

RUSSIAN BIOMEDICAL RESEARCH

2024, VOLUME 9, N 4

SCIENTIFIC AND PRACTICAL JOURNAL

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Рецензируемый

научно-практический журнал
РОССИЙСКИЕ БИОМЕДИЦИНСКИЕ ИССЛЕДОВАНИЯ
RUSSIAN BIOMEDICAL RESEARCH

Основан в 2016 году в Санкт-Петербурге

ISSN 2658-6584

eISSN 2658-6576

Выпускается 4 раза в год

Журнал реферируется РЖ ВИНИТИ

Издатели, учредители:

Федеральное государственное бюджетное
образовательное учреждение высшего образования
«Санкт-Петербургский государственный педиатрический
медицинский университет» Минздрава России (адрес:
194100, Санкт-Петербург, Литовская ул., д. 2),
Фонд НОИ «Здоровые дети — будущее страны» (адрес:
197371, Санкт-Петербург, ул. Парашютная, д. 31, к. 2,
кв. 53).

Журнал зарегистрирован Федеральной службой по
надзору в сфере связи, информационных технологий
и массовых коммуникаций (РОСКОМНАДЗОР)
ПИ № ФС77-74228 от 02 ноября 2018 г.

*Журнал входит в Перечень ведущих научных журналов
и изданий ВАК, в которых должны быть опубликованы
основные результаты диссертаций на соискание ученых
степеней кандидата и доктора наук (Распоряжение
№ 435-р от 15.11.2021).*

Журнал индексируется в РИНЦ. Договор
на включение журнала в базу РИНЦ: № 538-10/2016
от 06.10.2016, страница журнала в Российской научной
электронной библиотеке http://elibrary.ru/title_about.asp?id=62014

Проект-макет: Титова Л.А.

Layout project: Titova L.A.

Электронная версия / Electronic version

[http://www.gpmu.org/science/pediatrics-magazine/Russian_](http://www.gpmu.org/science/pediatrics-magazine/Russian_Biomedical_Research)
[Biomedical_Research, http://elibrary.ru](http://elibrary.ru)

Титова Л.А. (выпускающий редактор)

Варламова И.Н. (верстка)

Titova L.A. (Commissioning Editor)

Varlamova I.N. (layout)

Адрес редакции: Литовская ул., 2,
Санкт-Петербург, 194100;
тел./факс: (812) 295-31-55; e-mail: lt2007@inbox.ru

Address for correspondence:

2 Lithuania, Saint Petersburg 194100, Russian Federation
Tel/Fax: +7 (812) 295-31-55, e-mail: lt2007@inbox.ru

Статьи просьба направлять по адресу: avas7@mail.ru,
<https://ojs3.gpmu.org/index.php/biomedical-research>
Please send articles to: avas7@mail.ru,
<https://ojs3.gpmu.org/index.php/biomedical-research>

Формат 60 × 90/8. Усл.-печ. л. 11,5. Тираж 100 экз.
Распространяется бесплатно. Оригинал-макет изготовлен
ФГБОУ ВО СПбГПМУ Минздрава России.

Format 60 × 90/8. Cond.-printed sheets 11,5. Circulation 100.
Distributed for free. The original layout is made
Saint Petersburg State Pediatric Medical University.

Отпечатано ФГБОУ ВО СПбГПМУ Минздрава России
Литовская ул., 2, Санкт-Петербург, 194100.
Заказ 108. Дата выхода 27.12.2024.

Printed by Saint Petersburg State Pediatric Medical University.
2 Lithuania, Saint Petersburg 194100, Russian Federation.
Order 108. Release date 27.12.2024.

Полное или частичное воспроизведение
материалов, содержащихся в настоящем издании,
допускается только с письменного разрешения
редакции.
Ссылка на журнал «Российские биомедицинские
исследования / Russian Biomedical Research»
обязательна.

2024, ТОМ 9, № 4

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UDC 377+378.17+614.251.2+616-091.1-008.97
DOI: 10.56871/RBR.2024.93.48.001

INFECTIVE AGENTS IN FIXED ANATONICAL MATERIALS

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For citation: Zachinyaeva AV, Zachinyaev YaV, Gladin DP, Kirillova NP, Andreeva AN, Baranova TV. Infective agents in fixed anatonical materials. Russian Biomedical Research. 2024;9(4):5–8. DOI: <https://doi.org/10.56871/RBR.2024.93.48.001>

Received: 10.10.2024

Revised: 12.11.2024

Accepted: 17.12.2024

Abstract. The program of pre-graduate and postgraduate medical education involves the use of cadavers to teach anatomy by autopsy or examination of dissected samples. The preservation process of the biomaterial must ensure that it is free from damage, destruction and decomposition. Preservative solutions are used for this, but it remains unclear whether there is any risk of spread. microorganisms during the teaching of anatomy, research and autopsy procedures of fixed corpses. The results showed that the fixed cadaveric material, as well as preservative solutions, contain viable micromycetes. The study of the pathogenicity factors of fungi isolated from anatomical preparations showed that more than 80% of fungal strains have hydrolytic activity. This study highlights the importance of developing safe manipulation protocols to avoid possible infection and illness of staff and students.

Keywords: anatomical preparations, fungi, pathogenicity factors, enzymes

ИНФЕКЦИОННЫЕ АГЕНТЫ В ФИКСИРОВАННЫХ АНАТОМИЧЕСКИХ МАТЕРИАЛАХ

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Для цитирования: Зачиняева А.В., Зачиняев Я.В., Гладин Д.П., Кириллова Н.П., Андреева А.Н., Баранова Т.В. Инфекционные агенты в фиксированных анатомических материалах. Российские биомедицинские исследования. 2024;9(4):5–8. DOI: <https://doi.org/10.56871/RBR.2024.93.48.001>

Поступила: 10.10.2024

Одобрена: 12.11.2024

Принята к печати: 17.12.2024

Резюме. Программа додипломного и последипломного медицинского образования предполагает использование трупов для обучения анатомии путем вскрытия или изучения прозектированных образцов. Процесс консервации биоматериала должен гарантировать отсутствие его повреждений, разрушения и разложения. Для этого используются консервирующие растворы, однако остается неясным, существует ли какой-либо риск распространения микроорганизмов во время преподавания анатомии, исследований и процедур вскрытия фиксированных трупов. Результаты показали, что фиксированный трупный материал, а также консервирующие

растворы содержат жизнеспособные микромицеты. Изучение факторов патогенности грибов, выделенных из анатомических препаратов, показало, что более 80% штаммов грибов обладают гидролитической активностью. Это исследование подчеркивает важность разработки протоколов безопасных манипуляций во избежание возможного заражения и заболеваний персонала и студентов.

Ключевые слова: анатомические препараты, грибы, факторы патогенности, ферменты

INTRODUCTION

The human body has been used to teach anatomy since the Renaissance. In fact, the ancient Greek roots of the word “anatomy” mean “to cut” or “to separate”. Anatomy museums hold specimens of scientific interest. This excellent educational tool is used by anatomists when teaching future physicians. Modern methods of embalming human cadavers involve the use of formalin with the addition of glycerin, salts, disinfectants, and water. The embalming procedure should provide good preservation of organs and tissues with minimal structural changes to the corpse. Formalin is known to be a strong disinfectant. Its ability to inhibit the growth of bacteria and fungi even in low concentrations has been noted. This is due to the ability of formalin to attach to amino groups of protein molecules, which leads to changes and destruction of the molecular structure of proteins and nucleoproteins. It provides tissue hardness and inactivates enzymes responsible for postmortem autolytic processes [1–5].

Despite high efficacy and a wide range of antimicrobial activity, some microorganisms do not lose viability on formalin-treated surfaces, and some strains can even multiply in cadaver tissues [1]. For example, *Yaragalla* and *Rajput* found *Penicillium*, *Trichophyton* and *Aspergillus* species on skin and bone tissue of cadavers fixed with 5% formalin solution [6]. However, few studies have addressed the biological risk of manipulation of fixed cadaver and the spread of pathogens. N.A. Osman et al., S. Hayashi et al., Tabaac et al. showed the presence of pathogenic bacteria in 10 fixed cadavers used in practice for teaching anatomy: *Staphylococcus aureus*, *Enterococcus faecalis*, *Streptococcus pyogenes* [7, 8]. The presence of fungal species such as *Trichophyton*, *Microsporum*, *Candida* and *Cryptococcus* was also noted in the work of C. Molina et al. [9].

Another important aspect is the discoloration of anatomical preparations under the influence of fungal metabolites, which leads to their unusability. The sources of contamination of cadavers with various species of microscopic fungi are quite diverse and include room air, personnel and students on the department.

AIM

The aim of the present study was to investigate the fungal species in the air of the anatomy laboratory and to determine the presence of formalin-resistant fungi on the surface of cadavers and to evaluate their biological activity.

MATERIALS AND METHODS

Material was collected with sterile cotton swabs from anatomical preparations, from solutions for storing wet preparations and from cadaver preservation baths. Air sampling was carried out by artificial sedimentation. Samples were sown on Czapek's medium with subsequent cultivation at 28 °C (5–7 days). Species identification of fungi was carried out on the basis of cultural and morphological properties.

Taxonomic characters (morphology of reproductive structures, culture characteristics of colonies) were used to identify fungi. The names of fungal species are given according to the nomenclature of the Mycobank database [10].

Fungi isolated from anatomical preparations, wet preparation storage solutions, and cadaver preservation baths were analyzed for their ability to produce extracellular enzymes on solid medium. Protease activity was assessed by the formation of transparent zones around fungal colonies on skim milk medium [11]. To determine lipase activity, fungi were cultured on medium with Tween-80. Their enzymatic activity was evaluated by the formation of calcium oleate crystals. Hemolytic activity was evaluated by the formation of hemolysis zones on blood agar.

RESULTS AND DISCUSSION

The following micro-mycetes were isolated from the different materials.

- Air: *Aspergillus niger* Tiegh., *Penicillium lilacinum* Thom, *Aspergillus restrictum* Smitt, *Mucor ramosissimus*, *Aspergillus ustus* (Bainier), *Aspergillus flavus* Raper and Fennell, Gams, *Scopulariopsis brevicaulis* (Sacc.) Bainie, *Aureobasidium* spp., *Gliocladium* spp., *Trichoderma polysporum* Rifai.
- Solutions and flushes from cadaver preservation baths: *Gliocladium roseum* Bainier, *Gliocladium* spp.



Table 1

Enzymatic and hemolytic activity of the studied fungal species

Таблица 1

Ферментативная и гемолитическая активность изученных видов грибов

Виды грибов / Types of mushrooms	Количество штаммов / Number of strains	Количество штаммов, проявляющих гидролитическую активность / Number of strains exhibiting hydrolytic activity		
		протеаза / protease	липаза / lipase	гемолиз / hemolysis
<i>Aspergillus ustus</i>	5	2	1	2
<i>A. nidulans</i>	1	1	0	1
<i>A. niger</i>	3	3	3	3
<i>A. restrictum</i>	2	0	0	1
<i>A. flavus</i>	3	3	1	3
<i>Gliocladium roseum</i>	2	2	0	2
<i>Trichoderma polysporum</i>	4	3	4	2
<i>Scopulariopsis brevicaulis</i>	1	1	1	0

- Anatomical preparations: *Aspergillus nidulans* (Eidam), *Fonsecaea pedrosoi* (Brumpt).

It is interesting that the micromycete species isolated from the air environment of the anatomical laboratory were not detected in solutions or on anatomical preparations. Formalin-fixed preparations were covered with dense substrate mycelium. As a result of exposure to formalin vapors and low air exchange, no fungal growth occurred and no aerial mycelium was detected on the preparations. Thus, no contamination of the air environment with spores of fungi of the genus *Gliocladium*, as well as species of *A. nidulans* and *F. redrosoi* were recorded. Numerous metabolites produced by these fungi are dangerous for anatomical preparations. These are primarily quinones, which form stable complexes with natural polymers. As a result, anatomical preparations acquire coloration. In addition, volatile toxic isocyanates are formed, which are the main cause of the development of asthmatic status.

25 mycelial fungi isolated from anatomical preparations, wet preparation storage solutions and cadaver preservation baths were analyzed for their ability to produce extracellular enzymes on solid media. The following fungal species were tested: *Aspergillus niger lilacinum*, *A. nidulans*, *A. flavus*, *A. restrictum*, *A. ustus*, *Penicillium*, *Mucor ramosissimus*, *Scopulariopsis brevicaulis*, *Aureobasidium* spp., *Trichoderma polysporum*, *Gliocladium roseum*, *Fonsecaea pedrosoi*.

The study of the pathogenicity factors of micro-mycetes isolated from anatomical preparations showed that more than 80% of fungal strains have hydrolytic activity (Table 1).

Representatives of *Penicillium lilacinum*, *Mucor ramosissimus* and *Fonsecaea redrosoi* species showed no hydrolytic activity.

An important factor in the pathogenicity of such fungal species as *Aspergillus ustus*, *A. niger*, *A. flavus* are pro-

teases. The study of virulence factors of these fungi has shown that the main role in the development of pulmonary aspergillosis belongs to proteolytic enzymes — elastases, collagenases [12]. The ability to form extracellular phospholipases has been revealed in many opportunistic fungi that are causative agents of mycoses [13].

A pronounced hemolytic activity was found in 56% of fungal isolates. It has been proved that in a number of mycelial fungi hemolytic activity is the result of toxin production. Thus, S.J. Vesper et al. isolated the hemolytic agent stachylysin from *Stachybotrys chartarum* [14].

CONCLUSION

Thus, hydrolytic enzymes, which are pathogenicity factors, were detected in the majority of tested fungal cultures. Effective prevention of contamination of anatomical museums and departments by mycelial fungi is necessary, as it poses a serious health hazard to personnel.

ADDITIONAL INFORMATION

Author contribution. Thereby, all authors made a substantial contribution to the conception of the study, acquisition, analysis, interpretation of data for the work, drafting and revising the article, final approval of the version to be published and agree to be accountable for all aspects of the study.

Competing interests. The authors declare that they have no competing interests.

Funding source. This study was not supported by any external sources of funding.

ДОПОЛНИТЕЛЬНАЯ ИНФОРМАЦИЯ

Вклад авторов. Все авторы внесли существенный вклад в разработку концепции, проведение исследования и подготовку статьи, прочли и одобрили финальную версию перед публикацией.

Конфликт интересов. Авторы декларируют отсутствие явных и потенциальных конфликтов интересов, связанных с публикацией настоящей статьи.

Источник финансирования. Авторы заявляют об отсутствии внешнего финансирования при проведении исследования.

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UDC 616.517-031.81-08-07-053.2+616-092.6+612.79
DOI: 10.56871/RBR.2024.68.86.002

FEATURES OF SKIN MICROCIRCULATION IN PATIENTS WITH PSORIASIS

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For citation: Emelianov AS, Puzyrev VG, Kibalina IV, Emelianova AN. Features of skin microcirculation in patients with psoriasis. Russian Biomedical Research. 2024;9(4):9–15. DOI: <https://doi.org/10.56871/RBR.2024.68.86.002>

Received: 19.09.2024

Revised: 05.11.2024

Accepted: 17.12.2024

Abstract. Introduction. Psoriasis is a chronic inflammatory autoimmune skin disease involving the musculoskeletal system in the pathological process. This original study presents comparative results of studying the microcirculatory bed in the psoriatic papule and in a healthy area of the skin of patients with psoriasis. **The aim** was to study of the parameters of microcirculation in a pathological lesion of the skin in patients with psoriasis against the background of treatment under the influence of artificially created stress. **Materials and methods.** 16 patients with psoriasis aged 18 to 25 years who were on inpatient treatment at the Regional Skin and Venereological Dispensary in Chita were examined. Microcirculation was evaluated by laser speckle interferometry. Statistical analysis and visualization are performed in the R language (<http://cran.rproject.org>), version 4.2.3. **Results.** The dynamics of interlayer blood flow obtained by laser speckle interferometry in a state of artificially modulated stress in a healthy area of the skin significantly differ compared with microcirculation in the affected area. **Conclusion.** The revealed changes in the microcirculation of the skin contribute to the understanding of the pathogenetic links of the formation of a pathological focus in patients with psoriasis.

Keywords: psoriasis, microcirculation, psoriatic papules, pathogenesis

ОСОБЕННОСТИ МИКРОЦИРКУЛЯЦИИ КОЖИ У БОЛЬНЫХ ПСОРИАЗОМ

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Для цитирования: Емельянов А.С., Пузырев В.Г., Кибалина И.В., Емельянова А.Н. Особенности микроциркуляции кожи у больных псориазом. Российские биомедицинские исследования. 2024;9(4):9–15. DOI: <https://doi.org/10.56871/RBR.2024.68.86.002>

Поступила: 19.09.2024

Одобрена: 05.11.2024

Принята к печати: 17.12.2024

Резюме. Введение. Псориаз — хроническое воспалительное аутоиммунное заболевание кожи с вовлечением в патологический процесс опорно-двигательного аппарата. В данном оригинальном исследовании представлены сравнительные результаты изучения микроциркуляторного русла в псориатической папуле и в здоровом участке кожи пациентов с псориазом. **Цель исследования** — изучение параметров микроциркуляции в патологическом очаге кожи у пациентов с псориазом на фоне проводимого лечения при воздействии искусственно созданного стресса. **Материалы и методы.** Обследовано 16 пациентов с псориазом в возрасте от 18 до 25 лет, находившихся на стационарном лечении в ГУЗ «Краевой кожно-венерологический

диспансер» в г. Чите. Оценку микроциркуляции проводили методом лазерной спекл-интерферометрии. Статистический анализ и визуализация выполнены на языке R (<http://cran.rproject.org>) версии 4.2.3. **Результаты исследования.** Показатели динамики межслоевого кровотока, полученные методом лазерной спекл-интерферометрии, в состоянии искусственно модулированного стресса в здоровом участке кожи достоверно отличаются по сравнению с микроциркуляцией в пораженном участке. **Заключение.** Выявленные изменения микроциркуляции кожи вносят вклад в понимание патогенетических звеньев формирования патологического очага у пациентов с псориазом.

Ключевые слова: псориаз, микроциркуляция, псориатические папулы, патогенез

INTRODUCTION

Psoriasis is a chronic immune-mediated inflammatory skin disease characterized by impaired keratinization and inflammatory reactions in the dermis. The pathogenesis of dermatosis includes the interplay between environmental triggers, hereditary component, inflammatory and autoimmune reactions, which directly affects the alteration of skin microcirculation in psoriasis patients [2, 12]. According to the literature, autoantibodies and immune complexes in dermatosis contribute to vascular wall damage, which correlates with the duration, severity of the pathologic process and clinical symptoms of the disease. The main factors contributing to angiopathies in psoriasis are local skin damage, changes in interstitial metabolism, formation of hypersensitivity and changes in vascular permeability [3, 5].

Microcirculatory disorders in patients with psoriasis are caused by imbalance of hemostasis and coagulation [6]. Thus, scientific studies show an increase in the concentration of C-peptide, plasminogen, fibrinopeptide A, homocysteine and a decrease in the level of antithrombin III. The correlation between hemodynamic disturbance and the frequency of disease exacerbations was determined. Changes in the rheological properties of blood in patients are fixed in case of a long history of the disease, presence of foci of chronic infection, long-term intake of systemic glucocorticosteroids and cytostatics, complicated course of psoriasis.

The use of capillaroscopy contributes to a better study of microcirculatory parameters [1, 7, 8, 13]. Modern studies present the characteristics of microcirculatory disorders: at the progressive stage in psoriatic papules capillaries are thin, at the resolution of clinical symptoms they are dilated with a tortuous pattern. However, a 20% decrease in the number of functionally active capillaries was recorded at the border with healthy skin. The perivascular space is characterized by lymphocytic infiltration, edema, but numerous cytoplasmic outgrowths were detected on the endothelium. It is known that clinically healthy blood relatives with psoriasis have similar changes in microcirculation.

AIM

Study of microcirculation parameters in pathologic skin focus in patients with psoriasis on the background of the conducted treatment under the influence of artificially created stress.

MATERIALS AND METHODS

The study included 16 people with the diagnosis of “Disseminated psoriasis vulgaris of smooth skin and scalp, progressive stage, exacerbation” who were treated in the hospital on the basis of the State Institution of Health Care “Regional Skin and Venereological Dispensary” of the Ministry of Health of the Transbaikal Territory (Chita). All patients included in the study were prescribed standard systemic and topical therapy according to the Federal Clinical Recommendations of the Russian Society of Dermatovenereology and Cosmetology (RSDVC). Voluntary informed consent was obtained from all persons included in the study.

The study was performed by laser speckle interferometry in two stages. The first stage was at the moment of admission to the hospital, and the second stage was before discharge from the hospital. The stages included three periods, each of which lasted for three minutes: T1 — resting state, T2 — modulated stress, T3 — restorative resting state. Each period was accompanied by measurements of hemodynamic parameters. Stress was created by a color test implementing the Stroop effect. This method is designed to assess the formation of associative connections between cortical zones responsible for the perception of color and lettering. The mismatch between color and semantic meaning of words leads to a conflict of perception and, as a result, to stress. An mDLS (miniaturized Dynamic Light Scattering, Elfi-Tech, Rehovot, Israel) sensor attached to the skin recorded photons that were reflected from red blood cells moving in adjacent layers of blood flow (shear rate, or transverse velocity gradient). The first sensor was placed over the affected area of the outer surface of the forearm. The second sensor was placed above the first sen-

sor on healthy skin near the pathologic focus. The signal was integrated as three Hemodynamic Indexes (HI). The technique of spectral decomposition of the signal by Fast Fourier Transform (FFT) into frequency components associated with hemodynamic sources of different layer shear rates was used. The low-frequency (1–300 Hz) index (HI1) was determined by slow interlayer interaction, the high-frequency region (HI3) (3000–24 000 Hz) characterized fast layer shift processes. HI2 (300–3000 Hz) occupied an intermediate position. To evaluate the tendencies of blood flow redistribution between fast and slow processes, the HI1/HI3 ratio index was introduced. The summed index $HI = HI1 + HI2 + HI3$ demonstrated the volume of flow covered by sensor irradiation. The normalized indices RHI1, RHI2, RHI3 denote the relative contribution of each component to the overall dynamic processes ($RHI1 = HI1/HI$,

Table 1

Microcirculatory hemodynamic parameter prior to and after the treatment in healthy and affected areas of the skin

Таблица 1

Показатели микроциркуляторной гемодинамики до и после лечения на здоровом и пораженном участках кожи

Показатель / Parameter	Участок воздействия / Area of impact	Состояние покоя (T1) / Resting state (T1)	Уровень значимо- сти (p1) / Significance level (p1)	Состояние модулированного стресса (T2) / Modulated voltage state (T2)	Уровень значимости (p2) / Signifi- cance level (p2)	Восстановитель- ное состояние покоя (T3) / Restorative state of rest (T3)	Уровень значимо- сти (p3) / Significance level (p3)
Гемодинамический индекс (HI) / Hemodynamic Index (HI)	Здоровый участок / Healthy area	711±115	0,890	849±143	0,750	764±122	0,980
	Пораженный участок / Affected area	706±194		814±314		746±277	
Гемодинамический индекс 1 (HI1) / Hemodynamic Index 1 (HI1)	Здоровый участок / Healthy area	0,204±0,030	0,038	0,198±0,023	0,029	0,208±0,032	0,007
	Пораженный участок / Affected area	0,161±0,028		0,167±0,022		0,154±0,028	
Гемодинамический индекс 2 (HI2) / Hemodynamic Index 2 (HI2)	Здоровый участок / Healthy area	0,519±0,019	0,220	0,528±0,018	0,46	0,525±0,015	0,99
	Пораженный участок / Affected area	0,529±0,019		0,519±0,0257		0,525±0,0221	
Гемодинамический индекс 3 (HI3) / Hemodynamic Index 3 (HI3)	Здоровый участок / Healthy area	0,270±0,033	0,017	0,274±0,029	0,012	0,267±0,035	0,009
	Пораженный участок / Affected area	0,318±0,030		0,326±0,036		0,328±0,033	
Отношение HI1/HI3 / Ratio of HI1/HI3	Здоровый участок / Healthy area	0,710±0,141	0,064	0,673±0,105	0,018	0,715±0,145	0,020
	Пораженный участок / Affected area	0,514±0,119		0,5±0,115		0,479±0,113	

Note. Hemodynamic indices are dimensionless quantities. Statistical significance of comparing groups according to the paired Wilcoxon criterion: p1 – T1 (healthy area) and T1 (affected area), p2 – T2 (healthy area) and T2 (affected area), p3 – T3 (healthy area) and T3 (affected area).
Примечание. Гемодинамические индексы являются безразмерными величинами. Статистическая значимость сравнения групп по парному критерию Вилкоксона: p1 – T1 (здоровый участок) и T1 (пораженный участок), p2 – T2 (здоровый участок) и T2 (пораженный участок), p3 – T3 (здоровый участок) и T3 (пораженный участок).

