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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.

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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 ВИНТИ 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 ВИНТИ РАН-ის მონაცემთა ბაზებში. სტატიების სრული ტექსტი ხელმისაწვდომია EBSCO-ს მონაცემთა ბაზებშიდან.

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. Корректур авторам не высылаются, 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 computer-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 საქურაღებოლ!

რედაქციაში სტატიის წარმოდგენისას საჭიროა დაიცვათ 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 შედეგის 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 ფხიხლებში 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.

Atanas Andreev, Iliya Kolev, Igor Zazirnyi. COMPARISON OF THE CLINICAL RESULTS FROM THE RECONSTRUCTION OF ACL WITH AUTOGRAFT AND ALLOGRAFT TISSUE.....	6-12
Boldyreva Yu.V, Lebedev I.A, Zaharchuk E.V, Lykasov A.G, Tersenov G.O. VITAMIN D INSUFFICIENCY AS A RECENT PROBLEM FOR THE RESIDENTS OF TYUMEN CITY AND TYUMEN REGION.....	13-16
Valentyna Chorna, Lesya Lototska, Ruslan Karimulin, Anatolii Hubar, Iryna Khliestova. RISK FACTORS OF IN-HOSPITAL INFECTIONS OCCURRENCE IN HEALTHCARE INSTITUTIONS IN UKRAINE AND EU COUNTRIES.....	17-21
Aynur ALIYEVA, Deniz Tuna EDİZER. INVESTIGATION OF THE EFFECT OF SUDDEN HEARING LOSS ON VESTIBULAR TESTS.....	22-27
D. ADAMCHUK, M. KUZIEV, E. GURMAN, B. NIYAZMETOV. INFLUENCE OF PAPAVERINE AND COMMERCIAL DIETARY SUPPLEMENTS ON BLOOD GLUCOSE AND BODY WEIGHT IN OBESE DOGS.....	28-31
Yarov Yu. DYNAMICS OF PRO- AND ANTI-INFLAMMATORY CYTOKINES IN PATIENTS WITH GENERALIZED PERIODONTITIS ACCOMPANIED BY DIFFERENT REACTIVITY OF THE ORGANISM.....	32-36
Pantus A.V, Rozhko M.M, Paliychuk V.I, Kovalchuk N.Y, Melnyk N.S. MICROSTRUCTURE OF BIOPOLYMER MICRO-FIBROUS SCAFFOLD AND ITS INFLUENCE ON THE ABILITY TO RETAIN MEDICINES AND TISSUE REGENERATION.....	37-44
G. T. Atalykova, L. T. Saparova, S. N. Urazova, Y. M. Tsai, Syr. S. Zhukabayeva, Sof. S. Zhukabayeva. INTERIM ANALYSIS OF PRIMARY HEALTHCARE SPECIALISTS TRAINING IN THE UNIVERSALLY PROGRESSIVE MODEL OF HOME-BASED SERVICES: ANTICIPATED PROSPECTS IN THE SOCIAL AREA.....	45-48
J.A.Nasirli. RESULTS OF HIP REPLACEMENT IN PATIENTS WITH DYSPLASTIC COXARTHROSIS WITH VARIOUS SURGICAL ACCESS OPTIONS.....	49-53
Mariam Tevzadze, Sophio Kakhadze, Mikhail Baramia, Tamar Rukhadze, Zaza Khatashvili, Siroos Mirzaey. HORMONE-RECEPTOR -POSITIVE BREAST CANCER: DIFFERENT PROGNOSIS OF BONE METASTASIS AMONG MOLECULAR SUBTYPES.....	54-58
Hind S. Alsoghachi, Zeina A. Althanoon. THE THERAPEUTIC EFFECT OF ORAL INSULIN SENSITIZER METFORMIN ON LIPID PROFILE IN WOMEN WITH POLYCYSTIC OVARY SYNDROME.....	59-62
Gunduz Ahmadov Ahmad. ANALYSIS OF CLINICAL AND LABORATORY PARAMETERS CHILDREN WITH DIABETES MELLITUS TYPE 1 USING DIFFERENT TYPES OF INSULIN PREPARATIONS.....	63-65
Sopiko Azrumelashvili, Tina Kituashvili. QUALITY OF LIFE AND DISEASE COPING STRATEGIES IN PATIENTS WITH ROSACEA.....	66-72
Senthilkumar Preethy, Naoki Yamamoto, Nguyen Thanh Liem, Sudhakar S Bharatidasan, Masaru Iwasaki, Samuel JK Abraham. ROLE OF GUT MICROBIOME HOMEOSTASIS, INTEGRITY OF THE INTESTINAL EPITHELIAL CELLS, AND THE (ENDOGENOUS) BUTYRATE IN ENDURING A HEALTHY LONG LIFE.....	73-78
Aytekin ALIYEVA, Nasib GULIYEV, Bayram BAYRAMOV, Birsen YILMAZ. PRELIMINARY FINDINGS OF TLR2 AND TLR4 EXPRESSION IN PRETERM NEONATES WITH NECROTIZING ENTEROCOLITIS.....	79-84
Dotchviri T, Pitskhelauri N, Chikhladze N, Akhobadze K, Dotchviri T, Kereselidze M. FALL RELATED GERIATRIC TRAUMA TRENDS IN GEORGIA.....	85-90
Kekenadze M, Nebadze E, Kvirkvelia N, Keratishvili D, Vashadze Sh, Kvaratskhelia E, Beridze M. RISK FACTORS OF AMYOTROPHIC LATERAL SCLEROSIS IN GEORGIA.....	91-94
S.B.Imamverdiyev, E.C.Qasimov, A.F.Ahadov, R.N.Naghryev. COMPARATIVE RESULTS OF THE USE OF MODERN EXAMINATION METHODS IN THE EARLY DIAGNOSIS OF KIDNEY CANCER, IN DETERMINING THE STAGE OF INVASION, AND IN CHOOSING STRATEGIES FOR ITS RADICAL TREATMENT.....	95-99
Pritpal Singh, Suresh Chandra Akula, Prikshat Kumar Angra, Anup Sharma, Ashwani Kumar, Gagandeep Singh Cheema. A STUDY ON FACTORS AFFECTING THE INTENTIONS TO ACCEPT TELEMEDICINE SERVICES IN INDIA DURING COVID-19 PANDEMIC.....	100-103

