develop in children with JSS, as well as in JSH patients. We distinguish and describe four stages of mucous lesions. Secondary infection stomatitis was noticed in patients.

Key words. Juvenile scleroderma, children, oral mucous, histomorphological examination.

Introduction.

Juvenile scleroderma (JS) is a rare chronic connective tissue disorder characterized by stiffening of the skin and soft tissues, leading to fibrosis, systemic vasculopathy, and a large spectrum of internal organs involvement. The disease frequency was reported as one per million [1-7]. JS has two varieties: juvenile localized scleroderma (JLS), where internal organ involvement is not expected, and juvenile systemic sclerosis (JSS) [8-12]. JLS occurs approximately four times more frequently than JSS, unlike JSS, which did not develop Raynaud phenomenon and visceral damage. Both disease forms, however, may cause expressive functional organ insufficiency, aesthetic sequelae, and early infant disability [6,9,13].

Despite the skin and musculoskeletal tissue, joints of the trunk, head, and extremities, sclerodermatous lesions could be present as well in the oral cavity and perioral tissues [3,6,13]. Since JS is uncommon in children, many aspects of the disease remain unclear. Revision of recent findings shows that oro-facial manifestations of scleroderma (SL) have been reported both in systemic and localized disease forms [8-12]. Abnormal vascularity and alterations of the microcirculation of the oral cavity are additional damage factors for the gingival tissues in SI.

Numerous data on adult patients [2,3,14] showed that the mouth and face are frequently involved in SL. Patients often experience aesthetic concerns with skin sclerosis and telangiectasia, diminished mouth opening, altered dentition, and dry mouth. Mouth-related disability in adults with SL can be assessed by the Mouth Handicap in Systemic Sclerosis (MHISS) scale [15]. It was found out that 3 factors represent limitation induced by reduced mouth opening, dry mouth syndrome, and aesthetic concern. These data are directly associated with the main problems dentists face in caring for patients with SL:

1) oral mucosa involvement and ulcerations associated with dry mouth; 2) manducatory apparatus involvement responsible for dysphagia, retraction of lips, perioral streaks, and limitation in mouth opening; and 3) treatment-related adverse events [2].

The most common oral manifestations were limitation of mouth opening, widening of the periodontal ligament, and xerostomia in the meta-analysis study by M. Hadj Said and colleagues [14] among of 1187 orofacial manifestations (OFM) in adult patients with SL. The authors conclude that these ORM are probably more common than reported.

Oral lichen planus and its histopathological dates must be separated from morphea [16].

An unusual oral involvement was reported in a 13-year-old girl who consulted for progressive recession on the attached gingiva of her upper left incisors, produced white linear fibrotic areas with a scar-like appearance, atrophy of tongue papillae, gingival recession, and alveolar bone resorption [17]. She also presented a hypopigmented line on the left side of the skin of her upper lip, which continued through the vermilion and the lip mucosa, including the gingiva of the affected teeth. Clinical examination, blood tests, computerized axial tomography, echo-Doppler ultrasound, and histopathological evaluation confirmed the diagnosis of morphea. Treatment with methotrexate and systemic corticosteroids was conducted. After 24 months, no other lesions appeared.

Lopez Pineiro M, et al., in 2019, presented the case report on a 33-year-old African American woman [10] who presented with white discoloration of her superior gingiva and lip and a linear white patch that started along the gingiva; after the biopsy, the diagnosis of linear morphea involving the oral cavity was proved. Biopsy of the anterior maxillary bone was unremarkable. The latter case report serves as evidence of diagnostic difficulties, despite it being well known that linear scleroderma of the face (“en coupe de sabre”) usually affects the oral cavity with resorption of teeth, unilateral atrophy of the tongue, and xerostomia.

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Summing it up, the oral manifestations in juvenile scleroderma could be numerous, but its oral manifestations in juvenile scleroderma: clinical presentations and histopathological characteristics, frequency in the childhood population, and histopathological pattern are still in need to be studied thoroughly for evaluation of diagnostic criteria and treatment options.