Table 2

Microcirculatory hemodynamic parameter on response to stress stimulation in patients with psoriasis

Таблица 2

Показатели микроциркуляторной гемодинамики в ответ на стрессорную стимуляцию у больных псориазом

Показатель / Parameter	Участок воздействия / Area of impact	Состояние покоя (T1) / Resting state (T1)	Состояние покоя (T2) / Resting state (T2)	Состояние покоя (T3) / Resting state (T3)	Уровень значимости (p1) / Significance level (p1)	Уровень значимости (p2) / Significance level (p2)	Уровень значимости (p3) / Significance level (p3)
Гемодинамический индекс (HI) / Hemodynamic Index (HI)	Здоровый участок / Healthy area	711±115	849±143	764±122	0,003	0,018	0,004
	Пораженный участок / Affected area	709±296	814±314	746±277	0,48	0,64	0,93
Гемодинамический индекс 1 (HI1) / Hemodynamic Index 1 (HI1)	Здоровый участок / Healthy area	147±19,7	168±31,8	158±27,5	0,007	0,014	0,014
	Пораженный участок / Affected area	126±54,8	129±54,8	128±53,5	0,87	0,87	0,87
Гемодинамический индекс 2 (HI2) / Hemodynamic Index 2 (HI2)	Здоровый участок / Healthy area	370±64,1	448±73,4	401±65,6	0,004	0,033	0,005
	Пораженный участок / Affected area	416±212	421±176	433±204	0,85	0,85	0,85
Гемодинамический индекс 3 (HI3) / Hemodynamic Index 3 (HI3)	Здоровый участок / Healthy area	194±47,7	234±51,3	205±47,6	0,006	0,009	0,009
	Пораженный участок / Affected area	218±82	241±61,5	236±73,9	0,14	0,19	0,52
Отношение HI1/HI3 / Ratio of HI1/HI3	Здоровый участок / Healthy area	0,8±0,226	0,735±0,16	0,802±0,224	0,068	0,87	0,091
	Пораженный участок / Affected area	0,514±0,119	0,475±0,135	0,479±0,113	0,51	0,34	0,81

Note. Hemodynamic indices are dimensionless quantities. Statistical significance of comparing groups according to the paired Wilcoxon criterion: T1 and T2, p2 — T1 and T3, p3 — T2 and T3.

Примечание. Гемодинамические индексы являются безразмерными величинами. Статистическая значимость сравнения групп по парному критерию Вилкоксона: p1 — T1 и T2, p2 — T1 и T3, p3 — T2 и T3.

RHI2 = HI2/HI, RHI3 = HI3/HI). To evaluate the tendencies of blood flow redistribution between fast and slow processes, the HI1/HI3 ratio index was introduced.

Statistical analysis and visualization were performed in R language (<http://cran.rproject.org>) version 4.2.3. Assessment of the reliability of pairwise differences of all indicators between stages (T1, T2, T3) was performed using the Wilcoxon test. Decision on the statistical significance of hypotheses was made at the level of $p < 0.05$. Quantitative representation of indicators in the tables was performed in the format $M \pm SD$ (mean value $\pm$ standard deviation).

RESULTS AND DISCUSSION

In the first phase of the study before treatment, a significant number of subjects showed a decrease in the relative

normalized hemodynamic index RHI1 in all measurement periods: T1 (resting state) — healthy site = 0.00029, affected site = 0.00023 ($p=0.038$); T2 (modulated stress) — healthy site = 0.00023, affected site = 0.00021 ($p=0.029$); T3 (resting recovery state) — healthy site = 0.00027, affected site = 0.00021 ($p=0.007$). There was an increase in the normalized RHI3 index in the affected skin area compared to the healthy skin area: T1 (resting state) — 0.00038 and 0.00045 ($p=0.017$); T2 (modulated stress) — 0.00062 and 0.00064 ($p=0.012$); T3 (restorative resting state) — 0.00035 and 0.00044 ($p=0.009$) respectively (Table 1).

We have revealed changes in hemodynamic indices on the affected and healthy sites in response to stressor loading. Thus, on the healthy skin area in the period T2 (modulated stress) there was an increase in all normalized hemodynamic indices (RHI1 of the healthy site = 0.19788, affected site =

Table 3

Microcirculatory hemodynamic parameter on response to treatment in the T1 period

Таблица 3

Показатели микроциркуляторной гемодинамики в ответ на лечение в периоде T1

Показатель / Parameter	До терапии / Before therapy	После терапии / After therapy	Уровень значимости (p) / Significance level (p)
Гемодинамический индекс (HI) / Hemodynamic Index (HI)	703±406	713±242	0,86
Гемодинамический индекс 1 (HI1) / Hemodynamic Index 1 (HI1)	123±70	131±44,1	0,73
Гемодинамический индекс 2 (HI2) / Hemodynamic Index 2 (HI2)	375±221	367±128	0,80
Гемодинамический индекс 3 (HI3) / Hemodynamic Index 3 (HI3)	215±115	215±75,5	0,81
Отношение HI1/HI3 / Ratio of HI1/HI3	0,463±0,105	0,612±0,099	0,004

Note. Hemodynamic indices are dimensionless quantities. Statistical significance of comparing groups according to the paired Wilcoxon criterion.
Примечание. Гемодинамические индексы являются безразмерными величинами. Статистическая значимость сравнения групп по парному критерию Вилкоксона.

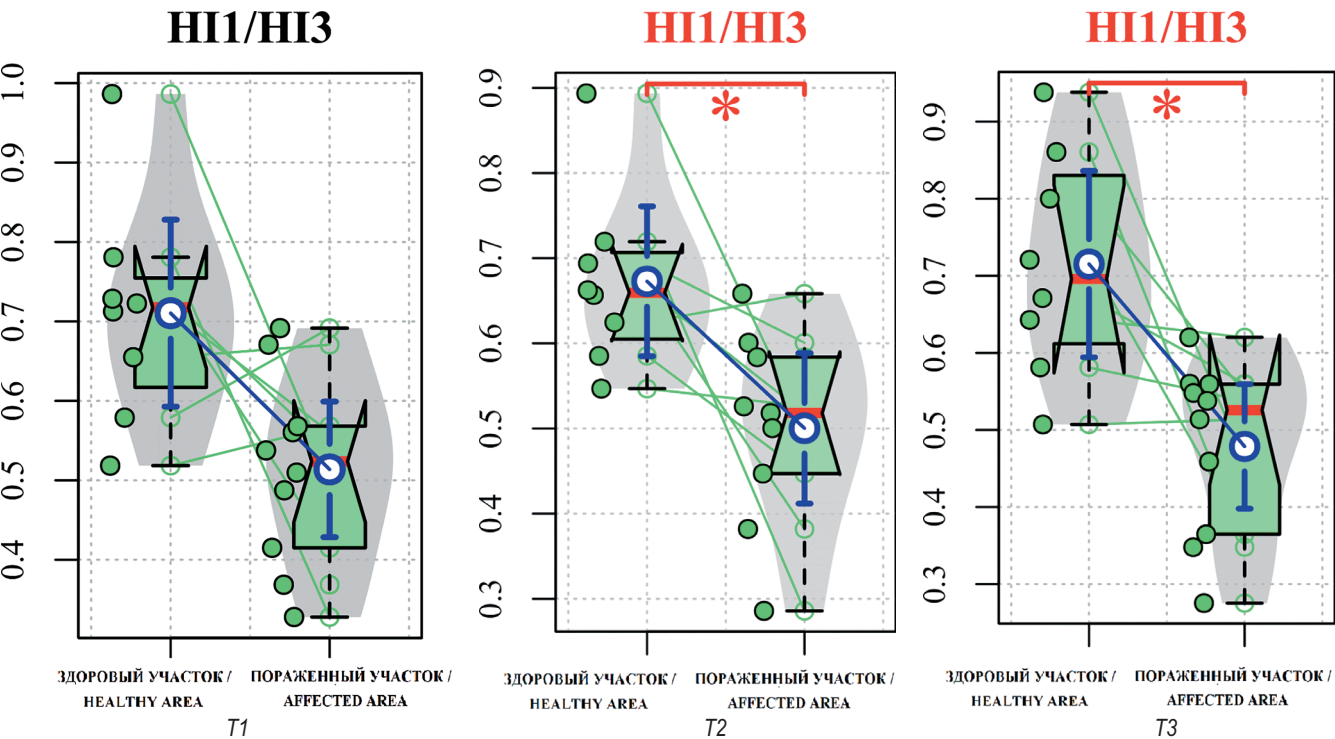


Fig. 1. Dynamics of the change in the ratio between slow and fast interlayer interactions in the HI1/HI3 ratio in healthy and affected areas by study period

Рис. 1. Динамика изменения соотношения между медленными и быстрыми межслоевыми взаимодействиями HI1/HI3 на здоровом и пораженном участках по периодам исследования

= 0.15848; RHI2 of the healthy site = 0.52768, affected site = 0.51720; RHI3 of healthy site = 0.29607, affected = 0.27562) with incomplete recovery of them at stage T3 (resting state recovery) (RHI1 of healthy site = 0.20681, affected site = 0.17158; RHI2 of healthy site = 0.52487, affected = 0.58043; RHI3 of healthy site = 0.26832, affected site = 0.31635). However, no statistical changes between slow and fast interlayer interactions were detected in the psoriatic focus both at rest

(T1) and under modulated stress (T2), which may indicate a lack of response in response to stress stimulation (Table 2). In the second phase of the study, incomplete recovery of the RHI index (RHI1 before treatment = 0.17496, after treatment = 0.18373; RHI2 before treatment = 0.53343, after treatment = 0.51473; RHI3 before treatment = 0.30583, after treatment = 0.30154) was observed after treatment in period T1 (resting state) (Table 3).

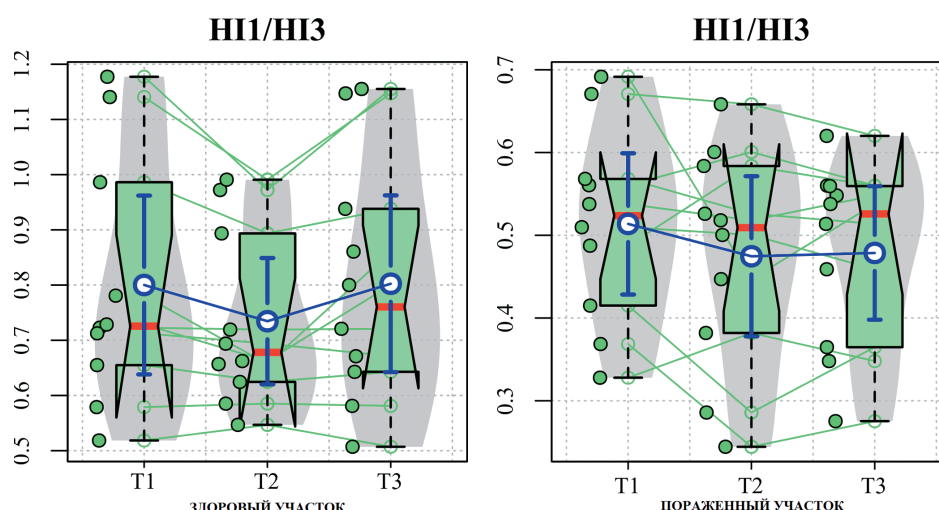


Fig. 2. Dynamics of the change in the ratio between slow and fast interlayer interactions in the HI1/HI3 ratio in healthy and affected areas of the skin

Рис. 2. Динамика изменения соотношения между медленными и быстрыми межслоевыми взаимодействиями HI1/HI3 на здоровом и пораженном участках кожи

How to explain the results obtained? It is known that the emerging local inflammation as well as the processes of neoangiogenesis change the character of blood flow in favor of turbulent flow [4], which affects hemodynamic functions: the hemodynamic index RHI1 decreases in all periods of measurement, while the RHI3 index increases on the affected skin area. This assumption is consistent with the results of studies [8, 10], the authors of which showed that the processes of inflammation and neoangiogenesis are caused by the appearance of cytokine-chemokine network. Based on this, we can conclude that a significant decrease in the HI1/HI3 ratio characterizes a change in the balance of interlayer velocity distribution (Fig. 1).

At the same time, the unequal response in the affected and healthy areas in response to the stressor load may be due to the processes of endotheliocyte maladaptation, the mechanoreceptors of which may have been blocked due to impaired wall blood flow, as well as specific proinflammatory cytokines, the action of which is caused by autoimmune inflammation [9–11] (Fig. 2).

CONCLUSION

1. Laser speckle interferometry-derived measures of interlayer blood flow dynamics demonstrated significant changes in the slow RHI1 and fast RHI3 components, unchanged by exposure to artificially induced stress.

2. At the healthy site, when the stress condition was induced, there was an increase in HI1 with incomplete recovery in the T3 period.

3. The observed change in microcirculation after the treatment is due to the reduction of systemic and local inflammation.

ADDITIONAL INFORMATION

Author contribution. Thereby, all authors made a substantial contribution to the conception of the study, acquisition, analysis, interpretation of data for the work, drafting and revising the article, final approval of the version to be published and agree to be accountable for all aspects of the study.

Competing interests. The authors declare that they have no competing interests.

Funding source. This study was not supported by any external sources of funding.

Consent for publication. Written consent was obtained from the patient for publication of relevant medical information within the manuscript.

ДОПОЛНИТЕЛЬНАЯ ИНФОРМАЦИЯ

Вклад авторов. Все авторы внесли существенный вклад в разработку концепции, проведение исследования и подготовку статьи, прочли и одобрили финальную версию перед публикацией.

Конфликт интересов. Авторы декларируют отсутствие явных и потенциальных конфликтов интересов, связанных с публикацией настоящей статьи.

Источник финансирования. Авторы заявляют об отсутствии внешнего финансирования при проведении исследования.

Информированное согласие на публикацию. Авторы получили письменное согласие пациентов на публикацию медицинских данных.

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UDC 612.63.01+618.2/3+664.644.5+577.151.02
DOI: 10.56871/RBR.2024.19.88.003

STUDY OF THE ACTIVITY OF DIGESTIVE ENZYMES OF BIOLOGICAL FLUIDS IN WOMEN DURING PREGNANCY

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For citation: Kolodkina EV, Lytaev SA. Study of the activity of digestive enzymes of biological fluids in women during pregnancy. Russian Biomedical Research. 2024;9(4):16–22. DOI: <https://doi.org/10.56871/RBR.2024.19.88.003>

Received: 19.09.2024

Revised: 05.11.2024

Accepted: 17.12.2024

Abstract. Introduction. The hydrolytic activity of biofluids during pregnancy has been studied. It was found that their content in blood serum, saliva, urine and coprofiltrate dynamically change from the end of pregnancy to the early postpartum period. It has been shown that digestive enzymes play an important role in the formation of the Mother–fetus interaction. **The purpose of the work** — to study the activity of digestive enzymes in peripheral blood serum, urine, saliva, coprofiltrate, amniotic fluid, umbilical cord blood in women during pregnancy after childbirth, to compare with that content in non-pregnant women. **Materials and methods.** The material for the study was taken from non-pregnant (n=45) and pregnant (n=82) women — new mothers aged from 18 to 35 years (2–3 days after childbirth). The dynamics of changes in the activity of hydrolases in biological fluids was studied. **Results.** A change in the activity levels of pepsinogen, amylase, alkaline phosphatase and lipase in biological fluids in women during pregnancy and in the postpartum period compared with those in non-pregnant women was revealed. **Conclusions.** In pregnant women, by the end of pregnancy, there is an increase in the activity of all hydrolases in blood serum, an increase in the activity of pepsinogen and lipase in urine, a significant increase in amylase in saliva and a decrease in the proteolytic and alkaline phosphatase activities of the coprofiltrate. The homogenate of placenta, umbilical cord blood and amniotic fluid is characterized by the highest activity of alkaline phosphatase.

Keywords: pregnancy, digestive enzymes, enzyme homeostasis, biological fluids, amniotrophic nutrition

ИЗУЧЕНИЕ АКТИВНОСТИ ПИЩЕВАРИТЕЛЬНЫХ ФЕРМЕНТОВ БИОЛОГИЧЕСКИХ ЖИДКОСТЕЙ У ЖЕНЩИН ВО ВРЕМЯ БЕРЕМЕННОСТИ

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Для цитирования: Колодкина Е.В., Лытаев С.А. Изучение активности пищеварительных ферментов биологических жидкостей у женщин во время беременности. Российские биомедицинские исследования. 2024;9(4):16–22. DOI: <https://doi.org/10.56871/RBR.2024.19.88.003>

Поступила: 19.09.2024

Одобрена: 05.11.2024

Принята к печати: 17.12.2024

Резюме. Введение. Изучена гидролитическая активность биологических жидкостей при беременности. Установлено, что их содержание в сыворотке крови, слюне, моче и копрофильtrate динамически меняется от конца беременности до раннего послеродового периода. Показано, что пищеварительные ферменты

играют важную роль в формировании взаимодействия «мать–плод». **Цель исследования** — изучить активность пищеварительных ферментов в сыворотке периферической крови, моче, слюне, копрофильtrate, амниотической жидкости, крови пуповины у женщин при беременности и после родов, сравнить с таковым содержанием у небеременных женщин. **Материалы и методы.** Материал для исследования брался у небеременных (n=45) и беременных (n=82) женщин — родильниц в возрасте от 18 до 35 лет (2–3-й день после родов). Изучалась динамика изменения активности гидролаз в биологических жидкостях. **Результаты.** Выявлено изменение уровней активности пепсиногена, амилазы, щелочной фосфатазы и липазы в биологических жидкостях у женщин при беременности и в послеродовой период по сравнению с показателями у небеременных женщин. **Выводы.** У беременных женщин к концу беременности наблюдается повышение активности всех гидролаз в сыворотке крови, увеличение активности пепсиногена и липазы в моче, существенное повышение амилазы в слюне и снижение протеолитической и щелочно-фосфатазной активностей копрофильtrата. Гомогенат плаценты, пуповинная кровь и амниотическая жидкость отличаются наиболее высокой активностью щелочной фосфатазы.

Ключевые слова: беременность, пищеварительные ферменты, ферментный гомеостаз, биологические жидкости, амниотрофное питание

INTRODUCTION

Different mechanisms are involved in the homeostasis of pepsinogen, amylase, alkaline phosphatase, and lipase, among which are the secretion and excretion of digestive gland hydrolases [5–8, 13, 16].

At present, it has been confirmed that digestive gland hydrolases are widely distributed in the biological media of the organism, which, being inducted into blood and lymph, are distributed according to the selective permeability of histohematic barriers, including the uteroplacental barrier, which supplies hydrolases to the amniotic fluid [1, 11, 14, 17–19, 21].

Digestive hydrolases are of particular importance in the system “maternal organism — placenta, amniotic fluid — fetus” [2–5, 8, 9].

Pregnancy establishes a relationship between the maternal body and the growing fetus. The fetus absorbs nutrients with amniotic waters that are hydrolyzed to monomers in the gastrointestinal tract (GIT) of the developing organism by enzymes that are recreted into the aquafetal environment (autolytic digestion) [10, 13, 15, 16, 20, 21].

The “fate” of secreted digestive enzymes in pregnant women, changes in the levels of enzyme activity in biological fluids throughout pregnancy and in the postpartum period have not been fully studied [12, 19, 20].

AIM

To study the activity of digestive enzymes in peripheral blood serum, urine, saliva, coprofiltrate, amniotic fluid, umbilical cord blood in pregnant and postpartum women and compare it with that in non-pregnant women.

MATERIALS AND METHODS

The study was conducted on the basis of the St. Petersburg State Budgetary Health Care Institution “Maternity Hospital No. 6 named after Prof. V.F. Snegirev”.

The material for the study was taken from non-pregnant (n=45) and pregnant (n=82) women. Maternity patients aged from 18 to 35 years.

The content and activity of enzymes (pepsinogen, amylase, lipase and alkaline phosphatase) were studied in peripheral blood serum, urine, oral fluid, coprofiltrate, amniotic fluid, umbilical cord blood in pregnant women at 39–40 weeks of pregnancy, in women on the 2–3rd day after delivery, and once in the control group.

All patients were informed about the purpose and methods and gave written voluntary informed consent to participate in the study (protocol No. 0608-23 of 07.08.2023 of the ethical committee meeting).

Total proteolytic activity was determined at low pH values of 1.5–2.0 by spectrophotometric (tyrosine) Kunitz-Northrop method. Amylolytic activity was determined by amyloclastic method according to Caraway. Lipolytic activity was determined by unified method using olive oil as a substrate. Alkaline phosphatase activity was determined by standard constant time method using a set of reagents from Lahema diagnosticum (Czech Republic).

Differences between the groups by the level of the studied signs were evaluated using the Mann-Whitney U-criterion. Differences were considered significant at the probability of error $p < 0.05$.

Statistical processing of the obtained data was carried out in Microsoft Excel 2003 spreadsheet environment, as well as Primer of biostatistics 4.03 and SPSS 11.0 programs.

RESULTS

As a result of these studies, it was revealed that the blood serum of pregnant women at 39–40 weeks of pregnancy contains 1.5–2 times more hydrolases than that of non-pregnant women (Table 1).

On the 2–3rd day after delivery in women the content of enzymes in the blood serum decreases, but remains higher than in the examined women of the control group. Apparently, this is due to the increased secretion of hydrolases in women during pregnancy [5, 6].

The study of digestive enzyme activity in the urine of the examined women revealed the following changes (Table 2).

At 39–40 weeks of pregnancy, the level of proteolytic and lipolytic activity of urine in women is significantly higher than in non-pregnant women ($p < 0.05$). On the 2–3rd day after delivery in women giving birth, there is a significant decrease in the enzymatic activity of this biological fluid for all the studied indicators, regardless of the increase of these enzymes in the antenatal period.

When studying the activity of digestive enzymes in saliva, it was revealed that the saliva of pregnant women has greater proteolytic activity than that of patients in the control group (Table 3).