Tchernev G. NEIGHBOURING MELANOMAS AND DYSPLASTIC NEVUS DEVELOPING SIMULTANEOUSLY AFTER CANDESARTAN INTAKE: NITROSAMINE CONTAMINATION/ AVAILABILITY AS MAIN CAUSE FOR SKIN CANCER DEVELOPMENT AND PROGRESSION.....	104-107
Michael Malyshev, Alexander Safuanov, Anton Malyshev, Andrey Rostovykh, Dmitry Sinyukov, Sergey Zotov, Anna Kholopova. DELAYED SURGERY FOR GIANT SPONTANEOUS RUPTURE OF THE DISTAL THORACIC AORTA CAUSED BY CYSTIC MEDIAL NECROSIS.....	108-111
Siranush Ashot Mkrtychyan, Artur Kim Shukuryan, Razmik Ashot Dunamalyan, Ganna Hamlet Sakanyan, Hasmik Avetis Varuzhanyan, Lusine Marsel Danielyan, Hasmik Grigor Galstyan, Marine Ararat Mardiyan. NEW APPROACHES TO THE EVALUATION OF HERBAL DRUG EFFICACY IN CHRONIC RHINOSINUSITIS TREATMENT SCHEME BASED ON CHANGES OF QUALITY-OF-LIFE CRITERIA.....	112-116
Musheghyan G.Kh, Arajyan G.M, Poghosyan M.V, Hovsepyan V.S, Sarkissian J.S SYNAPTIC PROCESSES IN THE ANTINOCICEPTIVE SOMATOSENSORY CORTEX SI OF THE BRAIN ACTIVATED BY THE VENTRAL POSTERIOR-LATERAL THALAMIC NUCLEUS IN A ROTENONE MODEL OF PARKINSON'S DISEASE.....	117-122
Tchernev G. A FLAVOUR OF DEATH: PERINDOPRIL INDUCED THICK MELANOMA AND BCC OF THE BACK. POTENTIAL ROLE OF THE GENERIC SUBSTANCE OR/-AND POSSIBLE NITROSAMINE CONTAMINATION AS SKIN CANCER KEY TRIGGERING FACTORS.....	123-125
Baimuratova M.A, Shertayeva A.Z, Madraimov N.B, Erkebay R.A, Diusebayev E.I. DISEASES OF PERIODONTAL TISSUES: MODERN CHALLENGES OF THE TIME.....	126-131