Our study was aimed at finding out the main clinical presentations and histopathological characteristics of oral cavity involvement in JS.

Purpose of the study.

Aim is to establish diagnostical features of juvenile scleroderma (JS) manifestation in children with clinical dental examination and histomorphological examination of the oral cavity.

To achieve this goal, we set the following objectives:**Objectives of the study.**

• To identify the main diagnostic signs of damage to the oral mucosa in children with juvenile scleroderma

• To study histomorphological features of lesions of oral mucosa tissues in children with juvenile systemic scleroderma

• To determine the dependence of mucosal lesions on the oral cavity on the duration and nature of the course of the underlying disease and the underlying therapy used.

Materials and Methods.

We examined 39 children at the age of 5 to 17 years old with JS, among them 9 children with juvenile systemic sclerosis (JSS) and 30 with juvenile localized scleroderma of the face and head (JSH). 12 of the children had a disease duration of over two years, and 27 children had a disease duration of less than two years. All children were on the treatment at the N.F. Filatov Clinical Institute of Children health University Children clinical hospital of the I.M. Sechenov First Moscow State Medical University in the department of rheumatology, where they received disease-modifying treatment with glucocorticosteroids and immunosuppressants.

The trial protocol was approved by the local ethics committee at FSAEI of HE I.M. Sechenov First Moscow State Medical University of the Ministry of Health of the Russian Federation (Sechenov University) – protocol №16-19. Before trial initiation, all children and their parents were given written informed consent to participate in the trial, examination, introduction of photographic protocols, and treatment.

The diagnosis and degree of severity of the disease, among the examined children, were established according to their complaints, clinical and laboratory studies, and the medical report of the pediatrician. In order to specify the activity of the disease, it is necessary to study in the blood serum: C-reactive protein (CRP), immunoglobulins (Ig), complement, rheumatoid and antinuclear factors, and antibodies to DNA.

Histomorphological and immunohistochemical examination of oral cavity mucousa. Material from the clinically modified mucosal site (n=19) and unmodified mucosal site (n=11) was taken in 19 children. Clinically modified mucosal sites were considered with a pronounced degree of thinning, compaction, and atrophy.

19 children got through a histo-morphological study of the oral mucosa, such as flushing and mucosal sections were examined to detect histological, morphological, immunohistochemical, and virus-optical shifts in the pathological focus and severity of the disease. It also could help to monitor the effectiveness of the local therapy better.

Morphological examination determines the density of the infiltrate of the lamina propria of the gingival mucosa, the structure of the cellular infiltrate: the number of lymphocytes, plasmocytes, macrophages, fibroblasts, eosinophils, and neutrophils.

In the immunohistochemical and virus-optical studies in paraffin sections using the direct immunofluorescent method, one finds a number of cells producing IgA, IgM, IgG, and IgE, as well as deposition of immune complexes and C3 complement components in the walls of the vessels.

Results.

We have examined 39 children with JS at the ages of 5 to 17 years, among them 9 children with juvenile systemic sclerosis (JSS) and 30 with juvenile localized scleroderma of the face and head (JSH). Diagnosis of JSS and JSH was established in accordance with the provisional classification criteria of JSS and classification of juvenile localized scleroderma. (PRES/ACR/ELAR, 2004).

During dental examination of the children, we found that all of them have skin lesions of the face, which are a frequent diagnostic syndrome of the juvenile systemic scleroderma. The skin syndrome in 60% (n=17) of patients is the first sign of JS, in 20% it occurs during the first year of the disease, and in the others, it joins later, after 2-6 years. The skin is cold, and dry, due to sweating and sebum, not formed in a crease, the pattern is smoothed. The color becomes parchment, or it acquires a shade of old ivory with areas of dyschromia and telangiectasias. The face is masklike, without mimicking and wrinkles. The specific lesions of the mucous membrane of the oral cavity were noted in all of our patients, both JSS and JSH. The main complaints in children are a difficult opening of the mouth, dryness, numbness of certain areas, burning, and change in taste. The mucous membrane of the oral cavity with JS, like the skin, undergoes three stages of development of the disease: complete swelling, induration, and atrophy (Figures 2A and 3B).