The indices of pepsinogen in saliva decreased in postpartum women in 1.8 times ($p < 0.05$) compared to those of

Table 1

Indicators of the activity of digestive enzymes in the blood of control group individuals, women at 39–40 weeks of pregnancy and postpartum women

Таблица 1

Показатели активности пищеварительных ферментов в крови у лиц контрольной группы, женщин на 39–40-й неделе беременности и родильниц после родов

Контингент исследуемых / Contingent of the studied	Пепсиноген, тир. ед/мл / Pepsinogen, tyr. units/ml	Амилаза, ед/мл / Amylase, units/ml	Щелочная фосфатаза, ед/мл / Alkaline phosphatase, units/ml	Липаза, ед/мл / Lipase, units/ml
1. Контрольная группа / Control group (n=45)	58,2±1,1	13,5±0,8	722,1±50,6	18,1±0,7
2. Беременные на 39–40-й неделе беременности / Pregnant women at 39–40 weeks of pregnancy (n=82)	60,2±4,1	23,0±1,7**	1182,3±106,4*	34,6±1,7**
3. Родильницы на 2–3-й день после родов / Maternity hospitals 2–3 days after delivery (n=82)	44,9±1,1*	19,6±0,8*	868,4±92,3	26,4±1,2**

Note: the reliability of differences with the indicators of the control group: * — $p < 0,001$; ** — $p < 0,05$.

Примечание: достоверность различий с показателями контрольной группы: * — $p < 0,001$; ** — $p < 0,05$.

Table 2

Indicators of the activity of digestive enzymes in the urine of individuals in the control group, women at 39–40 weeks of pregnancy and postpartum women

Таблица 2

Показатели активности пищеварительных ферментов в моче у лиц контрольной группы, женщин на 39–40-й неделе беременности и родильниц после родов

Контингент исследуемых / Contingent of the studied	Пепсиноген, тир. ед/мл / Pepsinogen, tyr. units/ml	Амилаза, ед/мл / Amylase, units/ml	Щелочная фосфатаза, ед/мл / Alkaline phosphatase, units/ml	Липаза, ед/мл / Lipase, units/ml
1. Контрольная группа / Control group (n=45)	4520,3±320,4	64,1±1,2	428,6±29,0	20,6±1,2
2. Беременные на 39–40-й неделе беременности / Pregnant women at 39–40 weeks of pregnancy (n=82)	9650,1±504,1**	67,2±1,4	410,9±36,2	41,2±1,6**
3. Родильницы на 2–3-й день после родов / Maternity hospitals 2–3 days after delivery (n=82)	3698,5±278,8*	41,2±0,9*	240,4±17,8**	27,5±1,5**

Note: the reliability of differences with the indicators of the control group: * — $p < 0,001$; ** — $p < 0,05$.

Примечание: достоверность различий с показателями контрольной группы: * — $p < 0,001$; ** — $p < 0,05$.



Table 3

**Indicators of the activity of digestive enzymes in saliva in the control group,
women at 39–40 weeks of pregnancy and postpartum women**

Таблица 3

**Показатели активности пищеварительных ферментов в слюне у лиц контрольной группы,
женщин на 39–40-й неделе беременности и родильниц после родов**

Контингент исследуемых / Contingent of the studied	Пепсиноген, тир. ед/мл / Pepsinogen, tyr. units/ml	Амилаза, ед/мл / Amylase, units/ml	Щелочная фосфатаза, ед/мл / Alkaline phosphatase, units/ml	Липаза, ед/мл / Lipase, units/ml
1. Контрольная группа / Control group (n=45)	1520,9±247,6	2385,3±264,7	215,6±22,3	64,8±7,0
2. Беременные на 39–40-й неделе беременности / Pregnant women at 39–40 weeks of pregnancy (n=82)	2612,9±218,1*	4781,6±423,8*	361,8±30,2	121,1±11,6*
3. Родильницы на 2–3-й день после родов / Maternity hospitals 2–3 days after delivery (n=82)	1463,3±221,6	3109,0±294,2**	475,3±31,6**	70,9±5,4

Note: the reliability of differences with the indicators of the control group: * — $p < 0,001$; ** — $p < 0,05$.

Примечание: достоверность различий с показателями контрольной группы: * — $p < 0,001$; ** — $p < 0,05$.

Table 4

**Indicators of the activity of digestive enzymes in coprofiltrate in the control group,
women at 39–40 weeks of pregnancy and postpartum women**

Таблица 4

**Показатели активности пищеварительных ферментов в копрофильтрате у лиц контрольной группы,
женщин на 39–40-й неделе беременности и родильниц после родов**

Контингент исследуемых / Contingent of the studied	Пепсиноген, тир. ед/мл / Pepsinogen, tyr. units/ml	Амилаза, ед/мл / Amylase, units/ml	Щелочная фосфатаза, ед/мл / Alkaline phosphatase, units/ml	Липаза, ед/мл / Lipase, units/ml
1. Контрольная группа / Control group (n=45)	442,2±20,5	19,5±0,8	6220,4±248,0	320,8±12,6
2. Беременные на 39–40-й недели беременности / Pregnant women at 39–40 weeks of pregnancy (n=82)	153,8±10,9*	44,4±3,9*	2236,6±158,6*	344,4±17,2
3. Родильницы на 2–3-й день после родов / Maternity hospitals 2–3 days after delivery (n=82)	315,3±16,8**	18,3±0,9	3229,2±122,1**	324,3±13,6

Note: the reliability of differences with the indicators of the control group: * — $p < 0,001$; ** — $p < 0,05$.

Примечание: достоверность различий с показателями контрольной группы: * — $p < 0,001$; ** — $p < 0,05$.

pregnant women at 39–40 weeks of pregnancy, which corresponds to the protein-producing function in the “mother–fetus” system (Table 3).

Amylolytic activity of saliva had a significant increase by 39–40 weeks of pregnancy (2-fold, $p < 0.001$) in women compared to controls. On the 2–3rd day after delivery, amylase activity decreased, not reaching the values in non-pregnant women.

Similar dynamics was observed with respect to salivary lipase activity, with an increase in the enzyme level at the end of pregnancy and a decrease in the postpartum period.

There was a significant increase in alkaline phosphatase activity of saliva at 39–40 weeks of pregnancy by 1.9 times

($p < 0.001$) in women compared with control parameters, with a further increase in the level of the enzyme in women on the 2–3rd day after delivery.

Indices of activity of digestive enzymes in coprofiltrate in the studied groups of women are presented in Table 4. There was a significant decrease in proteolytic and alkaline phosphatase activity of coprofiltrate in pregnant women on the 39–40th week of pregnancy and in laboring women on the 2–3rd day after delivery compared to the control group.

Amylolytic activity of coprofiltrate in pregnant women reaches values twice higher than in the control group by the end of pregnancy. After delivery, it becomes lower than the initial level and indicators of non-pregnant women.

Table 5

Indicators of the activity of hydrolases of amniotic fluid, umbilical cord blood, and placenta

Таблица 5

Показатели активности гидролаз амниотической жидкости, плаценты и пуповинной крови

Гидролитическая активность / Hydrolytic activity	Амниотическая жидкость / Amniotic fluid	Гомогенат плаценты / Placenta homogenate	Пуповинная кровь / Umbilical cord blood
Амилолитическая, ед/мл / Amylolytic, units/ml	16,3±0,7	9,2±0,5	36,7±4,5**
Щелочно-фосфатазная, ед/мл / Alkaline phosphatase, units/ml	3287,6±174,0	6906,2±208,1*	1282,1±316,2
Общая протеолитическая, тир. ед/мл / Common proteolytic, tyr. units/ml	566,4±39,1	759,0±25,5*	104,1±46,9*
Липолитическая, ед/мл / Lypolytic, units/ml	232,1±17,8	212,3±36,4	167,7±12,3**

Примечание: достоверность различий с показателями амниотической жидкости: * — $p < 0,001$; ** — $p < 0,05$.

Note: the reliability of differences with the indicators of the amniotic fluid: * — $p < 0,001$; ** — $p < 0,05$.

There were no significant differences in the lipolytic activity of coprofiltrate in women at the end of pregnancy and after childbirth compared to that in non-pregnant women.

Pregnancy ensures the circulation of digestive hydrolases in the system “maternal organism — placenta, amniotic fluid — fetus” for their subsequent participation in hematotropic nutrition and autolytic digestion of the fetus [5, 6, 15].

Amniotic fluid and umbilical cord blood have high hydrolytic activity. The extract from placenta contains hydrolases in a greater amount, taking into account the fivefold dilution of the homogenate (Table 5).

Thus, amylolytic activity in umbilical cord blood is 2 times higher than in amniotic fluid. The total proteolytic activity was significantly higher in the extract from placenta and amniotic fluid than in umbilical cord blood, indicating the concentrating ability of the placenta and amnion. The same pattern was observed with respect to lipase activity. At the same time, the content of alkaline phosphatase was particularly high in the extract from the placenta, and the amniotic fluid and cord blood contained almost as much of the enzyme as the maternal blood plasma before labor.

Thus, hydrolases secreted by digestive glands can participate in the organization of creator communication, formation of functional blocks of different purposes and functional systems of trophic and transport support for interorgan and interorganism interaction in the system “maternal organism — placenta, amniotic fluid — fetus”.

DISCUSSION

In the biological fluids of the system “mother — fetus — newborn — infant” selectively specific digestive enzymes, secreted in the maternal body, are distributed, detected by proteolytic, amylolytic, lipolytic, alkaline-phosphatase activi-

ties of blood plasma (serum), saliva, urine, coprofiltrate and amniotic fluid.

Our studies revealed a slight increase in pepsinogen activity in blood serum in pregnant women at 39–40 weeks of pregnancy with a subsequent decrease in the activity of the enzyme in laboring women on the 2–3rd day after delivery.

In pregnant women there was an increase in amylolytic, alkaline-phosphatase and lipolytic activities of blood serum in the III trimester compared to the indicators of the control group. In the postpartum period, enzyme activity decreased, not reaching the values of non-pregnant women.

The homeostasis of hydrolases synthesized by digestive glands is maintained by a system of interacting mechanisms, among which the renal excretion pathway is considered to be the most significant [8].

According to G.F. Korotko, the kidneys excrete a very significant amount of increased enzymes, while other pathways of enzyme excretion and degradation cannot compensate for their renal excretion from the body [8].

Our studies showed that the proteolytic activity of urine steadily increased towards the end of pregnancy, which is associated with increased enzyme excretion in urine and saliva.

Similar dynamics had lipolytic activity of urine, which increased by the end of pregnancy in all women who gave birth and remained higher than in non-pregnant women.

At 39–40 weeks of pregnancy, an increase in amylolytic and a decrease in alkaline phosphatase activity of urine was observed in women compared with the control group [5, 8].

In all pregnant women, the recreation of enzymes (amylase, lipase and pepsinogen) by the salivary glands is directly related to gestational age, with an increase in enzyme activity at the end of pregnancy and a decrease after delivery. Alkaline phosphatase activity increased significantly in the dynamics of pregnancy, with the greatest increase after delivery.

Excretory-recretory origin of hydrolytic activity of coprofiltrate is explained by the fact of detection of amylase, pepsinogen, lipase and alkaline phosphatase in feces. At 39–40 weeks of pregnancy, amylolytic activity increased in all women, while pepsinase and alkaline phosphatase activity decreased almost 3-fold ($p < 0.001$) compared to the values of non-pregnant women. There were no significant differences in lipolytic activity of coprofiltrate in pregnant women and laboring women.

The amnioplacental barrier is involved in the selective accumulation of digestive enzymes in amniotic fluid and in the placenta itself [5, 6, 15, 19].

We found that in placenta homogenate and amniotic fluid the content of enzymes is quite significant. Umbilical cord blood in comparison with placenta homogenate and amniotic fluid contains less enzymes: there is 6–7 times lower pepsinogen activity than in placenta, and 4–5 times lower than in amniotic fluid.

Our data indicate that the homeostasis of hydrolases is maintained due to their recreation and excretion from the body. In pregnancy, there is a dynamic change in the indicators of enzymatic activity of biological fluids, while homeostatic parameters are maintained at the level necessary for its development.

CONCLUSION

1. At the 39–40th week of pregnancy, women showed an increase in proteolytic, amylolytic, alkaline phosphatase and lipolytic activities of blood serum compared to the control group.

2. A significant increase in pepsinogen and lipase activity in urine was observed in women toward the end of pregnancy, followed by their decrease in postpartum women.

3. The greatest changes in saliva of pregnant women were observed with respect to amylase, the activity of which remained high in postpartum women.

4. There was a significant decrease in proteolytic and alkaline phosphatase activities of coprofiltrate in pregnant women at 39–40 weeks of pregnancy and in postpartum women at 2–3 days after delivery compared to the control group.

5. High activity of alkaline phosphatase is noted in placenta homogenate, umbilical cord blood and amniotic fluid. Total proteolytic activity is most pronounced in placenta homogenate and amniotic fluid.

ADDITIONAL INFORMATION

Author contribution. Thereby, all authors made a substantial contribution to the conception of the study, acquisi-

tion, analysis, interpretation of data for the work, drafting and revising the article, final approval of the version to be published and agree to be accountable for all aspects of the study.

Competing interests. The authors declare that they have no competing interests.

Funding source. This study was not supported by any external sources of funding.

Consent for publication. Written consent was obtained from the patient for publication of relevant medical information within the manuscript.

ДОПОЛНИТЕЛЬНАЯ ИНФОРМАЦИЯ

Вклад авторов. Все авторы внесли существенный вклад в разработку концепции, проведение исследования и подготовку статьи, прочли и одобрили финальную версию перед публикацией.

Конфликт интересов. Авторы декларируют отсутствие явных и потенциальных конфликтов интересов, связанных с публикацией настоящей статьи.

Источник финансирования. Авторы заявляют об отсутствии внешнего финансирования при проведении исследования.

Информированное согласие на публикацию. Авторы получили письменное согласие пациентов на публикацию медицинских данных.

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UDC 616.155.32+612.42+537.9+612.112.9+616-092.9
DOI: 10.56871/RBR.2024.32.92.004

CHANGES IN MORPHOMETRIC AND OPTICAL PARAMETERS OF RAT'S LYMPHOCYTES UNDER THE INFLUENCE OF COPPER-ZINC PYRITE ORE

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For citation: Nikitina AR, Ziyakaeva KR, Kayumova AF, Shamratova VG. Changes in morphometric and optical parameters of rat's lymphocytes under the influence of copper-zinc pyrite ore. Russian Biomedical Research. 2024;9(4):23–29. DOI: <https://doi.org/10.56871/RBR.2024.32.92.004>

Received: 23.09.2024

Revised: 30.10.2024

Accepted: 17.12.2024

Abstract. Introduction. It is well-established that morphological and optical characteristics of lymphocytes reflect their functional activity, making them suitable for assessing the status of the immune system. This is particularly significant as exposure to adverse environmental conditions, such as those associated with copper-zinc pyrite ore mining, can have negative effects on the body. The relevance of this issue is underscored by the potential risks faced by mining workers who come into contact with the ore, which contains heavy metal salts, and can lead to negative health outcomes. **The aim of this study** was to investigate the effects of copper-zinc pyrite ore on the surface area, nuclear area, and optical density of rat's lymphocytes of the peripheral blood. **Materials and methods.** The study utilized a sample of lymphocytes from the peripheral blood of rats, which were exposed to copper-zinc pyrite ore under controlled conditions. Measurements were taken of the aforementioned parameters, and statistical analysis was performed to determine any significant changes in these characteristics. In the study, we used computer morphometry to analyze the dimensional parameters and structural features of lymphocytes, as well as the optical properties of these cells, in rats that had been exposed to copper-zinc pyrite ore. In the study were used 70 male rats, aged three to four months and weighing an average of 210.5 ± 10.5 grams. The rats were divided into 5 groups based on the timing of their exposure to copper-zinc pyrite ore. The morphometric parameters of the lymphocytes were determined using computer morphometry by "MEKOS-C2" automated microscopy system (Russia), which was integrated with the AXIO Lab A1 microscope (ZEISS, Germany) for smear analysis. **Results.** During the experiment, the nuclear area of lymphocytes was increased, while its optical density decreased, the cytoplasmic area and optical density were decreased. **Discussion.** The findings suggest that exposure to copper-zinc pyrite ore was led to changes of lymphocyte morphology, specifically an increase of nuclear area. Further research is needed to understand the implications of these changes and their potential impact on immune function. The observed changes of the size and optical density of the cell nucleus could be due to a conversion of heterochromatin to active euchromatin and a decrease in the metabolic activity of the cytoplasm. **Conclusions.** The rearrangements in the morphometric parameters and optical properties of lymphocytes that have been observed may be the result of adaptive processes of rat's immune system under the influence of copper-zinc pyrite ore.

Keywords: lymphocytes, histograms, copper-zinc pyrite ore, optical density, rats

ИЗМЕНЕНИЕ МОРФОМЕТРИЧЕСКИХ И ОПТИЧЕСКИХ ПАРАМЕТРОВ ЛИМФОЦИТОВ КРЫС ПОД ВОЗДЕЙСТВИЕМ МЕДНО-ЦИНКОВОЙ КОЛЧЕДАННОЙ РУДЫ

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Для цитирования: Никитина А.Р., Зиякаева К.Р., Каюмова А.Ф., Шамратова В.Г. Изменение морфометрических и оптических параметров лимфоцитов крыс под воздействием медно-цинковой колчеданной руды. Российские биомедицинские исследования. 2024;9(4):23–29. DOI: <https://doi.org/10.56871/RBR.2024.32.92.004>

Поступила: 23.09.2024

Одобрена: 30.10.2024

Принята к печати: 17.12.2024

Резюме. Введение. Известно, что морфологические и оптические параметры отражают функциональную активность лимфоцитов, что позволяет использовать их для оценки состояния иммунной системы организма. Актуальность проблемы определяется тем, что при воздействии на человека неблагоприятных факторов среды, связанных с медно-цинковой колчеданной рудой, возникают отрицательные последствия для организма. Данные негативные эффекты могут наблюдаться у работников горнодобывающих предприятий при их контакте с рудой, так как в ее состав входят соли тяжелых металлов. **Цель работы** заключалась в исследовании площади поверхности лимфоцитов, площади и оптической плотности ядра и цитоплазмы лимфоцитов периферической крови крыс под воздействием медно-цинковой колчеданной руды. **Материалы и методы.** В работе с помощью компьютерной морфометрии в хроническом эксперименте изучены размерные показатели лимфоцитов и их структур, а также оптические свойства этих клеток у крыс, подвергнутых воздействию медно-цинковой колчеданной руды. В эксперименте использовали 70 нелинейных крыс-самцов 3-4-месячного возраста (средняя масса $210,5 \pm 10,5$ г). В соответствии со сроками воздействия руды крысы были разделены на 5 групп. Морфометрические параметры лимфоцитов определяли методом компьютерной морфометрии, с помощью комплекса автоматической микроскопии «МЕКОС-Ц2» (Россия), установленного в составе функций для анализа мазков на микроскопе AXIO Lab.A1 (ZEISS, Германия). **Результаты.** Во все сроки эксперимента происходило увеличение площади ядра лимфоцитов на фоне снижения его оптической плотности. Наблюдалось уменьшение оптической плотности и площади цитоплазмы лимфоцитов. **Обсуждение.** Наблюдаемые изменения площади и оптической плотности ядра лимфоцитов периферической крови, возможно, были обусловлены превращением гетерохроматина в активный эухроматин, а цитоплазмы — снижением ее метаболической активности. **Выводы.** Выявленные перестройки морфометрических показателей и оптических свойств лимфоцитов были обусловлены адаптивными процессами иммунной системы крыс при действии на организм руды.

Ключевые слова: лимфоциты, гистограммы, медно-цинковая колчеданная руда, оптическая плотность, крысы

INTRODUCTION

Recent studies have shown that certain indicators of peripheral blood lymphocytes, such as diameter, perimeter, and area, reflect not only morphological features of the cells but also their functional activity [1]. Additionally, optical properties of these cells can provide insight into the state of their internal structures.

A change in the range of variations in the size parameters of lymphocytes can serve as an indicator of impaired immunoreactivity of the body and the development of pathological processes in response to adverse environmental factors [1, 2]. It is therefore of great practical importance to study the morphometric and optical characteristics of peripheral blood lymphocytes in laboratory animals under exposure to salts of heavy metals, which are part of the ores that mining workers come into contact with. There are three major deposits in Bashkortostan that produce copper-zinc pyrite ore, and their composition contains approximately 60 harmful impurities, including salts of heavy metals like arsenic, antimony, mercury, and fluorine [3].

AIM

The aim of the study was to investigate the morphometric and optical features of lymphocytes, such as cell surface area, nuclear and cytoplasmic size, and optical density, in the peripheral blood of rats exposed to copper-zinc pyrite ore.

MATERIALS AND METHODS

The effect of copper-zinc pyrite ore on hematological parameters was studied in 70 white non-linear male rats aged 3–4 months and weighing 210.5 ± 10.5 grams. There were 5 experimental groups and one control group. Experimental rats received a water suspension of copper-zinc pyrite ore orally for 10, 20, 30, 45, and 60 days at a dose of 600 mg/kg body weight [4, 5]. During the experiment, we followed the principles outlined in the directives of the European Community (86/609/EEC), the Helsinki Declaration, and the “Rules for Carrying Out Work Using Experimental Animals” as well as the recommendations of the Bioethics Council of the Bashkir State Medical



University. Standard cages ($n=6$), with free access to food and water, were used for the animal husbandry in the vivarium at an average temperature of 24 ± 2 °C, in accordance with the guidelines of SP 2.2.1.3218 and Directive 2010/63/EU on the protection of animals used for scientific purposes. Blood was collected from the rat's tail vein. The animals were euthanized using decapitation and ether anesthesia [6]. A blood smear was stained by method Romanovsky–Giemsa. The morphometric parameters of lymphocytes were determined using computer morphometry of the "MEKOS-C2" automated microscopy system (Russia), which was installed as part of the smear analysis functions on the AXIO Lab A1 microscope (ZEISS, Germany). There were calculated all types of leukocytes, a database of their images was created, and after sorting, the data was transferred to MS Excel. Based on calculating the area of 200 cells in each sample, histograms were built to show the distribution of cells, which allowed for the average values and ratios of cell

proportions to be taken into account of leukocyte formula. The sample of the ore was provided by the Uchalinsky Mining and Processing Plant.

There were studied an optical density of the cytoplasm and nucleus of lymphocytes was studied. To estimate optical density parameters, the brightness distribution over the object was used, using the specific optical density index. The specific optical density index was measured in three spectral ranges of the video camera — blue, green, red, determined by the color of the rays absorbed by the substance. The total spectral range reflected the functional activity of the cell. There were calculated the integral optical density of the cytoplasm, optical density indices and specific total optical densities of lymphocytes [7].

The number and volume of rat's lymphocytes were analyzed using a veterinary semi-automatic hematology analyzer, Vet Exigo 19 (Sweden).