DYNAMICS OF PRO- AND ANTI-INFLAMMATORY CYTOKINES IN PATIENTS WITH GENERALIZED PERIODONTITIS ACCOMPANIED BY DIFFERENT REACTIVITY OF THE ORGANISM

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Abstract.

The aim of this research was to study the dynamics of pro- and anti-inflammatory cytokines in the blood and gingival fluid of patients with generalized periodontitis accompanied by different reactivity of the body after patch surgery.

The study included 216 people aged 45 between 55 years with a diagnosis of generalized periodontitis were examined. Depending on the condition of reactivity of the body, the patients were divided into three groups: 1 - normoreaction; 2- hyperreaction; 3 - hyporeaction. After the initial therapy, the patch was performed according to the indications. Blood sampling was performed after surgery on days 1, 2, 4, 6 and 9. The content of pro- (IL-1 β , IL-6, TNF α) and anti-inflammatory (IL-4) cytokines in blood and gingival fluid was defined by solid-phase enzyme-linked immunosorbent assay.

The results have shown that the normal reactivity of the organism is characterized by an increase in proinflammatory cytokines IL-1 β , IL-6, TNF α at the time of increasing necrosis of periodontal tissues, their decrease and increase in IL-4 with the appearance of markers of reparative processes in blood and gingival fluid. Hyperreactivity is characterized by a more pronounced early increase in pro- and anti-inflammatory cytokines of blood and gingival fluid (IL-1 β , IL-6, TNF α , IL-4) with a subsequent decrease below the initial values during the development of young connective tissue. In the case of hyporeactivity we can observe a late and less pronounced increase in all the cytokines in the blood and gingival fluid.

Correction of altered parameters in patients with generalized periodontitis accompanied by impaired (hyper- and hypo-) reactivity of the body with bringing them to the values which are typical for normoreactivity is considered to be a condition for optimizing wound healing after surgery and further stabilization of the periodontal tissues.

Key words. Generalized periodontitis, reactivity of the organism, postoperative period, cytokines.

Introduction.

The role of cytokines in the development of immunological and inflammatory reactions in periodontitis has been defined [1]. Cytokines are secreted mainly by blood cells and the immune system (polymorphonuclear leukocytes, macrophages, lymphocytes) and have autocrine (on the cells that produce them), paracrine (on cells in the microenvironment) and endocrine (on distant cells) effects [2]. Cytokines control the process of angiogenesis and regeneration [3]. The maximum local release of proinflammatory cytokines turns the protective mechanisms into pathological, uncontrolled ones, which cause damage to periodontal tissues and bone resorption [4]. A certain complex of cytokines, including IL-1, TNF α , IL-6, etc., determines the course of inflammation in the focus of tissue destruction that