Main diagnostic features of oral cavity mucosal damage in children with JS.

The defeat of the oral mucosa in patients with JS begins with the lips. A small swelling, along with edema of the mucous membrane and submucosal tissue, manifest this condition. In the stage of dense edema, the most frequent feature is a violation of the clear border of the red border of the lips. The second stage of the development of the JS is the stage of induration, which is characterized by a hardening of the patient's lips. In the atrophic stage, there are such characteristics as brown pigmentation, the mucous membrane is sharply thinned and dry, the elasticity is lost, and there is total atrophy of the mucous lips and the formation of microheilia (Figure 2B).

A characteristic symptom of scleroderma is a change in the tongue, with both the mucous membrane and the muscle layers, which leads to microglossia. In patients, due to atrophy of the filiform papillae, the surface of the tongue has a smoothed, polished appearance; thus, atrophic glossitis is developing.

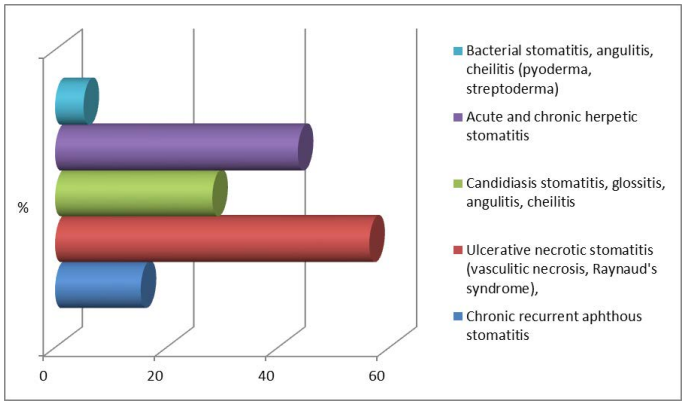


Figure 1. *Frequency and characteristic features of stomatitis in children with juvenile scleroderma.*

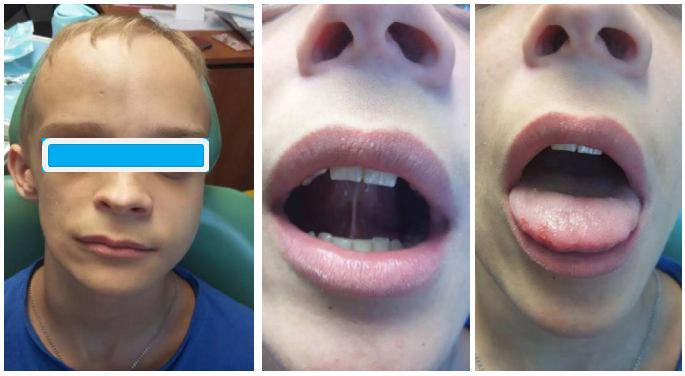
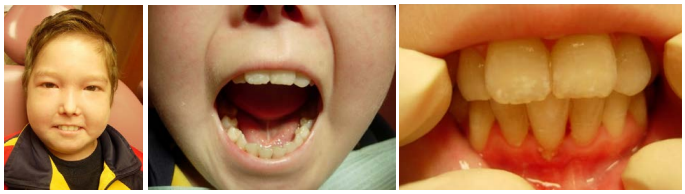


Figure 2. *12-year-old child, diagnosed with juvenile scleroderma.*

A. *Lesion like "en coup de sabre" in the maxilla-facial area.*

B. *Shortening of the frenum of the tongue in children with a duration of disease of more than 2 years suffering from systemic scleroderma.*