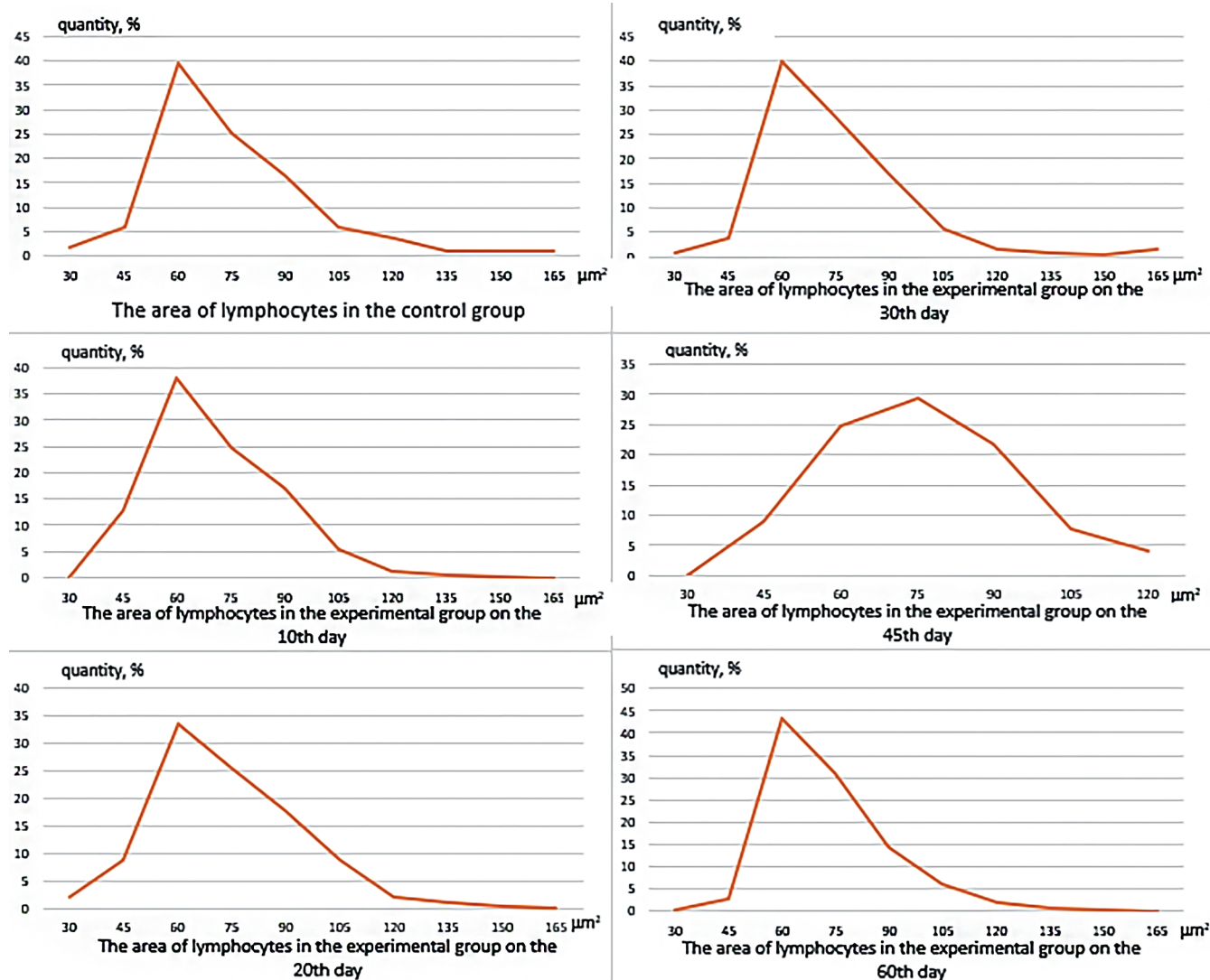


Fig. 1. Histograms of the distribution of the area of rat's lymphocytes exposed to copper-zinc pyrite ore

The data obtained were processed using the statistical software STATISTICA 12 (StatSoft, USA). Nonparametric the Mann–Whitney and the Kruskal–Wallis tests, were used to determine the statistical significance of differences between samples. The median value (Me) and the interquartile range (Q1, Q3) of lymphocytes volume were calculated. Differences were considered statistically significant if $p < 0.05$. Correlations between variables were assessed using the Spearman correlation coefficient, a nonparametric measure of association.

RESULTS

There are presented histograms of the distribution of rat's lymphocytes across the area occupied by cells on the glass area in the initial state and at various experimental time points are presented in Figure 1.

The distribution of cells area during the experiment under the influence of copper-zinc pyrite ore was characterized by imperfections and asymmetry. This was manifested by a shift of the peak of the distribution curve to the left and the presence of a "tail" extending to large values of the indicator.

During all study periods, the histogram of the area showed a maximum value of $60 \mu\text{m}^2$, except for 45 days. In control conditions, the proportion of small cells (less than or equal to $60 \mu\text{m}^2$) accounted for 48% of the total, and medium cells (less than or equal to $90 \mu\text{m}^2$), 43%. Together, these two groups accounted for more than 90% of circulating cells. The nature of the distribution curves changed slightly during the first period of the experiment. By the 30th day, based on the histograms of lymphocyte area, a shift in the apex was observed to the left, which was attributed to an increase in the proportion of larger cells within the overall population. The mean cell area did not statistically significantly change (Fig. 1).

On the 45th day, there was a slight modification to the shape of the histogram for the distribution. The curve for the lymphocyte region shifted towards larger values ($73 \mu\text{m}^2$), and the histogram became more symmetrical. This change in the proportion of cell fractions based on area led to an increase in the average size of lymphocytes. The proportion of medium-sized cells (between 75 and $90 \mu\text{m}^2$) was greater than 50% at this time, compared to other periods where the proportion of these cells did not exceed 43%. It should be noted that during this time, the number of lymphocytes in circulation increased (Table 1).

The study of intracellular parameters throughout the experiment revealed that the cell's area occupied by the nucleus increased significantly compared to the control group (Table 1). Conversely, the dynamics of the cytoplasmic area showed a decreasing trend starting from the 10th day, and in subsequent stages, the average cytoplasmic area of lymphocytes was significantly lower than in the control group. On the 10th day, it decreased by 35%, on the 20th day by 50%, on the 30th day by 30%, and on the 45th day by 25%. At the 60-day mark, it was still lower by 35% compared to the initial value. This decrease in cytoplasmic area, as evidenced by a comparison of nuclear-cytoplasmic ratios, occurred against a background of increased nuclear proportion, with the overall cell area remaining unchanged. The exception to this pattern was on the 45th day, when a maximum value of total cell surface area was recorded. This was due to a significant increase in nuclear area, compared to both the control and earlier study periods. Specifically, on the 10th, 20th, and 30th days, there were increases in 9, 18, and 7%, respectively. However, on the 45th and 60th days, the increases were in 23 and 9%.

The particular interest was an analysis of parameters that characterize the optical properties of cytoplasm and nuclei (Table 2).

Table 1

Rat's lymphocyte counts under the influence of copper-zinc pyrite ore, Me (Q1; Q3)

Indicators	Control group	Experimental group 10 days	Experimental group 20 days	Experimental group 30 days	Experimental group 45 days	Experimental group 60 days
Number of lymphocytes ($\times 10^9$ cells/l)	10,35 (9,00;12,40)	14,45 (10,75;17,90)*	11,30 (10,40;14,10)	12,10 (10,70;14,50)	16,70 (9,70;18,70)*	13,40 (10,10;16,40) *
The average area of lymphocytes, μm^2	64,00 (51,00;78,00)	63,00 (50,00;75,00)	62,00 (48,00;78,00)	62,00 (50,00;77,00)	72,00 (59,00;85,00) * Δ	61,00 (53,00;73,00)
The average area of the cytoplasm, μm^2	19,00 (13,00;26,00)	12,00 (8,00;18,00)*	09,00 (4,00;17,00)* Δ	13,00 (9,00;24,00)* $\blacksquare$	14,00 (9,00;24,00)* $\blacksquare$	12,00 (6,00;19,00)* $\blacksquare$
Average core area, μm^2	43,00 (34,00;52,00)	47,00 (36,00;58,00)*	51,00 (39,00;64,00)* Δ	46,00 (37,00;54,00)* $\blacksquare$	53,00 (43,00;65,00)* Δ $\blacksquare$	47,00 (41,00;57,00)*
The nuclear-cytoplasmic relationship, conventional units	2,12 (1,61;2,85)	3,53 (2,26;5,43)*	5,11 (2,81;10,32)* Δ	2,99 (1,80;4,32) * Δ $\blacksquare$	3,64 (2,07;6,26) * $\blacksquare$	3,71 (2,19;7,79) * $\blacksquare$ $\bullet$

Note: * — statistically significant difference in the indicator of the experimental group in relation to the value of the control group of rats ($p < 0.05$); Δ — to the value of the 10-day experimental group of rats ($p < 0.05$); $\blacksquare$ — to the value of the 20-day experimental group of rats ($p < 0.05$); $\bullet$ — to the value of the 30-day experimental group of rats ($p < 0.05$); Δ — to the value of the 45-day experimental group of rats ($p < 0.05$).



The informative value of studying optical properties lies in the fact that they reflect the peculiarities of the course of metabolism in the studied cells in normal and pathological processes. The revealed decrease of the optical density of the cytoplasm during the experiment compared with the control was indicate a decrease in viscosity of the cytoplasmic matrix (Table 2). At the same time, a direct correlation was established between total optical density and area of cytoplasm ($r=0,57$ in control, $r=0,56$ on 10th day, $r=0,52$ on 20th day, $r=0,69$ on 30th day, $r=0,59$ on 45th day, $r=0,77$ on 60th day). The value of the refractive index directly depends on the functional state of intracellular structures, it can be assumed that the decrease in area and optical density of cytoplasm observed during experiment compared to control was due to decrease in its functional activity under influence of ore [8]. On the 10th day, decrease in cytoplasmic area was 35% and specific total optical density decreased in 27.5%. On the 20th, 30th and 45th days, decrease was 50, 30 and 25%, respectively. On 60th day it was 35%.

Increase in nucleus size was combined with decrease in optical density in all spectral ranges during all periods of experiment (Table 2).

DISCUSSION

The study showed that intoxication of rats caused by exposure to copper-zinc pyrite ore was accompanied by an increase in the number of lymphocytes and changes in their morphometric and optical parameters. In the control group, the main proportion of circulating cells consisted of small and medium-sized lymphocytes, which corresponded

to information from literature sources [9]. On days 30th and 45th of the experiment, the population of lymphocyte was redistributed with an increase in proportion of larger cells combined on the 45th day with an increase in their number and nucleus size. This allowed us to assume that lymphocytes entering circulation were replenished with cells with enlarged nuclei. According to Davydkin I.L. and Semenov V.F., replenishment of population with larger cells could be due to immature thymocytes and natural killer cells [9, 10]. Intrapopulation rearrangement of lymphocytes and the appearance of groups of cells with different areas may indicate the development of an immune response to the effects of toxic substances in ore [1]. The study of intracellular components has made it possible to clarify information about the nature of these processes. Dynamic and objective indicators of cell state are size and optical density of nucleus [11]. It is known that size and shape of nucleus are determined not by amount of DNA but by modification of chromatin [11], and increase in area of nucleus is due to conversion of heterochromatin to euchromatin [12]. Therefore, increase in nuclear area and change in optical properties throughout study period can be considered as reflection of change in chromatin density due to transformation of inactive heterochromatin into active euchromatin. At the same time, the maximum activity of the nucleus occurred on the 45th day, manifested in the minimum optical density in the largest size of the nucleus and the cell as a whole.

Along with an increase in the size of the nucleus, a decrease in the optical density and area of the cytoplasm occurred under the action of the copper-zinc pyrite ore. At the same time, a positive correlation between these indicators

Table 2

Optical parameters of rat's lymphocytes under the influence of copper-zinc pyrite ore, Me (Q1; Q3)

Indicators	Control group	Experimental group 10 days	Experimental group 20 days	Experimental group 30 days	Experimental group 45 days	Experimental group 60 days
Integral optical density of the cytoplasm, conventional units	0,38 (0,26;0,50)	0,17 (0,12;0,28)*	0,12 (0,05;0,20)* Δ	0,30 (0,16;0,48)* Δ■	0,22 (0,12;0,36)* ■●	0,16 (0,07;0,25)* ●▲
The specific total optical density of the cytoplasm, conventional units	1,19 (0,96;1,47)	0,86* (0,74;1,01)	0,81* (0,64;1,02)	1,06* Δ ■ (0,81;1,62)	1,03* Δ ■ (0,79;1,29)	0,77* Δ ●▲ (0,61;0,97)
Specific optical density of the core according to the red component, conventional units	1,27 (1,06;1,51)	0,91* (0,76;1,14)	0,73* Δ (0,59;0,94)	1,04* Δ ■ (0,82;1,28)	0,70* Δ ● (0,62;0,83)	0,73* Δ ● (0,58;0,83)
Specific optical density of the core according to the green component, conventional units	1,73 (1,33;2,09)	0,81* (0,68; 0,99)	0,58* Δ (0,49;0,75)	1,33* Δ ■ (0,93;1,89)	0,55* Δ ● (0,47;0,66)	0,70* Δ ■ ●▲ (0,57;0,85)
Specific optical density of the core according to the blue component, conventional units	0,46 (0,32;0,60)	0,15* (0,12;0,20)	0,10* Δ (0,07;0,14)	0,37* Δ ■ (0,17;0,57)	0,09* Δ ● (0,06;0,13)	0,14* Δ ■ ●▲ (0,11;0,18)

Note: notation as in Table 1.



was revealed. Considering that the value of the refractive index directly depends on the concentration of chemical components of the intracellular substance and the state of cellular organoids, it can be assumed that the functional state of cytoplasmic structures and metabolic processes decreases during ore intoxication.

CONCLUSIONS

Based on the assumption that morphometric parameters objectively reflect the functional state of lymphocytes, we can discuss the restructuring of the cellular components of the immune system under the influence of copper-zinc pyrite ore. Upon activation of a cell, the structural organization of chromatin undergoes conformational changes, resulting in changes to its optical properties [13, 14]. As a result, the experimentally observed increase in nuclear size, combined with a decrease in optical density, may indicate changes in the degree of chromatin condensation due to copper-zinc pyrite ore, and, consequently, an increase in DNA activity [11, 15].

The observed changes in the size and optical characteristics of the nucleus are accompanied by a decrease in metabolic activity in the cytoplasm. As a result, structural and functional alterations in the lymphocyte population, aimed at the body's adaptation to the effects of copper-zinc pyrite ore, impact the nuclear apparatus but do not occur at the level of cytoplasmic processes.

ADDITIONAL INFORMATION

Author contribution. Thereby, all authors made a substantial contribution to the conception of the study, acquisition, analysis, interpretation of data for the work, drafting and revising the article, final approval of the version to be published and agree to be accountable for all aspects of the study.

Competing interests. The authors declare that there is no conflict of interest.

Funding source. The study had no sponsorship.

Ethics approval. The study was conducted in compliance with the "Rules of work using experimental animals". The study was approved by the local Ethics Committee of the Bashkir State University of the Ministry of Health of the Russian Federation, Protocol No. 5 dated 09/13/2017.

ДОПОЛНИТЕЛЬНАЯ ИНФОРМАЦИЯ

Вклад авторов. Все авторы внесли существенный вклад в разработку концепции, проведение исследования и подготовку статьи, прочли и одобрили финальную версию перед публикацией.

Конфликт интересов. Авторы заявляют об отсутствии конфликта интересов.

Источник финансирования. Исследование не имело спонсорской поддержки.

Этическое утверждение. Исследование проведено с соблюдением «Правил проведения работ с использованием экспериментальных животных». Исследование одобрено локальным этическим комитетом ФГБОУ ВО «Башкирский государственный университет» Минздрава России, протокол № 5 от 13.09.2017 г.

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UDC 616.31-001.17
DOI: 10.56871/RBR.2024.72.96.005

INJECTION USE OF PLATELET RICH PLASMA IN THE TREATMENT OF BORDERLINE SKIN BURNS

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For citation: Zinoviev EV, Derii EK, Kostyakov DV, Alekseev AA, Manukovskiy VA, Filimonov KA, Hromina SS. Injection use of platelet rich plasma in the treatment of borderline skin burns. Russian Biomedical Research. 2024;9(4):30–37. DOI: <https://doi.org/10.56871/RBR.2024.72.96.005>

Received: 04.09.2024

Revised: 21.10.2024

Accepted: 17.12.2024

Abstract. Introduction. The use of platelet-rich plasma is a promising method for treating burn patients. Today, there are many publications devoted to autodermoplasty in combination with the patient's blood plasma for deep skin burns, but less attention has been paid to the problem of borderline lesions. **Objective of the study** — to evaluate the improvement in the treatment efficacy of burn victims with borderline burns using platelet-rich plasma. **Materials and methods.** The work demonstrates the results of treatment of 40 patients with borderline skin burns, aged from 18 to 59 years, hospitalized at the State Budgetary Institution of St. Petersburg Research Institute of Emergency Medicine named after. I.I. Janelidze in the period from 2021 to 2023. The criterion for inclusion in the study was the area of a second degree burn wound according to ICD 10, with a total area of up to 15% of the body surface. The results of treatment with platelet-rich plasma were assessed on 2% of the area, which averaged 327.6 ± 15.2 cm². During the work, clinical, planimetric, cytological and histological research methods were used. **Results.** Our proposed method of a single injection of platelet-rich plasma into the area of a border burn wound made it possible to accelerate the time for the onset of epithelization by 19.2% ($p < 0.05$), the time for final healing of the wound by 25.1% ($p < 0.05$), and also reduce the incidence of infectious complications by 15% ($p < 0.05$). The obtained clinical and planimetric data were confirmed by cytological and histological studies. In fingerprint smears, by the twelfth day of observation, the number of neutrophils decreased by 33.7% ($p < 0.05$) and the number of fibroblasts and macrophages increased by 41.4% ($p < 0.05$) and 29.3% ($p < 0.05$) respectively. During the histological study, it was noted that the patients in the study group had less pronounced leukocyte infiltration, swelling of the dermis, and a more clearly formed collagen framework. **Conclusion.** The use of platelet-rich plasma makes it possible to achieve earlier relief of the inflammatory reaction and ensure an earlier transition to the regenerative phase of the wound process in the area of a border burn wound.

Keywords: burns, borderline burns, blood plasma, platelet-rich plasma, inflammation, regeneration

ИНЪЕКЦИОННОЕ ПРИМЕНЕНИЕ ОБОГАЩЕННОЙ ТРОМБОЦИТАМИ ПЛАЗМЫ ПРИ ЛЕЧЕНИИ ПОГРАНИЧНЫХ ОЖОГОВ КОЖИ

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Для цитирования: Зиновьев Е.В., Дерий Э.К., Костяков Д.В., Алексеев А.А., Мануковский В.А., Филимонов К.А., Хромина С.С. Инъекционное применение обогащенной тромбоцитами плазмы при лечении пограничных ожогов кожи. Российские биомедицинские исследования. 2024;9(4):30–37. DOI: <https://doi.org/10.56871/RBR.2024.72.96.005>

Поступила: 04.09.2024

Одобрена: 21.10.2024

Принята к печати: 17.12.2024

Резюме. Введение. Использование обогащенной тромбоцитами плазмы является перспективным методом лечения обожженных. На сегодняшний день существует множество публикаций, посвященных выполнению аутодермопластики в сочетании с плазмой крови пациента при глубоких ожогах кожи, однако меньше внимания уделено проблеме пограничных поражений. **Цель исследования** — оценить повышение эффективности лечения обожженных с пограничными ожогами с использованием плазмы, обогащенной тромбоцитами. **Материалы и методы.** В работе продемонстрированы результаты лечения 40 пациентов в возрасте от 18 до 59 лет с пограничными ожогами кожи, госпитализированных в ГБУ СПб НИИ СП им. И.И. Джанелидзе в период с 2021 по 2023 гг. Критерием включения в исследование было определение площади ожоговой раны II степени по МКБ-10 общей площадью до 15% поверхности тела. Результаты лечения плазмой, обогащенной тромбоцитами, оценивали на 2% площади, что в среднем составляло 327,6±15,2 см². В ходе выполнения работы были использованы клинический, планиметрический, цитологический и гистологический методы исследования. **Результаты.** Предложенный нами способ однократного инъекционного введения обогащенной тромбоцитами плазмы в область пограничной ожоговой раны позволил ускорить сроки начала эпителизации на 19,2% ($p < 0,05$), сроки окончательного приживления раны на 25,1% ($p < 0,05$), а также снизить частоту развития инфекционных осложнений на 15% ($p < 0,05$). Полученные клинические и планиметрические данные были подтверждены цитологическим и гистологическим исследованиями. В мазках-отпечатках к 12-м суткам наблюдения снизилось число нейтрофилов на 33,7% ($p < 0,05$) и увеличилось число фибробластов и макрофагов на 41,4% ($p < 0,05$) и 29,3% ($p < 0,05$) соответственно. В ходе проведения гистологического исследования было отмечено, что у пациентов исследуемой группы была менее выражена лейкоцитарная инфильтрация, отек дермы и более отчетливо сформирован коллагеновый каркас. **Заключение.** Использование обогащенной тромбоцитами плазмы позволяет достигнуть более раннего купирования воспалительной реакции и сократить длительность перехода к регенераторной фазе раневого процесса в области пограничной ожоговой раны.

Ключевые слова: ожоги, пограничные ожоги, плазма крови, обогащенная тромбоцитами плазма, воспаление, регенерация

INTRODUCTION

Human blood has been used for therapeutic purposes for more than a hundred years. In 1898, Swedish physicians Grafstrom and Elfstrom injected autologous blood in a salt solution to treat pneumonia and tuberculosis for the first time [5]. Subsequently, blood and its components were repeatedly used in the treatment of patients with acute and chronic diseases [4].

Among all variants of blood products use, plasma is of special importance in the context of wound defects treat-

ment, which is its liquid part containing form elements and tissue factors [6]. If we consider plasma therapy from the position of regenerative medicine, the most effective option is the use of platelet-rich plasma (PRP). In 2003, R.R. Akhmerov and R.F. Zarudiy developed a technique for obtaining platelet-rich plasma. Zarudiy developed a technique for obtaining this biological medication [3]. Subsequently, the technique became widespread and was actively used in clinical practice.

The main regenerative components contained in PRP include: transforming growth factor beta (TGF-β),

platelet-derived epidermal growth factor (PDEGF), vascular endothelial growth factor (VEGF), insulin-like growth factor 1 (IGF-1), fibroblast growth factor (FGF), and epidermal growth factor (EGF) [3]. Such an optimal composition of biological compounds forms favorable conditions for organ and tissue regeneration.

The use of PRP deserves special attention in burn patients. According to studies conducted under the guidance of V.G. Bogdan et al., PRP in combination with autodermoplasty increases the area of complete engraftment of the transplanted skin graft by more than 13% [1]. A team of authors from the I.I. Janelidze Research Institute of Emergency Medicine obtained similar data. They proved that the rate of regeneration significantly increases when PRP is combined with the transplantation of a perforated skin autoderm graft [2].

Notwithstanding a substantial number of scientific papers devoted to the treatment of deep burns by autodermoplasty combined with PRP, the problem of stimulation of borderline burn recovery has remained unresolved.

AIM

To evaluate the effectiveness of treatment in patients with borderline skin burns using PRP injections into the affected derma.

MATERIALS AND METHODS

The work is based on the analysis of treatment results in 40 patients with borderline skin burns, aged from 18 to 59 years, hospitalized at the I.I. Janelidze St. Petersburg Research Institute of Emergency Medicine in the period 2021-2023. The following parameters were chosen as inclusion criteria: age from 18 to 59 years, total area of borderline skin burns up to 15%. Exclusion criteria were also determined: patient's refusal to use platelet-rich autoplasm, oncological diseases detected in the last 5 years, pregnancy or breastfeeding, patient's intake of immunosuppressive drugs, confirmed carriage of HIV, syphilis, hepatitis B or C. Burned patients were divided into two groups. The first (control) group consisted of patients whose borderline burns were treated in accordance with the methods generally accepted in combustiology (ointment dressings with Levomekol water-soluble ointment and atraumatic wound coverings Activtex (Altex LLC, Russia)). The experimental group consisted of patients who received single injection of PRP in the amount of 2.8 ml for 1% of the border burn area on 5.9 ± 1.2 days of standard conservative treat-

ment. The mean age of patients in the control group was 35.3 ± 11.08 years, the area of burn wounds was $5.9 \pm 2.8\%$. The mean age of patients in the experimental group was 39.8 ± 9.55 years, the burn wound area in the group was $6.35 \pm 2.78\%$.