occurs in case of generalized periodontitis [5]. The formation of granulation tissue in the focus of chronic inflammation (periodontal pocket) is the result of the action of growth factors of different genetic orientation on its cellular elements, which are produced by macrophages, lymphocytes and fibroblasts [6]. The content of pro-inflammatory cytokines IL-1 β in the gingival fluid, which is the initiator of the cytokine cascade in periodontal tissues, becomes 3 times higher compared with a healthy person [7]. The level of anti-inflammatory cytokine IL-4 is significantly reduced, which is an unfavorable sign in the course of chronic periodontitis, as it leads to uncontrolled activation of macrophages and their production of IL-1, TNF α and other cytokines. The expression of IL-6 and IFN is significantly higher in the tissues of patients with inflammatory periodontal disease compared with the tissues of healthy individuals [8]. The content of IL-1 and TNF α in gingival fluid and peripheral blood serum was studied. It is shown that the level of IL-1 in the gingival fluid correlates with the depth of periodontal pockets. In addition, the level of IL-1 in the serum was significantly lower than in the gingival fluid, which indicates its importance in the pathogenesis of periodontal disease [9]. The aim of this research was to study the dynamics of pro- (IL-1 β , IL-6, TNF α) and anti-inflammatory (IL-4) cytokines in the blood and gingival fluid of patients with generalized periodontitis accompanied by normo-, hyper- and hyporeactivity of the body after patch surgery.

Materials and methods.

Research 216 people (82 men and 134 women) aged between 45 and 55 years with a diagnosis of generalized periodontitis of II, III degree of severity, chronic course were examined. The diagnosis was made on the basis of clinical examination, radiography, determination of periodontal samples in accordance with the International Classification of Diseases ICD-10. Depending on the state of reactivity of the body, the patients were divided into three groups: the first consisted of people with normoreaction (132 people, 61%); the second group contained patients with hyperreaction (46 people, 21%); the third one included patients with hyporeaction (38 people, 18%). The division of patients into groups depending on the state of the body's reactivity was carried out according to the differences in the dynamics of cytokines on day 1. All the patients underwent comprehensive treatment of generalized periodontitis in the amount recommended by the Ministry of Health of Ukraine - Order №566 from 23.11.04. "On Approval of the Protocols for the Provision of Medical Care". Patients with generalized periodontitis of II, III degrees of severity after initial therapy, underwent patch surgery according to the indications. Collection of gingival fluid was performed with standard paper pins (№25) by immersing them effortlessly into the periodontal pockets for 30 seconds in the area of the first lower molars. After that, the

pins were placed in sterile tubes with a volume of 1.5 ml of 0.5 ml of saline. Blood sampling was performed after surgery on the 1st, 2nd, 4th, 6th and 9th day in the morning on an empty stomach from the ulnar vein with a volume of 10 ml. The condition of cytokine regulation was determined by the content of IL-1 β , IL-6, TNF α , IL-4 by solid-phase enzyme-linked immunosorbent assay (ELISA) using commercial reagent kits ProCon IL-1 β , ProCon IL-6, ProCon TNF α , ProCon IL-4. Using a spectrophotometer, the optical density was measured over a given wavelength. Based on the obtained data, calibration curves were constructed for the corresponding cytokines and the results were read using an ELx800 Universal Microplate Reader (BIO-TEK INSTRUMENTS.INC).

The study was conducted in accordance with the principles of the Declaration of Helsinki adopted by the General Assembly of the World Medical Association (1997-2000), the Council of Europe Convention on Human Rights and Biomedicine (1997), the relevant provisions of the WHO, the International Code of Medical Ethics (1983).

Statistical processing of the obtained digital data was performed using the computer program Statistica 8.0 (STA862D175437Q).

Results and discussion.

The results of determination of cytokines IL-1 β , IL-6, TNF α , IL-4 in the blood of patients with generalized periodontitis after surgical treatment with normoreactivity of the body are presented in table 1. As can be seen from this table, the dynamics of these cytokines were unidirectional in their concentration. On the 1st and 2nd day after surgery, the largest increase in proinflammatory cytokines was observed: IL-1 β - 1.94 times, IL-6 - 1.46 times, TNF - 1.47 times ($p < 0.05$). On the 4th and 6th days, a decrease in the content of all proinflammatory cytokines in the serum was registered. On the 9th day, the content of all proinflammatory cytokines returned to normal. The dynamics of the anti-inflammatory cytokine IL-4 differed from that of IL-1 β , IL-6, TNF α . The content of IL-4, gradually increasing from 1 day of observation, reached its peak on the 6th day (the content was 1.77 times higher than the initial, $p < 0,05$). On the 9th day, the value of IL-4 remained 1.14 times higher than the initial one ($p > 0.05$). It is important to study the index of cytokine balance in the blood in patients with generalized periodontitis. The ICB is the ratio of the average values of healthy people to

Table 1. The Content of Cytokines IL-1 β , IL-6, TNF α , IL-4, IRC in the Blood in case of Normo-, Hyper- and Hyporeactivity of the Body after Surgery ($M \pm SE$).