C. *Plaque pockets of induction, sclerosis and atrophy on the mucous tongue.*



A **B** **C**

Figure 3. *The 13-year-old child diagnosed with systemic scleroderma.*

A. *Mask face, without mimicking and wrinkles, the skin is cold, dry, the color becomes parchment or acquires a shade of old ivory with areas of dyschromia and with telangiectasias.*

B. *Formation of the microstoma, violation of a clear boundary of the red border of the lips, sharp thinning, dryness, loss of elasticity, sharp thinning, persistent atrophy and immobility of the frenum of the tongue.*

C. *There is a local atrophy of periodontal tissues in the region of the tooth 4.1.*

There is a fast involving of a lingual frenulum to the process of atrophy and scleroderma, while its shortening and sharp immobility are noted-this is the earliest diagnostic sign of the manifestation of JS.

In the process of atrophy and sclerosis, the sublingual frenulum is involved particularly quickly, with its shortening, compacting, and sharp immobility, which is the earliest diagnostic sign of the manifestation of JS (Figures 2B and 3B).

Features of changes in the mucosa of the oral cavity in JS: loss of shine and elasticity, the presence of telangiectasias, a sharp thinning of the mucosa, and atrophy of periodontal tissue is often primary local, with a duration of the disease of more than 2 years; atrophy is generalized (Figure 3C).

The examinations conducted by us allowed us to establish the main diagnostic signs of the lesion of the mucosa of the oral cavity in children with JS and to divide it into 3 stages depending on the involvement of oral cavity mucous in the common sclerotic process (Table 1).

We observe the evolution of sclerotic changes in the oral mucosa - from the initial stage (edema, compaction) to the late stage (severe sclerosis and atrophy).

The defeat of the oral mucosa, in the initial stage (n = 12), took place in children with a disease duration of less than 2 years. Lesions of the oral mucosa, characteristic of the late stage (n = 9), occurred in children with JS debut at 4-6 years old, and appeared after 6-10 years of JS course, and also depended on the degree of immunological activity of JS.

Histological, morphological, and immunohistochemical changes in the oral mucosa in children with JS.

All clinical changes in the oral mucosa were confirmed by histomorphological studies of the oral mucosa. We were able to identify and track the pathology of the mucosa, which is observed only with scleroderma. Violations are described in the study of skin biopsy samples, well studied earlier, in contrast to the oral mucosa [18-20].

According to histomorphological studies of tissue from a pathologically altered area of the oral mucosa with JS, it was revealed:

- epithelial dystrophy, epithelial degeneration, hyalinosis, and reduction of the vascular bed in the submucosal layer of the epithelium (diagnostic signs of scleroderma)
- lymphocyte epithelial infiltration, which was much less common (a diagnostic sign of chronic tissue inflammation)
- vasculitis and vasculopathy of the vascular bed in the submucosal layer of the epithelium, deposition of the C3 component of complement and immune complexes (IgM and IgG) in the walls of blood vessels (a diagnostic sign of autoimmune tissue inflammation) (Table 2).

For a more detailed study of the pathology of the oral mucosa occurring in the own plate of the mucosa, we carried out morphometric and immunohistochemical studies. The data obtained showed that the cell density of the infiltrate increases to 9037+424 cells ($p < 0.01$) compared with unchanged tissue 5168+438. Among the cells of the infiltrate, the number of lymphocytes, plasmocytes, fibroblasts, and fibrocytes, neutrophils increases. The number of cells producing IgM and IgG increases, and the number of IgE cells increases slightly. In 72.63%, C3 deposition of the complement component and IgM and IgG immune complexes in the vessel walls is noted, which indicates autoimmune inflammation in the vascular endothelium (Table 3).

Infectious lesions of the oral mucosa in children with JS.