The research was approved by the local ethical committee of the I.I. Dzhanelidze St. Petersburg Research Institute of Emergency Medicine, protocol No. 1-8 of 10.10.2020. All patients signed an additional voluntary informed consent for treatment with PRP.

Effectiveness of the treatment was evaluated on burn areas covering about 2% of the body area, i.e. 327.6 ± 15.2 cm² on average. Clinical (daily examination, photofixation, control of the nature of detachment, epithelialization and graft healing) and planimetric methods were used in the research. The latter was performed according to the original method (patent of the Russian Federation No. 2798225 dated 03.08.2022). The depth of a burn wound was estimated by checking a vascular reaction and pain sensitivity. Features of reparative processes were profoundly analyzed by cytological and morphological methods. A cytological method was used to take swabs from the surface of burn wounds before treatment, as well as on the 3rd and 12th day. Skin biopsies were taken on the 3rd day after a single injection of PRP into the area of a border burn wound.

PRP was produced according to the following procedure (Fig. 1). At first, 1 ml of sodium citrate is drawn into a 10 ml syringe (Fig. 1, a), then 10 ml of the patient's whole venous blood is drawn into the same syringe (Fig. 1, b). The syringe is stirred by progressive movements and then transferred to a special tube (Fig. 1, c), which is centrifuged for 10 minutes at a speed of 2600 spins per minute. 4 layers are formed after this manipulation (Fig. 1, d): a — platelet-poor plasma; b — platelet-rich plasma; c — leucocyte film; d — erythrocyte suspension. Platelet-poor plasma was removed and was not used in present research. We transferred platelet-rich plasma (Fig. 1, e) and leucocyte film into a regular syringe for easier use (Fig. 1, f).

On average, we obtained 2.3 ± 0.2 ml of PRP out of 10 ml of whole venous blood. To determine the number of platelets in the final product, Sysmex KX-21N hematology analyzer (Japan) was used. Their average concentration was $1.043 \pm 41.7 \times 10^6$ cells/ μ l.

Statistical data were analyzed by STATISTICA 12.6 for Windows, as well as MS Excel. The nonparametric Mann-Whitney test was applied to compare quantitative indices in the studied groups, and Pearson's χ^2 test was used to compare frequency indices. An alternative hypothesis was accepted at $p < 0.05$.

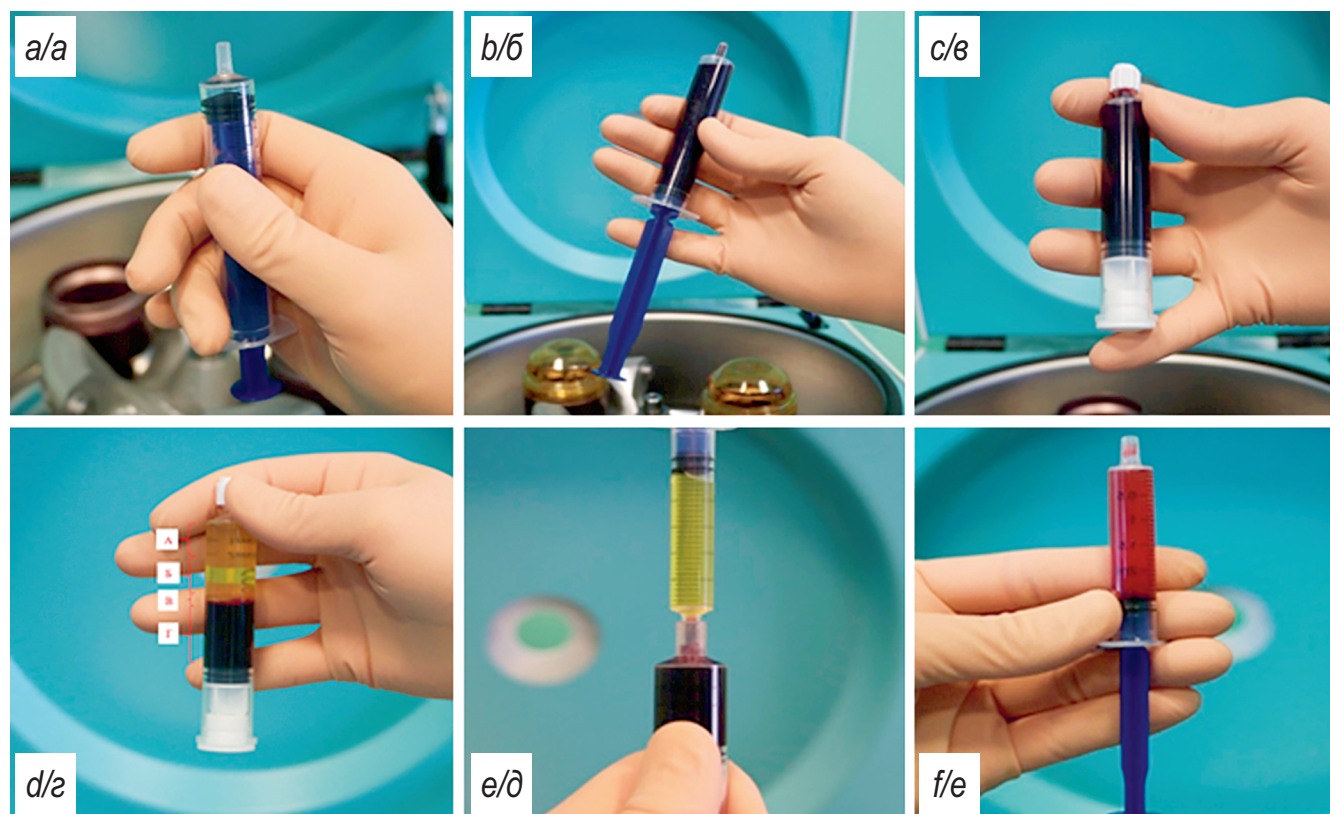


Fig. 1. Stages of obtaining platelet-rich autoplasm (explanations in the text)

Рис. 1. Этапы получения аутоплазмы, обогащенной тромбоцитами (пояснения в тексте)

Table 1

Features of the phases of the wound process taking into account a single injection of autoplasm enriched with platelets

Таблица 1

Особенности фаз раневого процесса с учетом однократного инъекционного введения аутоплазмы, обогащенной тромбоцитами

Группа наблюдения / Observation group	Средняя продолжительность периода (M±m), сутки / Average duration of the period (M±m), days			
	сосудистой реакции / vascular reaction	очистения раны / wound cleansing	начала эпителизации / beginning of epithelialization	окончательного заживления / final healing
Контрольная / Control	4,9±0,7	6,2±1,1	7,8±1,8	24,3±1,2
Исследуемая / Under study	4,7±0,4	5,9±1,2	6,3±1,4*	18,2±1,1*

Note: Mann-Whitney U test: * p < 0.05 compared to the control group.

Примечание: критерий U Манна-Уитни: * p < 0,05 по сравнению с контрольной группой.

RESULTS AND DISCUSSION

At stage 1 the duration of wound healing phases was assessed according to M.I. Kuzin (Table 1).

According to the results presented in Table 1, there were no significant differences in the timing and duration of a vascular reaction and wound cleansing, since PRP injection was carried out only after a wound had been cleaned. However, it was ascertained that the time of epi-

thelialization initiation in the experimental group reduced by 19.2% (p < 0.05). At the same time, final healing time of a border burn wound also decreased by 25.1% (p < 0.05).

Frequency of infectious complications was assessed next. The results presented in Figure 2 show that a single injection of platelet-rich autoplasm into the area of a border burn wound reduced the incidence of infectious complications by 15% (p < 0.05).

Частота осложнений /
Frequency of complications, %



Fig. 2. Frequency of wound infection in borderline burns taking into account the introduction of platelet-rich autoplasm

Рис. 2. Частота раневой инфекции при пограничных ожогах с учетом введения аутоплазмы, обогащенной тромбоцитами

Planimetric evaluation of a healing rate was one of the most important indicators in our work (Fig. 3).

The obtained data are presented in Figure 3. It allows us to conclude that a single injection of platelet-enriched autoplasm starting from the 5th day after the injection significantly accelerates epithelization of a border burn wound. Thus, by the 15th day it allows to reduce a wound

area by 3.7 times ($p < 0.05$) in comparison with the controls.

A cytological research of smears-prints before treatment, on the 3rd and 12th day after the beginning of treatment was carried out to confirm the obtained clinical data. Comparative data presented in Table 2 allow us to conclude that a single injection of platelet-enriched autoplasm on 5.9 ± 1.2 days after the burn allows to reduce the number of neutrophils by 18.8% by the 3rd day after the injection as well as to lower the content of neutrophil cells by 33.7% ($p < 0.05$) by the 12th day after the injection in comparison with the control group.

In addition, a reliable increase in the number of fibroblasts by the 12th day by 41.4% ($p < 0.05$) was observed ($p < 0.05$). The number of macrophages also showed a 29.3% growth ($p < 0.05$). When analyzing the percentage of lymphocytes, no significant dynamics and differences were found.

In order to confirm clinical, planimetric and cytological data, it was decided to perform histological examination of skin biopsy samples in both groups on the 3rd day after treatment (9th day from the moment of injury). When examining skin biopsy specimens with hematoxylin-eosin staining it is possible to conclude that neutrophilic and leukocytic infiltration and dermal edema were more pronounced in controls (Fig. 4).

To objectify a regenerative component of derma, Picro-Mallory staining was performed (Fig. 5).

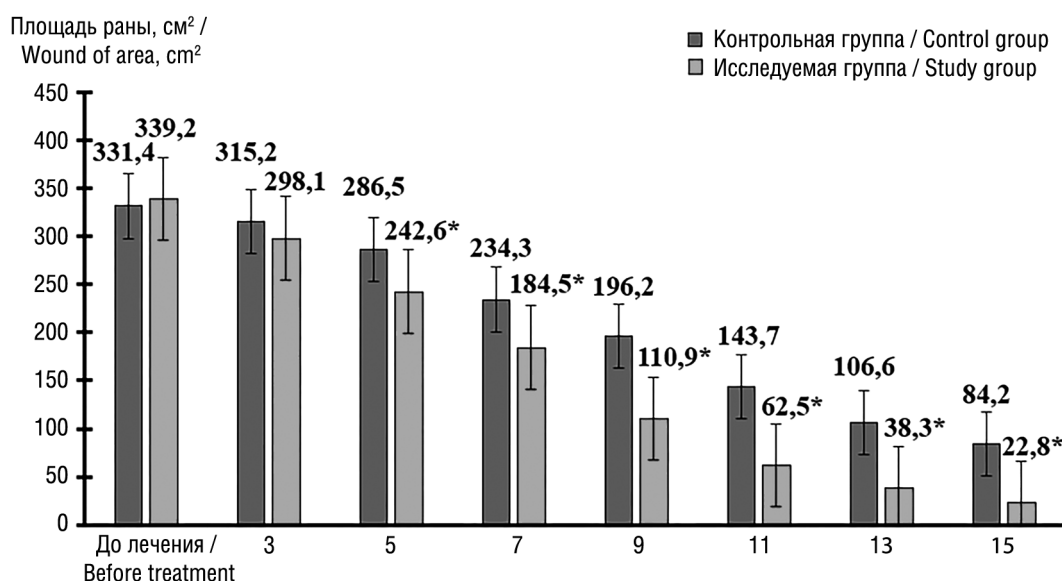


Fig. 3. Planimetric assessment of the healing dynamics of borderline burn wounds taking into account the introduction of autologous plasma enriched with platelets

Рис. 3. Планиметрическая оценка динамики заживления пограничных ожоговых ран с учетом введения аутоплазмы, обогащенной тромбоцитами

Table 2

Cytological picture of borderline burns taking into account the introduction of autoplasm enriched with platelets

Таблица 2

Цитологическая картина пограничных ожогов с учетом введения аутоплазмы, обогащенной тромбоцитами

Анализируемые параметры / Analyzed parameters	Содержание (M±m) в мазке-отпечатке, в срок (сутки)/% / Content (M±m) in smear-print, within a period (day)/%					
	контрольная группа / control group			исследуемая группа / study group		
	до начала лечения / before treatment	3-и	12-е	до начала лечения / before treatment	3-и	12-е
Нейтрофилы / Neutrophils	67,2±4,4	39,2±3,5	18,7±1,3	69,4±5,2	31,8±4,6	12,4±1,3*
Фibroбласты / Fibroblasts	2,2±0,5	2,9±1,2	22,4±1,9	2,3±0,6	3,7±1,1	31,1±2,2*
Макрофаги / Macrophages	12,3±2,1	13,8±1,4	20,3±1,9	13,5±2,7	15,3±1,2	28,7±2,1*
Лимфоциты / Lymphocytes	2,9±1,1	2,5±0,7	2,3±1,2	3,1±1,1	2,9±1,3	2,6±1,3

Note: Mann–Whitney U test: * p <0.05 compared to the control group.
Примечание: критерий U Манна–Уитни: * p <0,05 по сравнению с контрольной группой.

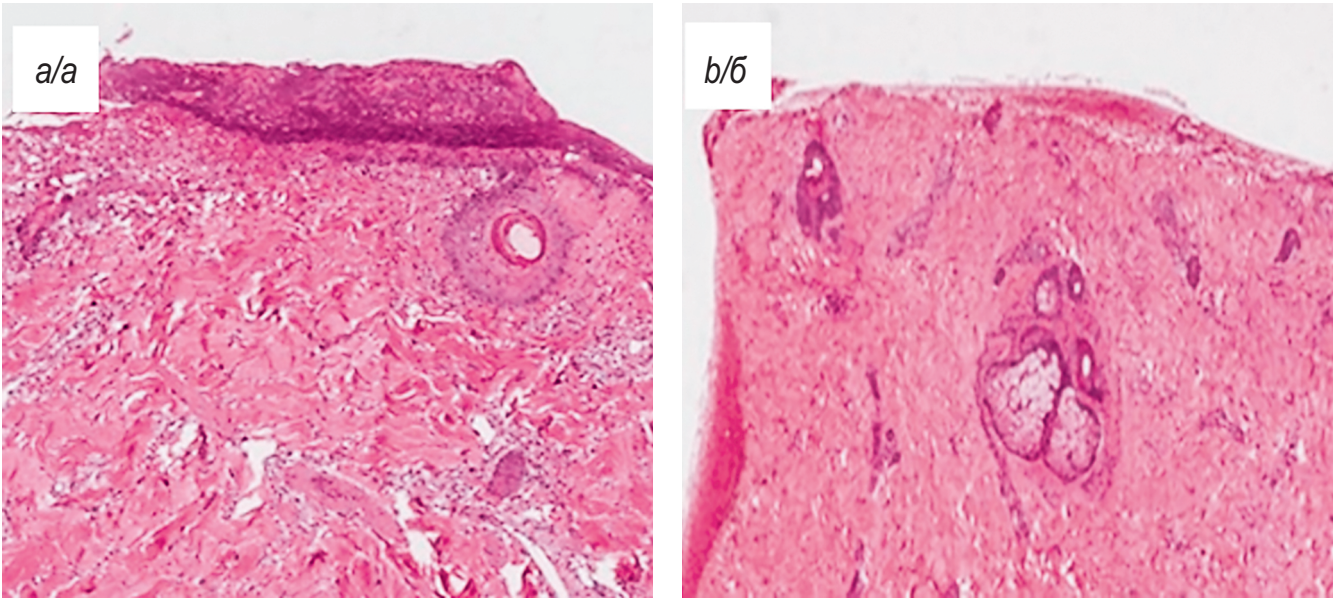


Fig. 4. Patients' skin on the 10th day after receiving a burn: a — without the introduction of autoplasm enriched with platelets; b — against the background of the injection of autoplasm enriched with platelets. Hematoxylin–eosin staining, ×100
Рис. 4. Кожа пациентов на 10-е сутки после получения ожога: а — без введения аутоплазмы, обогащенной тромбоцитами; б — на фоне инъекционного введения аутоплазмы, обогащенной тромбоцитами. Окраска гематоксилином–эозином, ×100

Skin biopsy specimens in the comparison group had a poorly developed collagen frame and no fibrin, which indicates less intensive reparative processes.

CONCLUSION

1. A single injection of PRP in combination with conservative treatment of borderline skin burns allowed to accelerate

terms of epithelialization on 19,2% (p <0,05), final wound healing on 25,1% (p <0,05), as well as to reduce the frequency of infectious complications on 15% (p <0,05).

2. The results of cytological and histological examinations confirm the clinical data indicating a decrease in the severity of inflammatory processes, as well as stimulation of regeneration in a border burn zone against the background of PRP administration. By the 12th day of observation, the

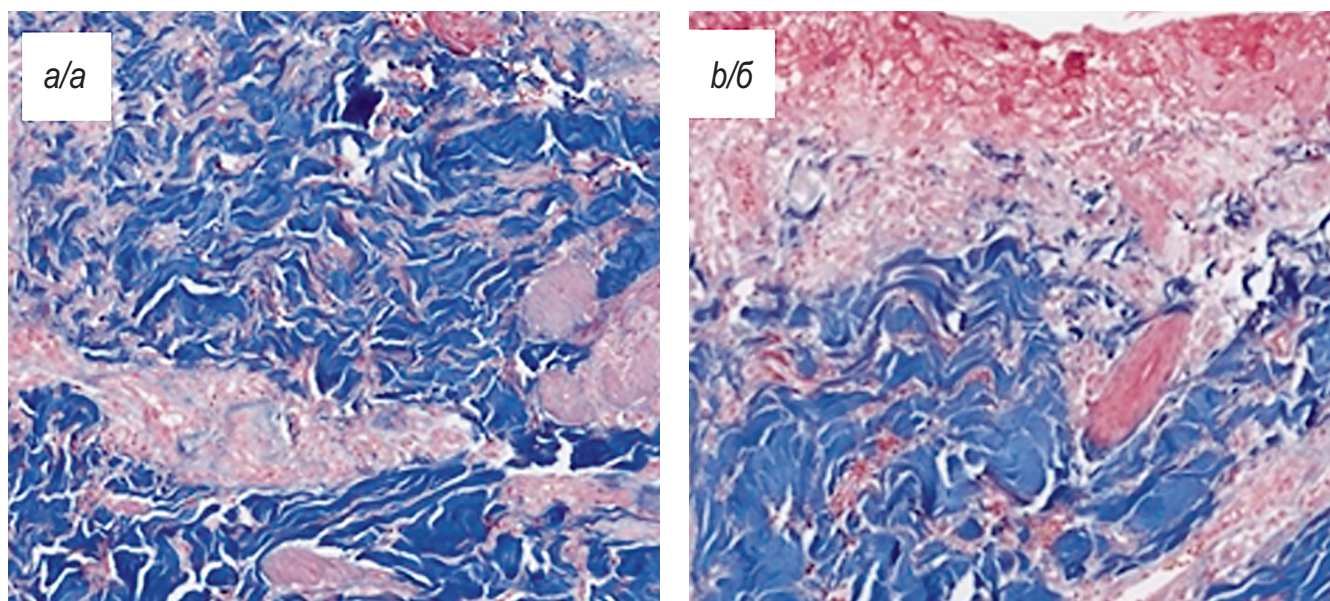


Fig. 5. Patients' skin on the 9th day after injury: *a* — without the introduction of platelet-rich autoplasm; *b* — against the background of the injection of platelet-rich autoplasm. Picro–Mallory staining, $\times 100$

Рис. 5. Кожа пациентов на 9-е сутки после получения травмы: *а* — без введения аутоплазмы, обогащенной тромбоцитами; *б* — на фоне инъекционного введения аутоплазмы, обогащенной тромбоцитами. Окраска Пикро–Маллори, $\times 100$

number of neutrophils decreased by 33.7% ($p < 0.05$) and the number of fibroblasts and macrophages increased by 41.4% ($p < 0.05$) and 29.3% ($p < 0.05$) respectively.

3. A single injection of PRP allows to stop an inflammatory reaction in the area of borderline burn wounds and accelerate a regenerative phase of a wound process, which, in turn, reduces the time of final skin recovery.

ADDITIONAL INFORMATION

Author contribution. Thereby, all authors made a substantial contribution to the conception of the study, acquisition, analysis, interpretation of data for the work, drafting and revising the article, final approval of the version to be published and agree to be accountable for all aspects of the study.

Competing interests. The authors declare that they have no competing interests.

Funding source. This study was not supported by any external sources of funding.

Consent for publication. Written consent was obtained from the patient for publication of relevant medical information within the manuscript.

ДОПОЛНИТЕЛЬНАЯ ИНФОРМАЦИЯ

Вклад авторов. Все авторы внесли существенный вклад в разработку концепции, проведение исследования

и подготовку статьи, прочли и одобрили финальную версию перед публикацией.

Конфликт интересов. Авторы декларируют отсутствие явных и потенциальных конфликтов интересов, связанных с публикацией настоящей статьи.

Источник финансирования. Авторы заявляют об отсутствии внешнего финансирования при проведении исследования.

Информированное согласие на публикацию. Авторы получили письменное согласие пациентов на публикацию медицинских данных.

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UDC 616.716.3-009
DOI: 10.56871/RBR.2024.85.46.006

CHARACTERISTICS OF THE TASTE SENSITIVITY OF THE TONGUE IN ELDERLY PEOPLE WHO HAVE SUFFERED COVID-19

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For citation: Shvetsov MM, Iordanishvili AK. Characteristics of the taste sensitivity of the tongue in elderly people who have suffered COVID-19. Russian Biomedical Research. 2024;9(4):38–43. DOI: <https://doi.org/10.56871/RBR.2024.85.46.006>

Received: 02.10.2024

Revised: 14.11.2024

Accepted: 17.12.2024

Abstract. Introduction. Many patients who have had COVID-19 report taste disorders that occur during the height of the disease, and sometimes persist for a certain time after recovery. Therefore, the study of taste sensitivity indicators in older people who have suffered a new coronavirus infection COVID-19 seems relevant for understanding the pathophysiological processes occurring in the human body. **Purpose of the study:** was to study the characteristics of the taste sensitivity of the tongue in elderly people who have suffered a new coronavirus infection COVID-19, based on a study of the thresholds of taste sensitivity of the tongue and electrogustometry. **Materials and methods.** The thresholds of taste sensitivity of the tongue, as well as indicators of electrogustometry of the tongue, were studied in 89 elderly people, who were divided into 2 study groups. Group 1 included 37 patients without pronounced psychosomatic pathology who did not suffer from the new coronavirus infection COVID-19. The 2nd main group of the study included 52 patients who underwent COVID-19 6 to 9 months ago. The patients of the 2 groups were divided into 2 subgroups, taking into account the presence or absence of complaints of impaired taste sensitivity during the course of COVID-19 disease. **The results of the study.** It was found that people who had a new coronavirus infection COVID-19, regardless of whether they had complaints of taste sensitivity disorders during the disease or not, 6 to 9 months after the disease, they had no differences in electrogustometry indicators. In patients who did not complain of taste disorders during the COVID-19 period, only an increase in the threshold of taste sensitivity of the tongue to salty was noted in the post-ovoid period, while in patients who complained of taste disorders during the COVID-19 disease, there was a significant increase in the thresholds of taste sensitivity of the tongue to all types of stimuli, although such an indicator for gorky was within the reference values. **Conclusion.** The data obtained indicate the peculiarities of the functioning of the taste analyzer in people who have suffered a new coronavirus infection COVID-19, and also indicate that an increase in the thresholds of taste sensitivity of the tongue in elderly patients may hinder the formation of a feeling of satiety and contribute to maintaining the desire to eat during the day, leading to difficulties with the regulation of diet therapy, an important component of the complex treatment of various psychosomatic pathologies.