Indexes	average value	Terms of Observation	Groups of patients		
			Normoreaction (n = 132)	Hyperreaction (n = 23)	Hyporeaction (n = 19)
IL-1 β , pg / ml	78,0 \pm 18,2	Initially	73,6 \pm 16,4	74,9 \pm 28,3	70,6 \pm 29,8
		1st day	142,1 \pm 20,8 *	206,4 \pm 41,4 * "	95,4 \pm 30,3
		2nd day	130,6 \pm 18,2 *	182,1 \pm 36,0 *	118,8 \pm 32,5
		4th day	125,9 \pm 18,0 *	140,8 \pm 30,8 *	106,5 \pm 28,4
		6th day	94,5 \pm 17,2	134,5 \pm 35,4	100,2 \pm 27,7
		9th day	74,2 \pm 16,0	68,8 \pm 26,7	67,9 \pm 27,0
IL-6, pg / ml	91,3 \pm 16,4	Initially	86,1 \pm 14,4	88,0 \pm 32,6	84,1 \pm 34,5
		1st day	126,4 \pm 18,0 *	151,3 \pm 34,4 *	98,3 \pm 35,8
		2nd day	115,2 \pm 17,6 *	136,5 \pm 36,6	112,4 \pm 38,3
		4th day	104,1 \pm 16,8	120,8 \pm 34,0	105,2 \pm 36,8
		6th day	96,5 \pm 15,0	118,1 \pm 34,2	96,9 \pm 34,2
		9th day	84,9 \pm 14,2	79,5 \pm 30,2	75,1 \pm 30,6
TNF α , pg / ml	80,5 \pm 14,5	Initially	75,9 \pm 12,8	76,4 \pm 34,2	73,1 \pm 35,1
		1st day	111,8 \pm 17,4 *	160,8 \pm 46,8 *	98,6 \pm 35,6
		2nd day	106,4 \pm 16,7 *	144,3 \pm 46,0	104,2 \pm 36,0
		4th day	104,8 \pm 16,5	128,1 \pm 45,4	80,9 \pm 34,3
		6th day	82,6 \pm 13,4	96,4 \pm 40,2	76,7 \pm 32,9
		9th day	77,1 \pm 12,6	72,9 \pm 36,0	69,5 \pm 30,7
IL-4, pg / ml	44,6 \pm 10,0	Initially	42,1 \pm 8,4	44,3 \pm 15,3	40,6 \pm 18,5
		1st day	50,6 \pm 8,8	92,9 \pm 24,4 *	55,3 \pm 19,3
		2nd day	54,4 \pm 9,2	50,8 \pm 16,8	51,6 \pm 18,0
		4th day	68,9 \pm 9,7 *	48,2 \pm 16,0	44,9 \pm 16,4
		6th day	74,5 \pm 10,0 *	37,5 \pm 15,5	30,6 \pm 15,1 "
		9th day	48,2 \pm 8,0	36,2 \pm 14,6	34,3 \pm 16,3
ICB (index of cytokene balance)		Initially	1,06 \pm 0,04	1,28 \pm 0,12	1,30 \pm 0,14
		1st day	2,34 \pm 0,07 *	2,08 \pm 0,20 *	1,76 \pm 0,16 * "
		2nd day	2,01 \pm 0,07 *	2,64 \pm 0,26 * "	2,72 \pm 0,18 * "
		4th day	1,68 \pm 0,06 *	1,95 \pm 0,19 * "	2,53 \pm 0,18 * "
		6th day	1,22 \pm 0,05 *	1,88 \pm 0,18 * "	2,08 \pm 0,16 * "
		9th day	1,16 \pm 0,05	1,44 \pm 0,16 "	1,63 \pm 0,15 * "

Note: * - $p < 0.05$ against the initial values

"- $p < 0,05$ against the values typical for normoreactivity of an organism.

the relative values of cytokines. As a result, the ICB in patients with GP initially, before the patch surgery, was equal to 1.06 ± 0.05 (table 1).