Such a pathological condition of the oral mucosa and prolonged basic treatment with drugs aimed at suppressing

Table 1. *Clinical characteristic of oral cavity mucous damage in children with JS in dependence with mouth shell mucous sclerosis stage.*

Localization of lesions of the oral mucosa at various stages of sclerosis	**Clinical symptoms of damage to the oral mucosa**
I – initial stage of damage to the oral mucosa (in the form of edema and unexpressed compaction) (n=12)	
- lip lesion	- initial violation of the “blurring” of the clear border of the red border of the lips - the appearance of single radial folds of the near-mouth region - There is a slight swelling of the mucous membrane and submucosal tissue in the vestibule of the mouth, resulting in pronounced embossed tooth prints.
- lesions of the oral mucosa	- Some swelling, hyperemia with still maintained suppleness, moderate hydration observed
- tongue lesion	- swelling of the mucous membrane and submucosal tissue (pronounced embossed tooth prints) on the lateral surfaces of the tongue - desquamative glossitis (partial desquamation of the epithelium of the tongue's mucous membrane) - the obstruction of the papillary layer of the tongue, is accompanied by swelling of the mucosa. - numbness of the tip of the tongue
- lesions of the hyoid frenum	- initial violations of pronunciation of sounds - sublingual frenum ischemia (whitening)
- lesions of the gum mucosa	- catarrhal gingivitis, with frequent exacerbations (hyperemia, bleeding, swelling of the gums)
II – stage of generalized damage to the oral mucosa (in the form of induction and compaction) (n=18)	
- lip lesion	- the red border becomes pale, tense with areas of hyperpigmentation - lip tissues acquire a moderately firm consistency, tighten - pronounced dryness of the lip mucosa (the presence of crusts, cracks, jam), frequent gluing of the lips. - the appearance of multiple radial folds, as if constricting the oral fissure, leading to "microheilia" - difficulty opening the mouth, leading to angular cheilitis
- lesions of the oral mucosa	- the mucosa acquires a paler shade, becomes more dense, anemic, and less malleable - moisturized, severe dryness
- tongue lesion	- desquamative glossitis (partial desquamation of the epithelium of the tongue mucosa), but the areas of desquamation of the epithelium are pale against the background of a dry sclerotic tongue surface, a taste disorder appears
- lesions of the hyoid frenum	- sharp whitening and compaction of the hyoid frenum, impaired mobility of the tongue
- lesions of the gum mucosa	- sharp cyanosis and compaction of the papillary gum - the emergence of a single "local gum recession"
III – late-stage lesions of the oral mucosa (in the form of atrophy and sclerosis) (n=9)	
- lip lesion	- complete loss of the border of the red border of the lips - sharp thinning of the lips, becoming dense and atrophic, sharply changing their shape, resembling strips of 2-3 mm or cords of a cyanotic shade - atrophy of the lips and narrowing of the mouth leads to a violation of their closure, and the teeth remain exposed - a symptom of "microstomy" - when you try to close your lips from tense, tightened skin in the near-mouth area of the face, inverted scars appear - the symptom is “incompletely tightened pouch” - speech impairment
- lesions of the oral mucosa	- sharp atrophy, thinning of the mucosa, and characteristic brown pigmentation are present - a complete loss of elasticity and suppleness, the mucous membrane of the cheeks, the vestibule of the mouth when trying to open the mouth, gathers in folds resembling tendon cords - the mucous membrane of the hard palate is strongly atrophied and thinned and tightly soldered with the periosteum, so the palatine suture is modified, acquiring a whitish-shiny hue, and palatine arches become like isolated tendon cords - the mucous membrane of the soft palate and the muscle layer is compacted and atrophied, which leads to impaired swallowing and pronunciation of sounds - deposition of calcifications in the submucosal layer, rarely in children, detected in 3 children
- tongue lesion	- pronounced manifestations of atrophy and sclerosis of the mucosa "atrophic glossitis", which leads to a violation of taste - sclerosis and muscle atrophy of the tongue macroglossia lead to swallowing and speech formation
- lesions of the hyoid frenum	- sharp shortening, as a result of severe sclerosis and atrophy, which leads to a restriction of the mobility of the tongue and impaired speech formation, food intake
- lesions of the gum mucosa	- atrophy and sclerosis of the papillary gum - “atrophic gingivitis”, “gum recession”