Keywords: elderly people, new coronavirus infection, COVID-19, consequences of a new coronavirus infection, oral cavity, tongue, taste sensitivity, electrogustometry, threshold of taste sensitivity of the tongue



ХАРАКТЕРИСТИКА ВКУСОВОЙ ЧУВСТВИТЕЛЬНОСТИ ЯЗЫКА У ПОЖИЛЫХ ЛЮДЕЙ, ПЕРЕНЕСШИХ COVID-19

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Для цитирования: Швецов М.М., Иорданишвили А.К. Характеристика вкусовой чувствительности языка у пожилых людей, перенесших COVID-19. Российские биомедицинские исследования. 2024;9(4):38–43. DOI: <https://doi.org/10.56871/RBR.2024.85.46.006>

Поступила: 02.10.2024

Одобрена: 14.11.2024

Принята к печати: 17.12.2024

РЕЗЮМЕ. Введение. Многие пациенты, переболевшие COVID-19, отмечают нарушения вкуса, которые наблюдаются в период разгара заболевания, а иногда сохраняются определенное время после выздоровления. Именно поэтому изучение показателей вкусовой чувствительности у людей старших возрастных групп, перенесших новую коронавирусную инфекцию COVID-19, представляется актуальным для понимания патофизиологических процессов, происходящих в организме человека. **Цель исследования** — изучить характеристику вкусовой чувствительности языка у пожилых людей, перенесших новую коронавирусную инфекцию COVID-19, на основании исследования порогов вкусовой чувствительности языка и электрогустометрии. **Материалы и методы.** Изучены пороги вкусовой чувствительности языка, а также показатели электрогустометрии языка у 89 людей пожилого возраста, которые были разделены на две группы исследования. В 1-ю группу вошли 37 пациентов без выраженной психосоматической патологии, которые не болели новой коронавирусной инфекцией COVID-19. Во 2-ю, основную, группу исследования вошли 52 пациента, которые 6–9 месяцев назад перенесли COVID-19. Пациентов 2-й группы разделили на две подгруппы с учетом наличия или отсутствия жалоб на нарушения вкусовой чувствительности в ходе болезни COVID-19. **Результаты исследования.** Установлено, что у людей, перенесших новую коронавирусную инфекцию COVID-19, независимо от того, имели ли они в ходе болезни жалобы на нарушения вкусовой чувствительности или нет, спустя 6–9 месяцев после болезни отсутствуют различия в показателях электрогустометрии. У пациентов, которые не предъявляли жалобы на нарушения вкуса в период COVID-19, в постковидный период отмечено только повышение порога вкусовой чувствительности языка на соленое, в то время как у пациентов, которые в период болезни COVID-19 жаловались на нарушения вкуса, отмечалось достоверное повышение порогов вкусовой чувствительности языка на все виды раздражителей, хотя такой показатель на горькое был в пределах референсных значений. **Заключение.** Полученные данные указывают на особенности функционирования вкусового анализатора у людей, перенесших новую коронавирусную инфекцию COVID-19, а также свидетельствуют, что повышение порогов вкусовой чувствительности языка у пожилых пациентов может препятствовать формированию чувства сытости и в течение суток способствовать сохранению желания употреблять пищу, приводя к сложностям с регулированием диетотерапии, важной составляющей комплексного лечения различной психосоматической патологии.

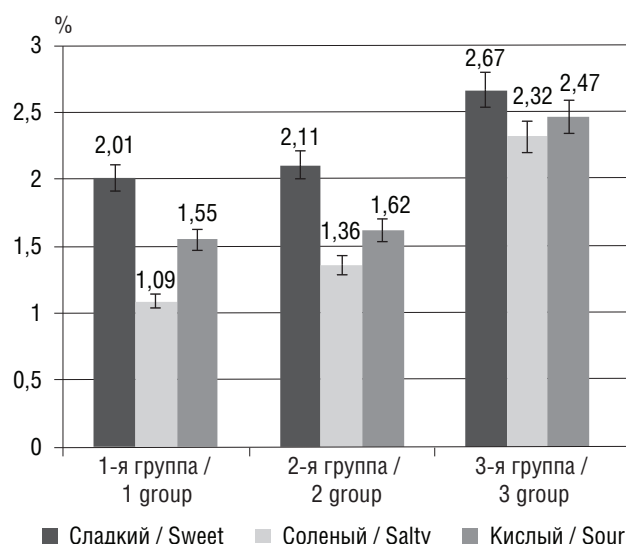
Ключевые слова: люди пожилого возраста, новая коронавирусная инфекция, COVID-19, последствия новой коронавирусной инфекции, полость рта, язык, вкусовая чувствительность, электрогустометрия, порог вкусовой чувствительности языка

INTRODUCTION

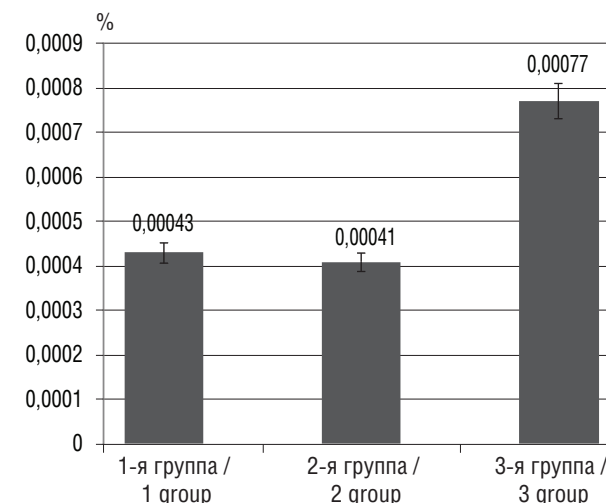
Currently, a new coronavirus infection (COVID-19) has become an integral part of people's life all over the world. COVID-19 emerged at the end of 2019, since then it has negatively affected the social life of society, as well as the health care system of almost all countries of the world [1,

2]. In recent years, domestic and foreign literature has provided diverse scientific information that people who suffered from COVID-19, regardless of a virus strain, have problems with organs and tissues of the masticatory apparatus, including the oral cavity [3, 4].

Hyposalemia, inflammatory periodontal pathology, cheilitis, stomatitis, candidiasis and hyperesthesia of teeth hard



a/a



b/b

Fig. 1. Indicators of taste sensitivity thresholds of the tongue for sweet, salty, sour (a) and bitter (b), % of the threshold solution of the irritant in the examined patients

Рис. 1. Показатели порогов вкусовой чувствительности языка на сладкое, соленое, кислое (а) и горькое (б), % порогового раствора раздражителя у обследованных пациентов

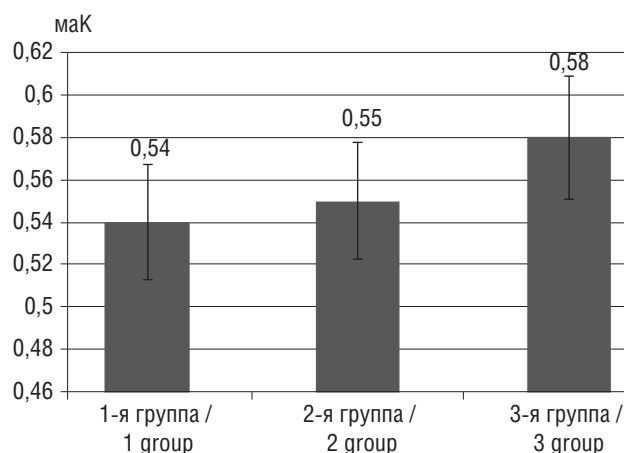


Fig. 2. Electrogustometry indicators in the examined patients, mАК

Рис. 2. Показатели электрогустометрии у обследованных пациентов, мАК

tissues are common in COVID-19 patients in the post-COVID period [5, 6]. Many patients who have survived COVID-19 note taste disturbances that are observed during the onset of the disease and sometimes persist for some time after recovery [7, 8]. These changes are especially characteristic in elderly and senile individuals [9]. That is why the study of taste sensitivity indicators in elderly people who have undergone a new COVID-19 coronavirus infection seems relevant for understanding the pathophysiological processes.

AIM

To investigate the characterization of tongue taste sensitivity in elderly people with new COVID-19 coronavirus infection, based on a study of tongue taste sensitivity thresholds and electro-gustometry.

MATERIALS AND METHODS

Clinical and physiological examination of tongue taste sensitivity thresholds of the tongue (TTST) as well as tongue electrogustometry indices were performed in 89 (28 men and 61 women) elderly people, who were divided into two study groups. The 1st, control group included 37 patients without significant psychosomatic pathology (12 men and 25 women aged 62 to 73 years), who had no new COVID-19 coronavirus infection. The 2nd, experimental group included 52 (16 men and 36 women aged 61 to 74 years) patients who had COVID-19 6 to 9 months ago. Group 2 patients were divided into two subgroups. Subgroup 2A consisted of 24 (5 males and 19 females) patients who reported impaired gustatory sensitivity during the course of the disease. Subgroup 2B consisted of 28 (11 males and 17 females) patients who did not have any changes in gustatory sensitivity after COVID-19. Patients of all groups did not suffer from endocrine pathology, did not undergo chemotherapeutic and radiation treatment due

to malignant neoplasms, as well as they did not suffer from any other diseases in decompensation stage.

Conventional methods of research were used, namely, thresholds of tongue gustatory sensitivity (TGS) for sweet, salty, sour and bitter stimuli were determined [10], and electrohustometry, i.e. determination of tongue sensitivity to direct electric current, was evaluated [11].

After the clinical study was completed, statistical evaluation of the obtained digital material was performed. The studied parameters are presented in the form of sample mean value and standard error of the mean value. Validity of differences between the mean values of independent samples was evaluated by means of parametric Student's criterion in case of normal distribution law and nonparametric Mann-Whitney criterion in case of deviation from normal distribution of indicators. The level of significance (p) was considered as achieved in all statistical analysis procedures; the critical level of significance was set at 0.05.

RESULTS AND DISCUSSION

According to literature and our findings, it is known that normally taste buds on the back of the tongue perceive 0.25–1.25% of sweet and salty solutions, 0.05–1.25% of acidic solutions and 0.0001–0.003% of bitter solutions [12, 13], while electrogustometry values are $0.35 \pm 0.08 \mu\text{A}$ [14]. An increase in TTST and electrogustometry indices increases with age, namely in elderly and old people, and the presence of any psychosomatic diseases adversely affects the above indices [15, 16]. This is especially evident in endocrine diseases, as well as after combined treatment of oropharyngeal tumors, more precisely, after chemotherapy and radiation therapy [17].

There were determined TTST rates in relatively healthy elderly people, as well as people of similar age who had a COVID-19 coronavirus infection and who did or did not experience impaired taste sensitivity during the course of the disease (Fig. 1).

Examination of TTST in patients of subgroup 2A revealed that sweet, sour, and bitter indices did not differ from each other ($p > 0.05$) and were similar to those determined in controls, while TTST for a salty taste was significantly higher. Taste sensitivity thresholds of the tongue in patients who had complaints of taste sensitivity disorders during COVID-19 (subgroup B) had a significant increase in sweet, sour, and bitter taste sensitivity thresholds ($p < 0.05$), although the bitter taste sensitivity thresholds did not exceed the reference values for an adult and could be considered physiologic, i.e. normal [18].

The study of tongue electrohustometry parameters showed that no significant differences were observed in all

groups of patients (Fig. 2), which may indicate the preserved physiologic sensitivity of tongue receptors. The average values of this index in patients of all examined groups ranged from 0.48 to 0.69 μA and amounted to $0.54 \pm 0.11 \mu\text{A}$.

The study of TTST and electrogustometry parameters confirmed the previously known facts that there is a slight increase of TTST parameters for all types of stimuli in elderly people, while the bitter sensitivity parameters remain within the reference values. It was reported that people who had a new COVID-19 coronavirus infection, regardless of whether they had complaints of taste sensitivity disorders during the disease or not, had no differences in electrogustometry indices 6–9 months after the disease. Those patients who did not complain about taste disturbances during COVID-19 showed only an increased TTST for salty in the post-CoVID-19 period, whereas patients who complained about taste disturbances showed a significant increase in TTST for all types of stimuli, with TTST for bitter being within reference values.

CONCLUSION

Summarizing the above, it should be concluded that elderly people who had a new COVID-19 coronavirus infection and complained about impaired taste sensitivity 6–9 months after the disease had objective evidence of increased TTST for all types of stimuli, with TTST for bitter stimuli being within reference values. Elderly people who had a new COVID-19 coronavirus infection and did not complain about taste sensitivity disorders had elevated TTST for salty stimuli. The obtained data allow us to characterize the peculiarities of the gustatory analyzer functioning in people who have undergone COVID-19, as well as to note that an increase in TTST may disturb a feeling of satiety. This usually preserves the desire to eat during the day, which may cause difficulties with diet regulation, especially in the complex treatment of various psychosomatic pathologies.

ADDITIONAL INFORMATION

Author contribution. Thereby, all authors made a substantial contribution to the conception of the study, acquisition, analysis, interpretation of data for the work, drafting and revising the article, final approval of the version to be published and agree to be accountable for all aspects of the study.

Competing interests. The authors declare that they have no competing interests.

Funding source. This study was not supported by any external sources of funding.

Consent for publication. Written consent was obtained from the patient for publication of relevant medical information within the manuscript.

ДОПОЛНИТЕЛЬНАЯ ИНФОРМАЦИЯ

Вклад авторов. Все авторы внесли существенный вклад в разработку концепции, проведение исследования и подготовку статьи, прочли и одобрили финальную версию перед публикацией.

Конфликт интересов. Авторы декларируют отсутствие явных и потенциальных конфликтов интересов, связанных с публикацией настоящей статьи.

Источник финансирования. Авторы заявляют об отсутствии внешнего финансирования при проведении исследования.

Информированное согласие на публикацию. Авторы получили письменное согласие пациентов на публикацию медицинских данных.

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UDC 616.31-001.17
DOI: 10.56871/RBR.2024.89.20.007

EFFECTIVENESS OF ANTI-SHOCK THERAPY IN THE TREATMENT OF EXTENSIVE BURNS IN CASE OF LONG-TERM COMPRESSION SYNDROME

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For citation: Sokolov NK, Zinoviev EV, Fistal EYa, Semiglazov AV, Derii EK, Sidelnikov von Essen VO, Kostyakova AV. Effectiveness of anti-shock therapy in the treatment of extensive burns in case of long-term compression syndrome. Russian Biomedical Research. 2024;9(4):44–47. DOI: <https://doi.org/10.56871/RBR.2024.89.20.007>

Received: 07.09.2024

Revised: 20.11.2024

Accepted: 17.12.2024

Abstract. The article analyzes the effectiveness of the use of crystalloid and colloid solutions, antihypoxants, antioxidants, and analgesics aimed at relieving the pathological processes of shock development in patients with extensive skin burns against the background of prolonged compartment syndrome. We conducted an experimental study that included 360 adult white outbred rats of both sexes, weighing 220–240 g, divided into groups depending on the treatment method. After modeling long-term compartment syndrome in animals, third-degree burns according to ICD-10 were reproduced, with a total area of 5, 10, 15, 20, 25, 30% of the body surface. The results were assessed after the administration of crystalloid and colloid solutions, as well as any substrate antihypoxants, both based on malic and fumaric acids — reamberin, mafusol, or polyoxifyumarin. As a result of our data, the most optimal statistical group of animals in the experiment was identified, with a skin burn area of 15% and the presence of long-term compression syndrome. During the study, the optimal volume of antishock infusion therapy was determined, which exceeded the calculated volume of infusions on the first day based on the Parkland scheme by almost 40% ($p < 0.01$).

Keywords: infusion therapy, burns, long-term compartment syndrome, shock

ЭФФЕКТИВНОСТЬ ПРОТИВОШОКОВОЙ ТЕРАПИИ ПРИ ЛЕЧЕНИИ ОБШИРНЫХ ОЖОГОВ НА ФОНЕ СИНДРОМА ДЛИТЕЛЬНОГО СДАВЛЕНИЯ

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Для цитирования: Соколов Н.К., Зиновьев Е.В., Фисталь Э.Я., Семиглазов А.В., Дерий Э.К., Сидельников фон Эссен В.О., Костякова А.В. Эффективность противошоковой терапии при лечении обширных ожогов на фоне синдрома длительного сдавления. Российские биомедицинские исследования. 2024;9(4):44–47. DOI: <https://doi.org/10.56871/RBR.2024.89.20.007>

Поступила: 07.09.2024

Одобрена: 20.11.2024

Принята к печати: 17.12.2024

Резюме. В статье проанализирована эффективность применения кристаллоидных и коллоидных растворов, антигипоксантов, антиоксидантов, а также анальгетиков, направленных на купирование патологических про-

цессов развития шока у пациентов, имеющих обширные ожоги кожи на фоне синдрома длительного сдавления. Нами было проведено экспериментальное исследование, в которое было включено 360 взрослых белых беспородных крыс обоего пола массой 220–240 г, распределенных на группы в зависимости от методики лечения. После моделирования синдрома длительного сдавления у животных были воспроизведены ожоги III степени, общей площадью 5, 10, 15, 20, 25, 30% поверхности тела. Результаты оценивались после введения кристаллоидных и коллоидных растворов, а также любых субстратных антигипоксантов, как на основе яблочной, так и фумаровой кислот — реамберина, мафусола или полиоксифумарина. Полученные данные позволили выделить наиболее оптимальную статистическую группу животных в эксперименте, с площадью ожога кожи 15% и наличием синдрома длительного сдавления. В ходе исследования было проведено определение оптимального объема проводимой противошоковой инфузионной терапии, превышающей расчетный объем инфузий в первые сутки, исходя из схемы Паркланда, почти на 40% ($p < 0,01$).

Ключевые слова: инфузионная терапия, ожоги, синдром длительного сдавления, шок

INTRODUCTION

Long-term compartment syndrome or crush syndrome (CS) is a complex of pathological reactions that occur as a result of prolonged mechanical compression of soft tissues. A distinctive feature of this type of injury is the severity of clinical manifestations and high mortality [2]. A specific difference in pathogenesis is the manifestation of endogenous intoxication with products of irreversible soft tissue ischemia or the consequences of reperfusion with components of their breakdown [3]. In recent years, special attention of researchers and clinicians has been attracted by victims with extensive burns against the background of CS [1]. There are algorithms for providing specialized medical care for each of the shock conditions, but no treatment regimens in case of their combination [4]. This determines the relevance of research in this area.

AIM

The aim of the study is to conduct an experimental analysis of the results of shock treatment using crystalloids, colloids, metabolic agents and analgesics in the acute phase of extensive burns against the background of CS.

MATERIALS AND METHODS

The experiment involved 360 white outbred adult rats of both sexes weighing 240–250 g. CS in the experimental animals was reproduced under anesthesia by compressing soft tissues of the right or left thigh for 4 hours using special metal vices. The area of compressive surface exerted a pressure force of 8–10 kg/cm², which corresponded to 5 cm². After modeling ischemia, deep third-degree burns were reproduced with an area of 5, 10, 15, 20, 25, 30% of the body surface. Skin burns were performed using the fol-

lowing method: in the back, using a KDB-22 light lamp with a power of 500 W, skin was heated to 85–90 °C. Thermometry was carried out using a thermocouple sensor of Electroline multimeter (China). The exposure did not exceed 20 s.

After reproduction of combined injury, intra-abdominal administration of crystalloid or colloid solutions with metabolic correctors of antihypoxic or antioxidant action was performed. In this case, the volume of infusion therapy was carried out using the Parkland formula:

$$V = 4 \cdot M \cdot \%,$$

where V is the volume of infusion, ml; M is the body weight of the animal, kg; % is the burn area (% of the total body surface area).

Statistical processing of data was carried out in accordance with generally accepted standards in scientific research. Quantitative parameters of the study groups were compared using Student's t-test. The significance criterion was $p < 0.05$.

RESULTS

The results of a comparative study of the mortality rate among animals with different volumes of infusion therapy in shock are presented in Table 1.

Analysis of the data in Table 1 leads to the conclusion that a group of animals with burn wounds of 15% of the body surface area is the most adequate model for assessing the effectiveness of intensive therapy.

The data on the comparative analysis of the mortality rate of animals relative to the area of deep skin burns are shown in Table 2. Based on them, we can conclude that the lowest mortality rate was 61.3% with volume of infusion therapy of about 100 ml/kg, which, in turn, correlated with the Parkland formula. When increasing the infusion therapy to 150 ml/kg and above, 100% mortality of experimental

animals is determined, as in the control group. The results obtained suggest that excessive infusion therapy disrupts the functioning of vital organs and functional systems.

It has been established that the probability of a fatal outcome in burn injury and long-term compartment syndrome depends on the volume of infusion therapy. The maximum survival of experimental animals with these lesions was recorded with the following infusion calculation: Volume of infusion (ml) = $6.5 \cdot M \cdot \%$, which, in turn, exceeds the Parkland formula by almost 40% ($p < 0.01$).

Table 3 shows that administration of synthetic colloids (139 kDa) and crystalloid solutions in a ratio of 2:3 and

Table 2

Mortality of rats with deep skin burns covering 15% of the body surface against the background of prolonged crush syndrome, taking into account the volume of infusions

Таблица 2

Летальность крыс при глубоком ожоге кожи площадью 15% поверхности тела на фоне синдрома длительного сдавления с учетом объема инфузий

Table 1

Mortality of rats with deep skin burns and crush syndrome

Таблица 1

Летальность крыс при глубоких ожогах кожи и синдроме длительного сдавления

Площадь ожога, % п.т. / Burn area, % b.s.	Показатель летальности, % / Mortality rate, %	
	без лечения / without treatment	с инфузионной терапией / with infusion therapy
5	25	—
10	85	—
15	100	77
20	100	90

Объем инфузии 0,9% NaCl, мл / Infusion volume 0.9% NaCl	Показатель летальности (M±m), % / Mortality rate (M±m), %
0	100±7,1
5	92,4±9,1
10	90,7±8,8
15	77,1±9,3
20	72,3±8,1
25	63,1±8,8
30	73,1±7,4
35	79,6±9,1
40	100±10,3

Table 3

Effect of infusions of crystalloid and synthetic colloid solutions on the mortality rate in deep burns of 15% of the body surface area against the background of crush syndrome

Таблица 3

Влияние инфузий кристаллоидных и синтетических коллоидных растворов на показатель летальности при глубоком ожоге площадью 15% поверхности тела на фоне синдрома длительного сдавления

Группы наблюдения / Observation groups	Показатель летальности (M±m, %) при инфузии по формуле / Mortality rate (M±m, %) with infusion according to the formula	
	Паркланда / Parkland	условно расчетной формуле (Паркланда + 40%) / conditionally calculated formula (Parkland + 40%)
Контроль (без лечения) / Control (no treatment)	100±0	100±0
0,9% NaCl	77,1±9,3	63,1±8,8 ¹
0,9% NaCl + ГЭК 130 (0,8:0,2) / 0,9% NaCl + HES 130 (0,8:0,2)	41,7±6,1 ^{1,2}	54,1±7,2 ¹
0,9% NaCl + ГЭК 130 (0,6:0,4) / 0,9% NaCl + HES 130 (0,6:0,4)	36,4±5,9 ^{1,2}	39,3±6,7 ^{1,2}
0,9% NaCl + ГЭК 130 (0,4:0,6) / 0,9% NaCl + HES 130 (0,6:0,4)	58,1±6,2 ¹	62,3±7,4 ¹
0,9% NaCl + ГЭК 130 (0,2:0,8) / 0,9% NaCl + HES 130 (0,2:0,8)	66,2±5,6 ¹	77,2±8,5 ¹
ГЭК 130 / HES 130	86,1±7,3 ¹	87,1±8,1 ²

Notes. Student's t-test: ¹ — $p < 0.05$ compared with the untreated group; ² — $p < 0.05$ compared with NaCl. HES — hydroxyethyl starch.