On the 1st day after the intervention, the balance index increased to 2.34 ± 0.07 ($p < 0.05$), which indicated a shift in balance towards the predominant activation of proinflammatory cytokines. Beginning with the 2nd day, the balance began to level off - the index decreased with a minimum value by the end of the observation, it was 1.16 ± 0.05 , which did not differ significantly from the initial value ($p > 0.05$). The results of the determination of cytokines (IL-1 β , IL-6, TNF α , IL-4) in gingival fluid in patients with generalized periodontitis after surgery with normoreactivity of the body are presented in table 2. As can be seen from this table, the dynamics of these cytokines in gingival fluid was similar to that in the serum of patients with GP of the first group and was characterized by their increase with maximum values of proinflammatory cytokines on the 1st day, anti-inflammatory - on the 6th day and subsequent normalization by the end of observation. The amplitude of changes in the studied parameters in the gingival fluid was more significant than in the blood, which indicates their greater informativeness to assess the state of cytokine regulation.

The results of finding cytokines IL-1 β , IL-6, TNF α , IL-4 in the blood of patients with generalized periodontitis after surgical treatment with hyperreactivity of the body are presented in table 1. As can be seen from this table, on the 1st day there was a

significant increase in pro- and anti-inflammatory cytokines ($p < 0,05$). The maximum level of IL-1 β was increased by 2.75 times compared to the initial level, the minimum increase of IL-6 was 1.72 times ($p < 0.05$). This increase in the content of cytokines on the 1st day in case of hyperreaction of the body was, on average, 1.43 times more significant in amplitude than in case of normoreaction. Subsequently, the level of all studied indicators decreased, on the 9th day reaching values below those of normoreactivity. Normalization of reduced cytokine levels was not observed until the end of the experiment. The dynamics of the index of cytokine balance (ICB) in patients with generalized periodontitis of the second group is interesting (table 1). Before the intervention, the ICB was 1.28 ± 0.12 , which indicates a more significant shift in the balance towards pro-inflammatory cytokines, despite the relatively high absolute levels of IL-4 in the blood of patients with GP accompanied by hyperreactivity. After the intervention, a significant increase in the balance index was noted, which indicates a significant shift towards the predominance of IL-1 β , IL-6, TNF. Beginning with the 2nd day, in all subsequent terms of observation, the ICB remained significantly higher than the initial value and the corresponding values which are typical for normoreactivity of the organism ($p < 0,05$). The results of determination of cytokines IL-1 β , IL-6, TNF α , IL-4 in gingival fluid in patients with generalized periodontitis after surgical treatment accompanied by hyperreactivity of the body are presented in table 2. It should

Table 2. The Content of Cytokines IL-1 β , IL-6, TNFI, IL-4 in the Gingival Fluid in case of Normal, Hyper- and Hyporeactivity of the Body after Surgery ($M \pm SE$).