Table 2. *Histomorphological pathological changes in the oral mucosa in juvenile scleroderma in children.*

Indicators of pathological histomorphological changes in the oral mucosa	**Quantitative indicators of biopsy (n=19)**
Epithelial dystrophy	n=12 (63,15%)
Acanthosis	n=7 (36,84%)
Spongsia	n=8 (42,11%)
Exacitosis	n=12 (63,15%)
Vascular bed reduction	n=9 (47,36%)
Vasculitis	n=7 (36,84%)
Vasculopathy	n=10 (52,63%)
Thickening of the walls of blood vessels	n=7 (36,84%)
Swelling of the stroma	n=6 (31,57%)
C_3 component deposition immune complexes (IgM и IgG)	n=14 (72,63%)

Table 3. *Morphometric and immunohistochemical parameters of the oral mucosa pathologically altered and unchanged in children with juvenile scleroderma (M+m).*

Morphometric and immunohistochemical parameters	**Pathologically altered mucosa (n=19)** **The average number of cells (for 1мм²)**	**Unchanged Mucous (n=11)** **The average number of cells (for 1мм²)**	**D**
Cellular density of infiltrate (average sum of all detected cells)	9037±424	5168±438	<0,01
Lymphocytes	3077±289	1991±209	<0,01
Immature plasmocytes	696±67	169±23	<0,01
Mature plasmocytes	836±75	397±81	-
Macrophages	589±39	421±95	-
Fibroblasts	1568±74	1228±61	<0,01
Fibrocytes	1958±95	902±145	<0,05
Eosinophils	114±17	37±33	<0,01
Neutrophils	199±31	23±19	<0,01
Producing cells: IgM IgG IgE	 658±59 495±35 63±12	 264±27 102±19 23±15	 <0,01 <0,01 -

D – differences between pathologically altered mucosa and unchanged

Table 4. *Lesions of the oral mucosa in children with juvenile systemic scleroderma with infectious stomatitis.*

stomatitis in children with juvenile scleroderma (history and reversibility)	Juvenile Scleroderma (n=39)
Chronic recurrent aphthous stomatitis	n=6 15,38%
Candidiasis stomatitis, glossitis, angulitis, and cheilitis	n=11 28,23%
Acute and chronic herpetic stomatitis	n=17 43,58%
Ulcerative necrotic stomatitis (vasculitic necrosis, Raynaud's syndrome),	n=22 56,41%
Bacterial stomatitis, angulitis, cheilitis (pyoderma, streptoderma)	n=2 5,12%

the autoimmune process often led to the secondary infection, accompanied by infectious diseases of the mucosa, and various stomatitis (Table 4, Figure 1).

Infectious stomatitis in children with juvenile scleroderma does not belong to the symptomatic criteria for damage to the oral mucosa, but they are much more common (from 5.12% to 43.58%) than in children who do not suffer from systemic diseases (according to the literature, 1-2% of the child population suffer from stomatitis) [11]. Sometimes in the same child, during periods of activity of the underlying disease, against the background of an increase in the doses of basic therapy, herpetic stomatitis and candidiasis stomatitis appear in the oral cavity, often simultaneously. This is very important information for rheumatologists, dermatologists, and dentists, especially when choosing drugs for the treatment of pathology of the oral mucosa in children with JS.

In addition to infectious complications, we diagnosed chronic recurrent aphthous stomatitis (15.38%), and ulcerative necrotic stomatitis (vasculitic necrosis, Raynaud's syndrome) (56.41%), which were considered symptomatic manifestations of autoimmune inflammation of the oral mucosa.

Discussion.