Примечания. t-критерий Стьюдента: ¹ — $p < 0,05$ по сравнению с группой без лечения; ² — $p < 0,05$ по сравнению с NaCl. ГЭК — гидроксиэтилкрахмал

crystalloids (0.9% NaCl) and synthetic colloid solutions of hydroxyethyl starch (130 kDa) in a ratio of 3:2 reduces the mortality rates of this category of animals by 40.7% ($p < 0.05$) and 23.8% ($p < 0.05$), respectively, compared to infusion with only physiological saline (0.9% NaCl solution).

CONCLUSION

1. The proportion of fatal outcomes in treatment of experimental animals with mechanical and thermal injury caused by extensive burns of the skin and CS of tissue in the acute phase can be reduced by adequate infusion therapy with colloid and crystalloid solutions. It was found that in the comparison group, where adequate infusion therapy was carried out according to the conditional formula (Parkland formula + 40% of the volume of infusion therapy), a tendency to a decrease in the number of fatal outcomes was noted.

2. The solution to the issue of the effectiveness of shock treatment in the acute phase of mechanical and burn shock is directly related to the performance of adequate infusion, including combined use of crystalloid and colloid solutions. At the same time, the mortality rate in the groups studied was reduced by 1.5–2 times ($p < 0.01$) compared to the group of animals where only crystalloid solutions were used.

ADDITIONAL INFORMATION

Author contribution. Thereby, all authors made a substantial contribution to the conception of the study, acquisition, analysis, interpretation of data for the work, drafting and revising the article, final approval of the version to be published and agree to be accountable for all aspects of the study.

Competing interests. The authors declare that they have no competing interests.

Funding source. This study was not supported by any external sources of funding.

Experiments with animals were carried out in accordance with international rules (Directive 2010/63/EU of the European Parliament and of the Council of the European Union of September 22, 2010 on the protection of animals used for scientific purposes).

ДОПОЛНИТЕЛЬНАЯ ИНФОРМАЦИЯ

Вклад авторов. Все авторы внесли существенный вклад в разработку концепции, проведение исследования и подго-

товку статьи, прочли и одобрили финальную версию перед публикацией.

Конфликт интересов. Авторы декларируют отсутствие явных и потенциальных конфликтов интересов, связанных с публикацией настоящей статьи.

Источник финансирования. Авторы заявляют об отсутствии внешнего финансирования при проведении исследования.

Эксперименты с животными проводили в соответствии с международными правилами (Директивой 2010/63/EU Европейского парламента и Совета Европейского союза от 22 сентября 2010 года по охране животных, используемых в научных целях).

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UDC 612.743+612.763
DOI: 10.56871/RBR.2024.95.20.008

ELECTROMYOGRAPHIC SIGNS OF AMBIDEXTRIA DEVELOPMENT PROGRESS

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For citation: Egorova AA, Beresneva VT, Gladin DP, Metlyaeva AV. Electromyographic signs of ambidextria development progress. Russian Biomedical Research. 2024;9(4):48–53. DOI: <https://doi.org/10.56871/RBR.2024.95.20.008>

Received: 30.09.2024

Revised: 01.11.2024

Accepted: 17.12.2024

Abstract. Introduction. The relevance of the work is due to the need to develop ambidexterity as a manual skill of future surgeons in order to speed up the performance of operations and minimize trauma to the specialist, as well as reduce the risk of blood-borne infections. Ambidexterity can be developed by performing special exercises at home, and an objective assessment of changes in the state of the neuromuscular apparatus can be carried out using surface electromyography. **The aim** of the study is to develop an effective version of exercises for the development of fine motor skills using EMG assessment of the dynamics of the functional state of the motor units of the muscles of the forearms of the non-dominant hand. **Materials and methods.** The ten-day experiment involved 10 people aged 18–23 years, who were evenly divided into two groups, which once a day performed exercises to develop fine motor skills of the fingers, and the second group additionally performed exercises to develop interhemispheric connections. EMG registration was carried out by electromyograph Biopac Student LAB Basic Systems. The reliability of differences in dependent samples was determined using the nonparametric Mann–Whitney criterion; for dependent samples, the Wilcoxon criterion was used. **Results.** Performing fine motor skills training in combination with exercises that activate the work of both hemispheres of the brain more effectively contributes to the development of motor skills of the non-working hand. The formation of interhemispheric interactions increases the number of involved motor units and the degree of their synchronization. **Conclusion.** The development of interhemispheric connections allows for more effective mastery of manipulations with the non-working hand due to the involvement of a larger number of motor units in the process of muscle contraction.

Keywords: ambidexterity, electromyography, fine motor skills

ЭЛЕКТРОМИОГРАФИЧЕСКИЕ ПРИЗНАКИ ПРОГРЕССА РАЗВИТИЯ АМБИДЕКСТРИИ

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Для цитирования: Егорова А.А., Береснева В.Т., Гладин Д.П., Метляева А.В. Электромиографические признаки прогресса развития амбидекстрии. Российские биомедицинские исследования. 2024;9(4):48–53. DOI: <https://doi.org/10.56871/RBR.2024.95.20.008>

Поступила: 30.09.2024

Одобрена: 01.11.2024

Принята к печати: 17.12.2024

Резюме. Введение. Актуальность работы обусловлена потребностью формирования амбидекстрии как мануального навыка будущих хирургов для ускорения выполнения операций, минимизации травматизации

специалиста, а также снижения риска заболевания гемоконтактными инфекциями. Амбидекстрию можно развивать с помощью выполнения специальных упражнений дома, а объективную оценку изменений состояния нервно-мышечного аппарата проводить с помощью поверхностной электромиографии (ЭМГ). **Цель исследования** — разработка эффективного варианта упражнений для развития мелкой моторики с применением ЭМГ-оценки динамики функционального состояния двигательных единиц мышц предплечий неведущей руки. **Материалы и методы.** В десятидневном эксперименте участвовали 20 человек в возрасте 18–23 лет, которые были равномерно разделены на две группы, обе из которых один раз в сутки выполняли упражнения для развития мелкой моторики пальцев рук, вторая группа при этом дополнительно выполняла упражнения для развития межполушарных связей. Регистрация ЭМГ осуществлялась при помощи электромиографа Biopac Student LAB Basic Systems. Достоверность различий зависимых выборок определяли с помощью непараметрического критерия Манна–Уитни, для зависимых выборок применяли критерий Уилкоксона. **Результаты.** Выполнение тренинга по развитию мелкой моторики в сочетании с упражнениями, активирующими работу двух полушарий головного мозга, более эффективно способствует развитию моторики нерабочей руки. Формирование межполушарных взаимодействий увеличивает количество вовлеченных двигательных единиц и степень их синхронизации. **Выводы.** Развитие межполушарных связей позволяет более эффективно осваивать манипуляции нерабочей рукой за счет вовлечения в процесс сокращения мышц большего числа двигательных единиц.

Ключевые слова: амбидекстрия, электромиография, мелкая моторика

INTRODUCTION

Formation of manual skills is one of the elements of training surgeons in higher medical educational institutions [1]. Using not only the right but also the left hand — ambidexterity — allows not to transfer instruments from one hand to the other during surgeries, thereby having the ability to perform surgical manipulations with the non-dominant hand [2]. Ambidexterity also contributes to the more productive learning process, reduces the overall level of emotional stress and mental strain [3, 4]. The ability to use non-dominant hand minimizes trauma to the specialist, reduces the risk of various blood-borne infections. Ambidexterity in surgeons lowers the level of the patient's discomfort, increases speed and quality of the procedure, helping to reduce indicators of surgical stress and patient's rapid recovery [5].

Manual skills are usually developed using special simulators [6]. However, ambidexterity can be effectively developed by performing special exercises at home [7]. Electromyography (EMG) is used in biomechanics, ergonomics and sports research to objectively assess changes in the state of motor units (MU) [7,8]. EMG is a suitable method for assessing physiological processes occurring in the neuromuscular system during the development of special motor skills of non-dominant hand [9].

AIM

The aim of the study is to develop effective version of exercises for the development of fine motor skills using EMG — assessment of the dynamics of functional state

of motor units of muscles of the forearms of non-dominant hand.

MATERIALS AND METHODS

The ten-day experiment involved 20 people aged 18 to 23 years, who were evenly divided into two groups. Both groups performed exercises once a day to develop fine motor skills of the fingers, used in rehabilitation of patients after upper limb injuries [11]. The second group additionally performed exercises aimed at developing interhemispheric connections [12].

The changes in the state of MU of the non-dominant hand were assessed using surface EMG (recorded using BIOPAC STUDENT LAB BASIC SYSTEMS electromyograph). Statistical analysis of the data was performed using the STATISTICA program, version 6.0. The reliability of differences in dependent samples was determined using the nonparametric Mann–Whitney criterion; for dependent samples, the Wilcoxon criterion was used.

RESULTS

After a week of the experiment, the time of completing tasks with non-dominant hand (Table 1) decreased in both groups. Moreover, the students in the second group showed more significant progress compared to those in the first group.

The results of the dynamics of amplitude and frequency of the total bioelectrical activity of muscles of non-dominant hand of students in the first and second groups before the study and after a week of performing the exercises are presented in Tables 2 and 3.

Table 1

Time of completing tasks to assess fine motor skills of the non-dominant hand before and after completing a set of exercises in the first and second experimental groups

Таблица 1

Время выполнения заданий для оценки мелкой моторики неведущей рукой до и после выполнения комплекса упражнений в первой и второй экспериментальных группах

Выполняемое задание / Task to be performed	Общая выборка до выполнения комплекса, с / Total sample before the execution of the complex, sec	1-я группа после выполнения комплекса, с / 1 st group after completing the complex, sec	2-я группа после выполнения комплекса, с / 2 nd group after completing the complex, sec
Застегнуть пуговицы / Button up	43	22	18
Продеть нитку в иголку / Thread a needle	25	17	13
Вставить стержень в отверстие пуговицы (бусины) и поднять ее / Insert the rod into the hole of the button (bead) and lift it up	17	12	8
Достать спичку из коробки и зажечь ее / Take a match out of the box and light it	12	9	7
Собрать монеты с плоской поверхности, положить их в кошелек / Collect coins from a flat surface and put them in a wallet	15	10	6
Стереть ластиком предварительно нарисованные крестики / Erase the previously drawn crosses with an eraser	9	5	3
Отвинтить гайку рукой / Unscrew the nut by hand	9	5	3
Намотать нитку на катушку / Wind the thread onto the spool	8	4	3

Table 2

Maximum amplitude of oscillations on the electromyogram of the non-working hand before and after performing a set of exercises

Таблица 2

Максимальная амплитуда осцилляций на электромиограмме нерабочей руки до и после выполнения комплекса упражнений

Группа / Group	До эксперимента / Before the experiment		После эксперимента / After the experiment	
	момент максимального сокращения, мкВ / moment of maximum contraction, μ V	момент максимального расслабления, мкВ / moment of maximum relaxation, μ V	момент максимального сокращения, мкВ / moment of maximum contraction, μ V	момент максимального расслабления, мкВ / moment of maximum relaxation, μ V
1	783 $\pm$ 362	250 $\pm$ 167	844 $\pm$ 366	104 $\pm$ 37,9
2	792 $\pm$ 38,1	180 $\pm$ 8,3	1052 $\pm$ 43,7*	81 $\pm$ 2,6*

* $p \leq 0.05$, statistically significant differences, Mann-Whitney test.

* $p \leq 0.05$, статистически значимые отличия, критерий Манна-Уитни.

The mean amplitude and frequency of EMG oscillations in both groups before the study did not differ statistically significantly. After exercises, the amplitude in both groups changed in a similar way: during maximum contraction it became higher, and at the moment of relaxation it was lower than before the experiment. In students of the second group, the changes were statistically significantly different from the data before the experiment.

The frequency of EMG oscillations after a week of training changed in a similar way. In this case, students of the first group showed a significant decrease in the frequency of oscil-

lations only under conditions of maximum relaxation relative to the background. Meanwhile, in individuals of the second group, statistical differences in the frequency of oscillations on the EMG were significant both against the background of maximum contraction and with maximum relaxation.

DISCUSSION

We have shown that the motor skills of non-dominant hand of a healthy person can be significantly improved as a result of a week of training, if the exercises are performed

Table 3

Maximum oscillation frequency on the electromyogram of the non-working hand before and after performing a set of exercises

Таблица 3

Максимальная частота осцилляций на электромиограмме нерабочей руки до и после выполнения комплекса упражнений

Группа / Group	До эксперимента		После эксперимента	
	момент максимального сокращения, мкВ / moment of maximum contraction, μ V	момент максимального расслабления, мкВ / moment of maximum relaxation, μ V	момент максимального сокращения, мкВ / moment of maximum contraction, μ V	момент максимального расслабления, мкВ / moment of maximum relaxation, μ V
1	343 $\pm$ 20	110 $\pm$ 18,2	369 $\pm$ 24,5	44 $\pm$ 5,3*
2	347 $\pm$ 24,5	79,2 $\pm$ 10,6	460,9 $\pm$ 43,7 *	35 $\pm$ 5,6*

* $p \leq 0,05$, статистически значимые отличия, критерий Манна–Уитни.

* $p \leq 0.05$, statistically significant differences, Mann–Whitney test.

once a day every day. Not only the time of completing test tasks to assess fine motor skills improves, but the electrical activity of the forearm MU also changes: amplitude and frequency of oscillations during contraction increase. Students in the second group showed higher values of the maximum amplitude and frequency of contraction on the EMG. This means that as a result of the development of interhemispheric interactions, a larger number of neuromotor units were recruited, and their impulse activity increased [13].

It is shown that bimanual hand movements are associated with a symmetric facilitation of neural activity mediated by both increased intrahemispheric connectivity and enhanced transcallosal coupling of SMA and M1. The supplementary motor area is a key structure that stimulates or suppresses activity in the motor cortical network controlling uni- and bilateral hand movements [14].

The frequency and amplitude of EMG oscillations during maximum relaxation, which mainly reflect the activity of the end plates of muscle, were also lower in students of the second group. This indicates a more pronounced decrease in the tonic impulses of MU as a result of fatigue [15]. It has been previously established that the proportion of the amplitude of low- and high-frequency ranges significantly correlates with relative levels of phosphate, which may be a consequence of depletion of energy reserves in myocytes [16].

CONCLUSION

1. Exercises aimed at developing interhemispheric connections allow mastering manipulations with non-dominant hand more effectively.

2. Transcallosal coupling contributes to the involvement of a larger number of MU in contraction.

3. As a result of more effective contraction, fatigue develops in the muscles, leading to a decrease in neuronal impulses.

ADDITIONAL INFORMATION

Author contribution. Thereby, all authors made a substantial contribution to the conception of the study, acquisition, analysis, interpretation of data for the work, drafting and revising the article, final approval of the version to be published and agree to be accountable for all aspects of the study.

Competing interests. The authors declare that they have no competing interests.

Funding source. This study was not supported by any external sources of funding.

Consent for publication. Written consent was obtained from the patient for publication of relevant medical information within the manuscript.

ДОПОЛНИТЕЛЬНАЯ ИНФОРМАЦИЯ

Вклад авторов. Все авторы внесли существенный вклад в разработку концепции, проведение исследования и подготовку статьи, прочли и одобрили финальную версию перед публикацией.

Конфликт интересов. Авторы декларируют отсутствие явных и потенциальных конфликтов интересов, связанных с публикацией настоящей статьи.

Источник финансирования. Авторы заявляют об отсутствии внешнего финансирования при проведении исследования.

Информированное согласие на публикацию. Авторы получили письменное согласие пациентов на публикацию медицинских данных.

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UDC 616.314.18-007+57.022+612.017.2
DOI: 10.56871/RBR.2024.16.51.009

IMPROVING THE EFFECTIVENESS OF PHYSIOLOGICAL ADAPTATION OF PATIENTS TO COMPLETE REMOVABLE DENTURES USING ELECTROMYOGRAPHIC BIOFEEDBACK

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For citation: Chepurayeva OS, Shemonaev VI, Klauchek SV. Improving the effectiveness of physiological adaptation of patients to complete removable dentures using electromyographic biofeedback. Russian Biomedical Research. 2024;9(4):54–60. DOI: <https://doi.org/10.56871/RBR.2024.16.51.009>

Received: 20.09.2024

Revised: 11.11.2024

Accepted: 17.12.2024

Abstract. Introduction. Complete absence of teeth is a very common pathology, especially in the elderly, and removable dentures are mainly used for its treatment. Various local and general mechanisms are used to reduce the process of adaptation to dentures in patients with complete absence of teeth. We suggest using the principle of biofeedback, which is safe, does not require medical support, and optimizes the adaptation process by activating the human body's own reserves, through active patient involvement and conscious training of the musculoskeletal system. **The aim of the study** is to optimize the adaptation process of primary prosthetic patients with complete removable plate prostheses using the principle of biofeedback. **Materials and methods.** The research was aimed at substantiating the effectiveness of the biofeedback method to optimize the adaptation of patients to removable dentures after complete tooth loss. The study involved 50 elderly people (60–74 years old). All patients were treated for complete absence of teeth with removable dentures, but the patients of the main group received biofeedback therapy at the treatment stages to optimize adaptation. **Results.** When comparing the results of the group receiving traditional treatment and the group using correction with biofeedback, it was found that the adaptation to full removable plate prostheses occurred faster in the second group. According to electromyography and gnathodynamometry data, patients receiving biofeedback therapy at the treatment stages had already adapted to full removable plate prostheses on day 14. We have proved the effectiveness of the implementation of the proposed technology to optimize the process of adaptation to removable dentures. **Conclusion.** Based on the results of objective physiological and subjective studies, it can be seen that the use of the author's algorithm based on the principles of biofeedback makes it possible to shorten the period of adaptation of patients to complete removable plate prostheses, thereby optimizing the process of getting used to complete removable orthopedic structures.

Keywords: electromyographic biofeedback, complete absence of teeth, physiological adaptation to removable plate prostheses

ПОВЫШЕНИЕ ЭФФЕКТИВНОСТИ ФИЗИОЛОГИЧЕСКОЙ АДАПТАЦИИ ПАЦИЕНТОВ К ПОЛНЫМ СЪЕМНЫМ ЗУБНЫМ ПРОТЕЗАМ С ИСПОЛЬЗОВАНИЕМ ЭЛЕКТРОМИОГРАФИЧЕСКОЙ БИОЛОГИЧЕСКОЙ ОБРАТНОЙ СВЯЗИ

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Для цитирования: Чепуряева О.С., Шемонаев В.И., Клаучек С.В. Повышение эффективности физиологической адаптации пациентов к полным съемным зубным протезам с использованием электромиографической биологической обратной связи. Российские биомедицинские исследования. 2024;9(4):54–60. DOI: <https://doi.org/10.56871/RBR.2024.16.51.009>

Поступила: 20.09.2024

Одобрена: 11.11.2024

Принята к печати: 17.12.2024



Резюме. Введение. Полное отсутствие зубов является весьма распространенной патологией, особенно у пожилых людей, для ее лечения в основном применяют съемные пластиночные протезы. Для сокращения процесса адаптации к протезам у пациентов с полным отсутствием зубов используют различные локальные и общие механизмы. Мы же предлагаем использовать принцип биологической обратной связи (БОС), который безопасен, не требует медикаментозной поддержки, оптимизирует процесс адаптации за счет активизации собственных резервов организма человека путем активного вовлечения пациента и осознанной тренировки мышечного звена зубочелюстной системы. **Цель исследования** — оптимизация процесса адаптации первично протезируемых пациентов полными съемными пластиночными протезами с использованием принципа БОС. **Материалы и методы.** Исследования были направлены на обоснование эффективности применения метода БОС для оптимизации адаптации пациентов к съемным пластиночным протезам после полной потери зубов. В исследовании приняли участие 50 человек пожилого возраста (60–74 года). Всем пациентам было проведено лечение полного отсутствия зубов съемными пластиночными протезами, но пациенты основной группы на этапах лечения для оптимизации адаптации получали терапию с БОС. **Результаты.** При сравнении результатов группы, получающей традиционное лечение, и группы, использующей коррекцию с БОС, установлено, что у второй группы адаптация к полным съемным пластиночным протезам наступила быстрее. У пациентов, получающих БОС-терапию, на этапах лечения уже на 14-й день по данным электромиографии и гнатодинамометрии наступила адаптация к полным съемным пластиночным протезам. Нами доказана эффективность внедрения предложенной технологии оптимизации процесса адаптации к съемным зубным протезам. **Заключение.** По результатам объективных физиологических и субъективных исследований видно, что применение авторского алгоритма, основанного на принципах БОС, позволяет сократить период адаптации пациентов к полным съемным пластиночным протезам и тем самым оптимизировать процесс привыкания к полным съемным ортопедическим конструкциям.

Ключевые слова: электромиографическая биологическая обратная связь, полное отсутствие зубов, физиологическая адаптация к съемным пластиночным протезам

INTRODUCTION

Restoration of chewing function, dental aesthetics and quality speech in the complete absence of teeth is one of the urgent tasks of modern dentistry. Removable dentures are mainly used to treat the complete absence of teeth. Adaptation to removable dentures is different for each individual patient, and often even a correctly manufactured denture with good fixation does not guarantee rapid adaptation [1–4]. The process of adaptation to removable dentures is influenced by many factors: atrophy of the alveolar process, physiological characteristics of the patient's body as a whole, and psychological characteristics of each individual patient [5–7]. Various local and general mechanisms are used to reduce the adaptation time to removable dentures in patients with a complete absence of teeth. A significant share of the influence is exerted by topical medications. A number of authors recommend using various adhesive agents, modified adhesive compositions [8–10]. Foreign literature describes digital technologies for the manufacture of complete removable dentures, which improve their quality and accelerate the process of getting used to them [11, 12].

When choosing a method for optimizing patient adaptation to complete removable dentures, we proceeded from the fact that the principle of biofeedback is safe. It also does not require medication support, optimizes the adaptation process by activating the human body's own reserves through active patient involvement and conscious training of muscles of the stomatognathic system [13–15]. Thus, it seems relevant to use biofeedback to optimize adaptation to complete removable dentures.

AIM

The aim of the study is to optimize the adaptation process of primary prosthetic patients with complete removable dentures using the principle of biofeedback.

MATERIALS AND METHODS

Two groups of individuals were surveyed to determine the effectiveness of the approach we developed to optimize the adaptation process. The 1st group (control group) received traditional treatment, while the 2nd group (main group) received biofeedback therapy. Each group included 25 patients.