Indexes	Terms observation	Groups of patients		
		normoreaction (n = 132)	Hyperreaction (n = 23)	Hyporeaction (n = 19)
IL-1 β , pg / ml	Initially	27,3 \pm 1,4	29,4 \pm 2,3	26,2 \pm 2,4
	1st day	68,1 \pm 2,8 *	76,6 \pm 4,0 * "	28,9 \pm 2,6 "
	2nd day	59,0 \pm 1,8 *	62,4 \pm 3,8 * "	34,8 \pm 3,1 * "
	4th day	52,9 \pm 1,9 *	58,6 \pm 3,6 * "	29,1 \pm 2,8 "
	6th day	34,5 \pm 1,5 *	36,8 \pm 3,0 * "	27,4 \pm 2,7 "
	9th day	28,2 \pm 1,4	27,6 \pm 2,8	25,9 \pm 2,7,0
IL-6, pg / ml	Initially	123,6 \pm 5,4	124,7 \pm 9,6	122,1 \pm 9,5
	1st day	264,4 \pm 8,0 *	298,4 \pm 10,0 * "	144,3 \pm 9,8 "
	2nd day	189,5 \pm 7,3 *	146,8 \pm 9,4 * "	152,4 \pm 10,3 * "
	4th day	134,1 \pm 6,1	1329,9 \pm 8,6	141,2 \pm 9,9
	6th day	128,6 \pm 5,0	124,1 \pm 8,7	139,9 \pm 9,8
	9th day	124,9 \pm 4,8	121,5 \pm 8,2	120,5 \pm 9,6
TNF, pg / ml	Initially	45,4 \pm 4,8	46,6 \pm 9,1	44,3 \pm 8,8
	1st day	116,2 \pm 7,1 *	160,8 \pm 10,1 * "	58,9 \pm 8,9 "
	2nd day	101,0 \pm 6,7 *	74,4 \pm 9,7 * "	60,2 \pm 9,0 "
	4th day	85,9 \pm 5,1 *	62,1 \pm 9,4 * "	67,9 \pm 9,3 * "
	6th day	62,7 \pm 4,4	46,4 \pm 8,7 "	46,7 \pm 8,9 "
	9th day	47,3 \pm 4,2	42,8 \pm 8,6	42,5 \pm 8,7
IL-4, pg / ml	Initially	16,9 \pm 2,4	17,8 \pm 5,3	16,6 \pm 5,5
	1st day	21,8 \pm 2,8	42,7 \pm 5,8 * "	25,3 \pm 6,3
	2nd day	24,9 \pm 2,2	34,8 \pm 5,5 * "	28,1 \pm 7,0
	4th day	48,1 \pm 3,7 *	32,2 \pm 5,4 * "	34,7 \pm 8,4 * "
	6th day	54,5 \pm 3,8 *	27,4 \pm 5,2 * "	25,6 \pm 7,1 "
	9th day	18,1 \pm 2,2	14,6 \pm 4,6	14,3 \pm 4,8

Note: * - $p < 0.05$ against the initial values

"- $p < 0,05$ against values at normoreactivity of an organism.

be noted that the dynamics of the cytokines in gingival fluid was similar with this in the serum of patients of the second group - on the 1st day there was a significant increase in all the pro- and anti-inflammatory cytokines ($p < 0,05$). However, the amplitude of the increase was significantly higher than in the blood and in comparison, with cases of normoreactivity of the organism ($p < 0,05$).

The dynamics of pro- and anti-inflammatory cytokines (IL-1 β , IL-6, TNF α , IL-4) in the blood of patients with generalized periodontitis accompanied by hyporeactivity of the body are presented in table 1. On the 1st day the level of all the studied parameters compared to initial values increased ($p > 0,05$). The peak of anti-inflammatory IL-4, the content of which in the blood increased by 1.36 times ($p > 0,05$). The maximum values of proinflammatory cytokines - IL-1 β , IL-6, TNF α - were registered on the 2nd day of observation. However, the amplitude of changes in these parameters relative to the original data was comparatively small. Thus, the level of IL-1 β increased by 1.68 times, IL-6 - by 1.34 times and TNF - by 1.43 times ($p > 0,05$). The specified amplitude of growth of all the indicators in all the terms of supervision was the smallest in comparison with those which are typical for normo- and hyperreactivity of an organism. Prior to the intervention, the ICB was 1.30 ± 0.14 , which indicates a more significant shift in the balance towards proinflammatory cytokines, despite the relatively low absolute levels of IL-1 β , IL-6, TNF in the blood of patients with GP accompanied by hyporeactivity (table 1). After the intervention, a significant increase in the index of cytokine balance was observed both in relation to its initial value and in relation to the one, typical for normoreactivity of the body ($p < 0,05$). A significant imbalance of pro- and anti-inflammatory cytokines in the direction of the predominance of IL-1 β , IL-6, TNF α persisted until the end of observations. The dynamics of cytokines in the gingival fluid of patients with generalized periodontitis accompanied by hyporeactivity of the body are presented in table 2. It should be taken into consideration that the dynamics of all the studied cytokines in gingival fluid was similar to that in the serum of patients with GP of the third group and was characterized by an increase in the content of IL-1 β , IL-6, TNF α , IL-4 after surgery on periodontal tissues. The rise of the studied cytokines was later and less pronounced in comparison with that of normoreactivity of the organism. Although, the amplitude of changes in all the studied parameters in the gingival fluid was more significant than in the blood. Thus, amplitude of growth of all the indicators in all the terms of supervision was the smallest in comparison with typical for normo- and hyperreactivity of an organism.