Current literature evidence that in scleroderma, processes of sclerosis of the mucosa are irreversible and lead to severe suffering of patients, due to the limitation of the mobility of the tongue, soft palate, reduction of the depth of the vestibule of the mouth, speech impairment, changes in taste sensations, thinning of the mucosa, and easy traumatism [3,8,10,11,14,21-24]. The majority of investigations are performed in adult patients with systemic sclerosis (SS) or morphea. Our research is based on children with scleroderma. Significant mucous abnormalities of the oral cavity were detected, including large infiltrates containing lymphocytes, plasmocytes, fibroblasts, and neutrophils. In 72.63% of patients, C3 deposition of the complement component and IgM and IgG containing immune complexes were found in the vessel walls of the oral cavity. These changes indicate an autoimmune origin of inflammation in the endothelium. These changes were unique in JSS and JSH patients. Patients with JS exhibit a reduction in the vascular bed. Vasculitis was found in 1/3 of the cases, and vasculopathy in 52,63%. Abnormal microcirculation was described previously [25], but in adults with SS. Antonacci A. (2024) [26] examined the vessels of the oral mucosa by capillaroscopy, and established the presence of vasculitis, and described the diagnostic sign of SS - vascular reduction.

A histomorphological study of oral mucousa in patients with JS showed epithelial degeneration. Where have classified into 4 stages, according to the severity of lesions.

Other investigations [25,27] and meta-analysis [28] demonstrate the prevalence of oral mucosa changes in scleroderma patients. We have not found such detailed descriptions of immunological changes occurring in the cells of the vessels of the submucosal layer of the oral mucosa, so we could speculate that our research in JS is the first one.

We also observed concomitant secondary infection in the form of fungal and viral infections, probably caused by therapy with glucocorticosteroids and immunodepressants. This problem has received little attention from researchers [6].

According to our data, the degree of involvement of the oral mucosa in children with JS depends on the disease duration and intensity of immunosuppresive therapy. Similar findings are present in literature [1,3,4,5-7,15,24,26]. Study by Pedowska M. (2021) presents morphea lesions in the oral cavity in adults. There are descriptions of stomatologic changes in patients with hemiscleroderma of the face, but they are focused on bone and soft tissue lesions [27,29].

Conclusion.

The results of studying the state of the oral mucosa in patients with JS showed that signs of the damage of the mucous membrane of the oral cavity were detected in 100% of observed JS patients. Lesions of mucose appear at the earliest stages of the disease and are associated with the development of dystrophic and atrophic processes, and abnormal vascularization. Mucosal dystrophic and vascular abnormalities develop in children with JSS, as well as in JSH patients. We distinguish four stages of mucous lesions and secondary infection stomatitis.

Conflicts of Interest.

The authors declare no conflict of interest.

Author contributions:

Skakodub Alla Anatolyevna: Research concept and design, collection and/or assembly of data, data analysis and interpretation, writing the article.

Osminina Maria Kirilovna: Collection and/or assembly of data, writing the article.

Geppe Natalia Anatolievna: Research concept and design, final approval of article.

Admakin Oleg Ivanovich: Data analysis and interpretation, critical revision of the article.

Kozlitina Yaliya Aleksandrovna: Critical revision of the article, final approval of article.

Goryaynova Anastasia Vladimirovna: Collection and/or assembly of data.

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სკლეროდერმიის მქონე ბავშვებში პირის ღრუს მდგომარეობის კლინიკური და მორფოლოგიური მახასიათებლები.

არასრულწლოვანთა სკლეროდერმია (JS) არის შემაერთებელი ქსოვილის იშვიათი ქრონიკული დაავადება, რომელიც ხასიათდება კანისა და რბილი ქსოვილების გამკვრივებით, მათ შორის პირის ღრუს და პერიორალური ქსოვილების, რაც იწვევს ფიბროზის, შინაგანი ორგანოების ფართო სპექტრის დაზიანებას, კოსმეტიკური დეფექტების და ადრეული ინვალიდობის განვითარებას ბავშვებში.