Conclusion.

In general, the results of this study showed that for patients with generalized periodontitis accompanied by normoreactivity of the body after surgery it is typical to have an increase in proinflammatory cytokines at the time of increasing necrosis of periodontal tissues, their reduction and IL-4 increase with the appearance of markers of reparative processes in the blood and gingival fluid. In case of hyperreactivity of the body in patients with generalized periodontitis after surgery there is a more pronounced early increase in blood and gingival fluid of pro-

and anti-inflammatory cytokines, followed by a decrease below baseline during the development of young connective tissue. If patients with generalized periodontitis have hyporeactivity of the body after surgery, there is a late and less pronounced increase in pro- and anti-inflammatory cytokines in the blood and gingival fluid. Our studies confirm the important role of cytokine regulation in postoperative wound healing. We have shown that different conditions of reactivity of the organism preconditions different in amplitude and timing type of changes in pro- and anti-inflammatory cytokines during the postoperative period in patients with generalized periodontitis. Correction of altered parameters in patients with generalized periodontitis accompanied by impaired reactivity of the body with bringing them to values, typical for normoreactivity is considered to be a condition for optimizing mucosal wound healing after surgery and further stabilization of the periodontal tissues.

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РЕЗЮМЕ

ДИНАМИКА ПРО- И ПРОТИВОВОСПАЛИТЕЛЬНЫХ ЦИТОКИНОВ У БОЛЬНЫХ ГЕНЕРАЛИЗОВАННЫМ ПАРОДОНТИТОМ ПРИ РАЗЛИЧНОЙ РЕАКТИВНОСТИ ОРГАНИЗМА
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Целью данного исследования стало изучение динамики про- и противовоспалительных цитокинов в крови и десневой жидкости у больных генерализованным пародонтитом с различной реактивностью организма после проведения лоскутной операции.

Обследовано 216 пациентов в возрасте от 45 до 55 лет с генерализованным пародонтитом. В зависимости от состояния реактивности организма больные были разделены на три группы: 1 - нормореакция; 2- гиперреакция; 3 - гипореакция. После инициальной терапии, проводили по показаниям лоскутную операцию. Забор крови и десневой жидкости производили после хирургического вмешательства на 1-е, 2-е, 4-е, 6-е и 9-е сутки. Методом твердофазного иммуноферментного анализа определяли содержание про- (ИЛ-1 β , ИЛ-6, ФНП α) и противовоспалительных (ИЛ-4) цитокинов.

Результаты показали, что для нормореактивности организма характерным является повышение провоспалительных

цитокинов ИЛ-1 β , ИЛ-6, ФНП α в момент нарастания некроза тканей пародонта, их снижение и повышение ИЛ-4 при появлении маркеров репаративных процессов. Для гиперреактивности - более выраженное раннее повышение в крови и десневой жидкости про- и противовоспалительных цитокинов (ИЛ-1 β , ИЛ-6, ФНП α , ИЛ-4) с последующим снижением ниже исходных значений в период развития молодой соединительной ткани. Для гипореактивности – позднее и менее выраженное повышение всех цитокинов в крови и десневой жидкости.

Коррекция измененных показателей у больных генерализованным пародонтитом на фоне нарушенной (гипер- и гипо-) реактивности организма с приведением их к значениям при нормореактивности рассматривается как условие оптимизации заживления раны после хирургического лечения и дальнейшей стабилизации процесса в тканях пародонта.

Ключевые слова: генерализованный пародонтит, реактивность организма, послеоперационный период, цитокины