ამ კვლევის მიზანი იყო პირის ღრუს ლორწოვანის ქსოვილის დაზიანების ჰისტომორფოლოგიური თავისებურებების შესწავლა არასრულწლოვანთა სკლეროდერმიით (JS) ბავშვებში.

ჩვენ დავაკვირდით 5-დან 17 წლამდე ასაკის 39 პაციენტს (9 არასრულწლოვანთა სისტემური სკლეროზით - JSS და 20 არასრულწლოვანთა სკლეროდერმიით - სს), რომლებსაც ჩაუტარდათ სტომატოლოგიური გამოკვლევა და პირის ღრუს ლორწოვანის მორფოლოგიური გამოკვლევა. .

პირის ღრუს ლორწოვანი გარსი პაციენტებში JS-ით აღინიშნა დაზიანების ნიშნები დაკვირვებულთა 100%-ში. ლორწოვანი გარსის დაზიანებები გაჩნდა დაავადების ადრეულ სტადიაზე და თან ახლდა დისტროფიული და ატროფიული პროცესების განვითარება, ასევე პათოლოგიური სისხლძარღვები. პაციენტთა 72,63%-ში პირის ღრუს სისხლძარღვების კედლებში გამოვლინდა კომპლემენტის C3 კომპონენტის დეპოზიტები, ასევე IgM და IgG შემცველი იმუნური კომპლექსები.

პირის ღრუს ვასკულიტი აღმოჩენილია პაციენტების მესამედში, ხოლო ვასკულოპათია გამოკვლეულთა 52,63%-ში. დისტროფიული და სისხლძარღვთა ცვლილებები ლორწოვან გარსში განვითარდა ორივე პაციენტში JSS და JUSH. ჩვენ გამოვავლინეთ და აღვწერეთ ლორწოვანი გარსის დაზიანების ოთხი ეტაპი. პაციენტებს ასევე აღენიშნებოდათ მეორადი ინფექციური სტომატიტი

საკვანძო სიტყვები: არასრულწლოვანთა სკლეროდერმია, ბავშვები, პირის ღრუს ლორწოვანი გარსი, ჰისტომორფოლოგიური კვლევა.

Клинико-морфологическая характеристика состояния ротовой полости у детей со склеродермией.

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Аннотация

Ювенильная склеродермия (ЮС) — это редкое хроническое заболевание соединительной ткани, характеризующееся уплотнением кожи и мягких тканей, включая ротовую полость и периоральные ткани, что приводит к фиброзу, поражению широкого спектра внутренних органов, косметическим дефектам и ранней инвалидности у детей.

Целью данного исследования было изучение гистоморфологических особенностей поражений тканей слизистой оболочки ротовой полости у детей с ювенильной склеродермией (ЮС).

Наблюдались 39 пациентов с ЮС (9 с ювенильным системным склерозом — ЮСС и 20 с ювенильной

склеродермией головы — ЮСГ) в возрасте от 5 до 17 лет, у которых проводилось стоматологическое обследование и морфологическое исследование слизистой оболочки ротовой полости. Слизистая оболочка ротовой полости у пациентов с ЮС демонстрировала признаки повреждения у 100% наблюдаемых. Поражения слизистой проявлялись на самых ранних стадиях заболевания и сопровождались развитием дистрофических и атрофических процессов, а также аномальной васкуляризацией. У 72,63% пациентов выявлялись отложения компонента комплемента C3, а также иммунные комплексы, содержащие IgM и IgG, в стенках сосудов ротовой полости.

Васкулит ротовой полости был обнаружен у трети пациентов, а васкулопатия — у 52,63% обследованных. Дистрофические и сосудистые изменения слизистой оболочки развивались как у пациентов с ЮСС, так и с ЮСГ. Мы выделили и описали четыре стадии поражений слизистой оболочки. У пациентов также наблюдались вторичные инфекционные стоматиты.

Ключевые слова: ювенильная склеродермия, дети, слизистая оболочка ротовой полости, гистоморфологическое исследование.