In accordance with the Standards of Medical Care, the condition of all patients met the following criteria and signs: complete absence of teeth on one or both jaws; absence of sharp bone prominences (exostoses); absence of pronounced atrophy of the alveolar process (with complete absence of teeth on one or both jaws). Complete absence of teeth on the upper jaw with a high alveolar process of the upper jaw, uniformly lined with dense mucosa, with well-defined maxillary tuberosity, deep palate, poorly expressed torus or its absence allowed to classify patients as type I according to the Schroeder classification. Complete absence of teeth on the lower jaw with a pronounced alveolar ridge, when the transitional fold is located far its crest, allowed to classify patients as type I according to the Keller classification. Healthy oral mucosa is moderately flexible, moderately mobile, pale pink, well-moistened. This allowed us to classify patients as I class according to the Supple classifica-

tion. In addition, the patients did not have pathology of the temporomandibular joint and masticatory muscles.

The patient's adaptation correction was carried out for 10 days. It included: author's complex of myogymnastic exercises (invention patent RU 2812832 C1 dated 02.02.2024), author's method of training patients with complete absence of teeth using the principles of biofeedback (invention patent RU 2802148 C1 dated 22.08.2023), author's training plastic base with a plastic roller (utility model patent RU 202617 U1 dated 01.03.2021). Myogymnastics was carried out taking into account the individual physiological characteristics of the maxillofacial area of patients and using a plastic roller with a plastic base specially developed by us (utility model patent RU 213341 U1 dated 07.09.2022) [16–18].

Medical check-up of patients at the stages of treatment included: dental check-up of the maxillofacial area and the

Table 1

Results of the assessment of patient adaptation at the stages of treatment with the traditional method and using correction with biological feedback according to gnathodynamometry data ($M \pm m$)

Таблица 1

Результаты оценки адаптации пациентов на этапах лечения традиционным методом и с использованием коррекции с биологической обратной связью по данным гнатодинамометрии ($M \pm m$)

Срок наблюдения / Observation period	Контрольная группа, с традиционным лечением / Control group, with conventional treatment (n=25)		Основная группа, с использованием БОС-терапии на этапах лечения / The main group, using biofeedback therapy at the stages of treatment (n=25)		t-критерий Стьюдента / Student's t-test	P
	сила сокращения жевательных мышц, Н / force of contraction of masticatory muscles, N					
	сторона / side		сторона / side			
	правая / right	левая / left	правая / right	левая / left		
Первое посещение / First visit	90,5±2,6	93,6±2,5	90,5±2,6	93,6±2,5	0,27	0,8
Шестое посещение / Sixth visit	91,0±2,3	93,6±3,3	92,0±2,3	94,5±2,3	0,61	0,5
3 дня после наложения протеза / 3 days after the prosthesis is applied	90,4±2,5	95,3±2,1	98,3±2,5	97,3±2,1	2,7	0,00005*
7 дней после наложения протеза / 7 days after the prosthesis is applied	100,4±1,5	105,3±2,2	115,4±2,5	116,3±2,1	4,18	0,000064*
14 дней после наложения протеза / 14 days after the prosthesis is applied	110,1±2,1	111,5±1,6	125,1±4,1	125,5±3,6	3,9	0,00017*
30 дней после наложения протеза / 30 days after the prosthesis is applied	130,1±4,3	131,1±3,2	139,1±2,3	139,1±2,2	2,35	0,02*
60 дней после наложения протеза / 60 days after prosthesis placement	135,5±6,3	134,1±4,1	140,1±4,1	139,6±6,3	0,5	0,6

* Differences in the same indicators between groups are statistically significant ($p < 0.05$).

* Различия одноименных показателей между группами статистически достоверны ($p < 0,05$).

oral cavity itself, palpation, gnathodynamometry (GDM), electromyography (EMG), autonomic nervous system (ANS) testing, modified technique for assessing adaptation to orthopedic dental structures "AOS", OHIP-14-Ru questionnaire for assessing the quality of life, and maladjustment coefficient (MC).

Statistical analysis of the data was performed using the STATISTICA 7.0 software package. The normality of distribution was assessed using the Kolmogorov-Smirnov test followed by the parametric method. Differences were considered significant at $p \leq 0.05$.

RESULTS

The vegetative Kerdo index (KI) values in patients of both clinical groups before the start of treatment did not differ significantly (mean value was 10.0), which was additional evidence of the similarity of these clinical groups. On the first day after insertion of a complete removable denture, an increase in heart rate (HR) and, accordingly, KI

(sympathicotonia) from 60.5 to 65.8% was recorded in both study groups. On the seventh day after insertion of a denture, the HR and KI values in the main group approached normal values, and in the control group, sympathicotonia was observed, which is characteristic of a stress state ($p < 0.05$ with the first group). During control visits after 30 and 60 days of treatment, patients in both clinical groups had KI values within normal limits.

The gnathodynamometry values in patients of both groups before the start of treatment did not differ significantly (mean value was 92N), which was additional evidence of the similarity of these groups (Table 1).

On the first day after denture insertion, a slight increase in the chewing force from 1.5 to 1.8% was recorded in both clinical groups, both on the functionally dominant and non-dominant chewing sides. On the 7th and 14th days after insertion of a complete removable denture, the pressure force was partially restored, but when using the traditional approach, it was only 102.4 ± 7.7 N. At the same time, in patients of the second

Table 2

Results of the assessment of patient adaptation at the stages of treatment with the traditional method and using correction with biofeedback according to electromyography data of the masticatory muscles ($M \pm m$)

Таблица 2

Результаты оценки адаптации пациентов на этапах лечения традиционным методом и с использованием коррекции с биологической обратной связью по данным электромиографии жевательных мышц ($M \pm m$)

Срок наблюдения / Observation period	Контрольная группа, с традиционным лечением / Control group, with conventional treatment (n=25)		Основная группа, с использованием БОС-терапии на этапах лечения / The main group, using biofeedback therapy at the stages of treatment (n=25)		t-критерий Стью- дента / Student's t-test	P
	электромиография, мкВ / electromyography, μ V					
	сторона		сторона			
	правая	левая	правая	левая		
Первое посещение / First visit	52,0 $\pm$ 6,1	41,0 $\pm$ 6,5	53,0 $\pm$ 5,2	42,0 $\pm$ 5,1	0,12	0,9
Шестое посещение / Sixth visit	150,1 $\pm$ 6,5	120,0 $\pm$ 5,4	140,0 $\pm$ 7,6	100,0 $\pm$ 5,5	1,04	0,3
3 дня после наложения протеза / 3 days after the prosthesis is applied	160,5 $\pm$ 5,5	120,0 $\pm$ 4,5	100,9 $\pm$ 5,7	70,0 $\pm$ 4,6	7,57	0,00001*
7 дней после наложения протеза / 7 days after the prosthesis is applied	130,2 $\pm$ 4,4	100,0 $\pm$ 5,3	70,1 $\pm$ 3, 5	60,8 $\pm$ 5,6	9,53	0,000001*
14 дней после наложения протеза / 14 days after the prosthesis is applied	110,0 $\pm$ 5,5	80,1 $\pm$ 4,4	55,3 $\pm$ 3,6	50,4 $\pm$ 4,5	7,74	0,000001*
30 дней после наложения протеза / 30 days after the prosthesis is applied	53,3 $\pm$ 3,6	50,2 $\pm$ 3,4	52,5 $\pm$ 2,6	50,4 $\pm$ 2,1	2,23	0,8
60 дней после наложения протеза / 60 days after prosthesis placement	50,6 $\pm$ 0,7	50,2 $\pm$ 0,8	50,1 $\pm$ 0,4	50,8 $\pm$ 0,6	0,62	0,54

* Различия одноименных показателей между группами статистически достоверны ($p < 0.05$).

* Differences in the same indicators between groups are statistically significant ($p < 0.05$).

group it was 115.3 ± 8.9 N ($p < 0.05$ with the first group). During control visits after 30 and 60 days of treatment, the GDM values were recorded in patients of both clinical groups within the normal limits. However, during treatment using the principle of biofeedback, the values of the force of chewing pressure of the muscles were higher than in the first group.

The bioelectrical activity (BEA) of the studied muscles was examined using the method of total electromyography (Table 2). Standard wireless sensors were used, which were placed along the course of muscle fibers on the right and left above the motor point of the masseter muscle.

As a result of assessing the EMG parameters in the control group, at maximum muscle stress, a high-frequency curve was recorded with average amplitude of 52.0 ± 6.1 μ V on the right, and 41.0 ± 6.5 μ V on the left before prosthetics of the masseter muscle itself. Meanwhile, in the main group, values were 53.0 ± 5.2 μ V on the right side, and 42.0 ± 5.1 μ V on the left. Bioelectrical activity in men and women differed slightly, and therefore the electromyography data of men and women were considered together.

The next day after insertion of a removable denture (6th visit), according to the results of the EMG: in the control group, at maximum muscle stress, a high-frequency curve was recorded with amplitude of contraction of the masticatory muscle itself of 150.1 ± 6.5 μ V on the right side, and 120.0 ± 5.4 μ V on the left. At the same time, in the main group, values were 140.0 ± 7.6 μ V on the right side, and 100.0 ± 5.5 μ V on the left. It is seen that in patients of the main and control groups there was a "jump" in the bioelectrical activity of the masticatory muscles immediately after insertion of a removable denture, since it is a strong irritant.

On the third day after insertion of a removable denture in the control group, at maximum muscle stress, a high-frequency curve was recorded on the EMG of the masticatory muscle itself with average amplitude of 160.5 ± 5.5 μ V on the right side, and 120.0 ± 4.5 μ V on the left before prosthetics. Meanwhile, in the main group, values were 100.9 ± 5.7 μ V on the right side, and 70.0 ± 4.6 μ V on the left. It is evident that in patients of the main and control groups of the study, according to the bioelectrical activity of the masticatory muscles of the right and left sides, signs of asymmetry of the indicators are preserved.

On the seventh day after insertion of a removable denture in the control group, at maximum muscle stress, a high-frequency curve was recorded on the EMG with average amplitude of 130.2 ± 4.4 μ V on the right side, and 100.0 ± 5.3 μ V on the left before prosthetics of the masticatory muscle itself. At the same time, in the main group, values were 70.1 ± 3.5 μ V on the right side, and 60.8 ± 5.6 μ V on the left. It is seen that in patients of the main group, the bioelectrical activity of the masticatory muscles of the right and left sides approached the initial values. Also, the indicators on the right and left are almost the

same (which indicates a good prognosis for adaptation), while this is not observed in patients in the control group.

On the fourteenth day after insertion of a removable denture in the control group, at maximum muscle stress, a high-frequency curve was recorded on the EMG with average amplitude of 110.0 ± 5.5 μ V on the right side, and 80.1 ± 4.4 μ V on the left before prosthetics of the masticatory muscle itself. Meanwhile, in the main group, values were 55.3 ± 3.6 μ V on the right side, and 50.4 ± 4.5 μ V on the left. It is evident that in patients of the main group, the bioelectrical activity of the masticatory muscles of the right and left sides approached the initial values. Also, the indicators on the right and left are almost the same (which indicates the onset of adaptation in the main group), while this is not observed in patients in the control group.

On the thirtieth day after insertion of a removable denture in the control group, at maximum muscle stress, a high-frequency curve was recorded on the EMG with average amplitude of 53.3 ± 3.6 μ V on the right side, and 50.2 ± 3.4 μ V on the left before prosthetics of the masticatory muscle itself. At the same time, in the main group, values were 52.5 ± 2.6 μ V on the right side, and 50.4 ± 2.1 μ V on the left. The masticatory muscles of the subjects in both groups work symmetrically, which is confirmed by the symmetry of their strength indicators and can be considered a sign of successful adaptation.

On the sixtieth day after insertion of a removable denture, a high-frequency curve was recorded on the EMG in the control group at maximum muscle stress with average amplitude of 50.6 ± 0.7 μ V on the right side, and 50.2 ± 0.8 μ V on the left before the prosthesis the masticatory muscle itself. Meanwhile, in the main group, the EMG values were 50.1 ± 0.4 μ V on the right side, and 50.8 ± 0.6 μ V on the left. In patients of the main and control groups, the bioelectrical activity of the masticatory muscles of the right and left sides is almost the same. The masticatory muscles of the subjects in both groups work symmetrically, which is confirmed by the symmetry of their strength indicators and can be considered a sign of successful adaptation.

When analyzing the data of the assessment of patients in both groups after insertion of removable dentures using the "Maladjustment Scale" (MC — maladjustment coefficient), it is shown that on the day of denture insertion in the first (control) group, MC was equal to an average of 122.4 ± 0.3 . In the second group MC was 107.2 ± 0.3 . During medical check-up of patients on the 7–14th day after insertion of removable dentures in the first (control group) and second (main group, patients received biofeedback therapy) groups, the MC was 110 ± 6.2 and 48.0 ± 4.3 , respectively. This indicates a relatively more favorable course of the adaptation process in patients in the case of using the myogymnastic complex with biofeedback in treatment. Medical check-up of patients on the 30th–60th day after denture insertion revealed a further decrease in

KDA values to 6.3 ± 0.4 in the main group and to 4.1 ± 0.3 in the comparison group. It should be noted that adaptation is considered to have occurred already at values of KDA less than 10. Thus, it is obvious that patients of the main group have a higher degree of adaptation to removable dentures ($p < 0.05$).

Before treatment, the OHIP-14-Ru questionnaire scores (the "Quality of Life Questionnaire") were higher than 56 points in both groups and amounted to 65 ± 7.4 . Immediately after denture insertion, the OHIP-14-Ru questionnaire scores in the first (main) group were slightly higher than 56 points and amounted to 57 ± 5.7 points. In the second group (comparison group), the scores were 55 ± 5.4 points, indicating a satisfactory level of quality of life ($p < 0.001$).

According to the data of electromyography and gnathodynamometry of the masticatory muscles, adaptation in patients of the main group occurred on the 14th day after denture insertion, and in patients of the control group — only on the 30th day after fixation of the complete removable denture.

Thus, the application of biofeedback at the stages of treatment of patients with a complete absence of teeth using removable dentures reduces the level of maladaptive impact of dental manipulations on chewing function. In addition, this approach ensures more complete and accelerated restoration of the main physiological characteristics of masticatory muscles of stomatognathic system.

CONCLUSION

Based on the results of objective physiological and subjective studies, it can be seen that using the author's algorithm based on principles of biofeedback makes it possible to shorten the period of adaptation of patients to complete removable dentures, thereby optimizing the process of getting used to complete removable orthopedic structures.

The tactics we have developed for managing patients with complete absence of teeth include a complex of myogymnastic exercises, method for training patients with complete absence of teeth using principles of biofeedback, as well as the use of technical devices we have proposed (a training plastic base with a plastic roller). This tactic allows us to optimize the process of adaptation to removable dentures. Therefore, it is advisable to include it in the protocol for dental treatment of patients with complete absence of teeth.

ADDITIONAL INFORMATION

Author contribution. Thereby, all authors made a substantial contribution to the conception of the study, acquisition, analysis, interpretation of data for the work, drafting and revising the article, final approval of the version to be published and agree to be accountable for all aspects of the study.

This publication is part of the dissertation research for the degree of candidate of medical sciences of Olga Sergeevna Chepurayeva.

Competing interests. The authors declare that they have no competing interests.

Funding source. This study was not supported by any external sources of funding.

Consent for publication. Written consent was obtained from the patient for publication of relevant medical information within the manuscript.

ДОПОЛНИТЕЛЬНАЯ ИНФОРМАЦИЯ

Вклад авторов. Все авторы внесли существенный вклад в разработку концепции, проведение исследования и подготовку статьи, прочли и одобрили финальную версию перед публикацией.

Данная публикация является частью диссертационного исследования на соискание степени кандидата медицинских наук Ольги Сергеевны Чепуряевой.

Конфликт интересов. Авторы декларируют отсутствие явных и потенциальных конфликтов интересов, связанных с публикацией настоящей статьи.

Источник финансирования. Авторы заявляют об отсутствии внешнего финансирования при проведении исследования.

Информированное согласие на публикацию. Авторы получили письменное согласие пациентов на публикацию медицинских данных.

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UDC 619+616.995.122+612.015+576.895.122+597.58
DOI: 10.56871/RBR.2024.17.57.010

ON THE TREMATODE FAUNA OF FISH OF THE FAMILY *PERCIDAE* IN THE LAKE VEROYARVI OF LENINGRAD REGION

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For citation: Makarov DV, Frolova OV. On the trematode fauna of fish of the family Percidae in the lake Veroyarvi of Leningrad Region. Russian Biomedical Research. 2024;9(4):61–67. DOI: <https://doi.org/10.56871/RBR.2024.17.57.010>

Received: 27.09.2024

Revised: 31.10.2024

Accepted: 17.12.2024

Abstract. Introduction. The lakes of the Vsevolozhsky District of the Leningrad Region are considered to be popular places of tourist importance, where intensive amateur fishing is conducted. Data on the parasite fauna of the fish species most commonly found in the biocenoses are important in ichthyopathology and medicine. **The aim** of the study was to determine the systematic affiliation of trematode larvae in fish of the family *Percidae* from Lake Veroyarvi in the Vsevolozhsky District of the Leningrad Region and to assess the safety of objects of fishing by the presence of trematode larvae pathogenic to humans. **Materials and methods.** The material was collected in the summer and autumn of 2022–2023. 15 individuals of perch (*Perca fluviatilis*) were studied by the method of complete parasitological autopsy. Fixation and staining of the detected trematode metacercariae were performed using carmine acetic acid. The fixed samples were studied using an XSP-128-201 binocular microscope. **Results.** Metacercariae of the family *Diplostomidae* were found in the eyes of 14 out of 15 individuals of the perch. Numerous metacercariae of the *Strigeidae* family have been identified in the connective tissue membrane of the swim bladder, the parenchyma of the ovary, and mesentery of fish. Based on the analysis of the literature data, the life cycles, vertebrate and invertebrate hosts of the identified trematodes are considered. The first intermediate hosts are gastropods; fish of the *Percidae* family are the second intermediate hosts. Vertebrates, mainly birds, act as the final hosts. **Conclusion.** Larvae of trematodes of the families *Diplostomidae* and *Strigeidae*, which do not pose a danger to humans, have been identified in the organisms of fish of the *Percidae* family in Lake Veroyarvi, Leningrad Region.

Keywords: Trematode fauna, family *Diplostomidae*, family *Strigeidae*, family *Percidae*, ichthyopathology

О ТРЕМАТОДОФАУНЕ РЫБ СЕМЕЙСТВА *PERCIDAE* ОЗЕРА ВЕРОЯРВИ ЛЕНИНГРАДСКОЙ ОБЛАСТИ

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Для цитирования: Макаров Д.В., Фролова О.В. О трематодофауне рыб семейства *Percidae* озера Вероярви Ленинградской области. Российские биомедицинские исследования. 2024;9(4):61–67. DOI: <https://doi.org/10.56871/RBR.2024.17.57.010>

Поступила: 27.09.2024

Одобрена: 31.10.2024

Принята к печати: 17.12.2024

Резюме. Введение. Озера Всеволожского района Ленинградской области относят к популярным местам туристического значения, на которых ведется интенсивное любительское рыболовство. Данные о паразитофауне наиболее часто встречающихся видов рыб в рассматриваемых биоценозах имеют значение в ихтиопатологии и медицине. **Цель исследования** — определение систематической принадлежности личинок трематод

в рыбах семейства Окуневые (*Percidae*) из озера Вероярви Всеволожского района Ленинградской области и оценка безопасности объектов рыболовства по наличию в них личинок трематод, патогенных для человека.

Материалы и методы. Сбор материала проведен летом и осенью 2022–2023 гг. в полевых условиях. Методом полного паразитологического вскрытия исследовано 15 особей окуня обыкновенного (*Perca fluviatilis*). Фиксацию и окрашивание обнаруженных метацеркарий трематод проводили с использованием уксуснокислого кармина. Изучение фиксированных образцов осуществляли с использованием бинокулярного микроскопа XSP-128-201. **Результаты.** В глазах 14 из 15 особей окуня обыкновенного обнаружены метацеркарии семейства *Diplostomidae*. В соединительнотканной оболочке плавательного пузыря, паренхиме яичника и брыжейке рыб выявлены многочисленные метацеркарии семейства *Strigeidae*. На основании анализа литературных данных рассмотрены жизненные циклы, позвоночные и беспозвоночные хозяева обнаруженных трематод. Первыми промежуточными хозяевами являются брюхоногие моллюски, рыбы семейства Окуневые — вторые промежуточные хозяева. В роли окончательных хозяев выступают позвоночные животные, преимущественно птицы. **Выводы.** В организмах рыб семейства *Percidae* в озере Вероярви Ленинградской области определены личинки трематод семейств *Diplostomidae* и *Strigeidae*, не представляющие опасность для человека.

Ключевые слова: трематодофауна, семейство *Diplostomidae*, семейство *Strigeidae*, семейство *Percidae*, ихтиопатология

INTRODUCTION

One of the most clinically significant groups of parasitic organisms are trematodes (class *Trematoda*). Representatives of this class of flatworms have a variety of adaptations to parasitism and are of enormous importance in the biosphere. In addition, many types of trematodes are parasites of humans and economically significant animal species [1, 2, 12, 16].

The reservoirs of the Vsevolozhsky district of the Leningrad region are popular for tourism. Due to the spread of recreational fishing, the question arises about the safety of eating caught fish [5, 10]. Most studies on parasite fauna of fish in large bodies of water of commercial and fishery importance [8]. The parasite fauna of fish living in small lakes of the Karelian Isthmus of the Leningrad Region, both stagnant and flowing, is currently little studied. This work focuses on the study of trematodes that are important in ichthyopathology and medicine. For the first time, data on the parasite fauna of fish of the family *Percidae* in Lake Veroyarvi in the Leningrad Region are provided.

AIM

To determine the systematic affiliation of trematode larvae in the organisms of fish of the family *Percidae* in Lake Veroyarvi in the Leningrad Region and to assess the safety of fisheries based on the presence of trematode larvae pathogenic to humans.

MATERIALS AND METHODS

The basis for this work was the material collected in the summer and autumn (June to September) of 2022–2023 in

Lake Veroyarvi, Vsevolozhsky District, Leningrad Region. Collection, primary processing and study of the material were carried out in field conditions. The body length and weight of 15 common perch (*Perca fluviatilis*, family *Percidae*) were assessed. A complete parasitological dissection of the fish was performed to detect parasites of different systematic groups [3] using an MBS-10 stereomicroscope (LZOS, Russia). After the isolation of trematode larvae, they were processed in accordance with the generally accepted method [15]. Acetic carmine was used to fix and stain metacercariae [15]. The fixed samples were studied at the Department of Medical Biology of St. Petersburg State Pediatric Medical University using a binocular microscope XSP-128-201 (Optitech, China). Photo and video recording was carried out using a digital camera C510 (Levenhuk). To determine the systematic affiliation of parasites, a guide to parasites of freshwater fish was used [9]. Morphometric studies were carried out in ImageJ software. For calibration, a transmitted light micrometer object (LOMO, Russia) with a division value of 0.01 mm was used.

RESULTS AND DISCUSSION

During a parasitological dissection of 15 common perches, ranging in size 93 to 180 mm, weighing 9 to 89 g, larvae of the family *Diplostomidae* were found in eyes of 14 individuals: the genus *Diplostomum* (Fig. 1, 2) and the genus *Tylodelphys* (Fig. 3).

To determine the systematic classification of trematode metacercariae, the number, location, and shape of calcareous bodies (elements of the secondary excretory system) were taken into account [15]. Detection of calcareous bodies

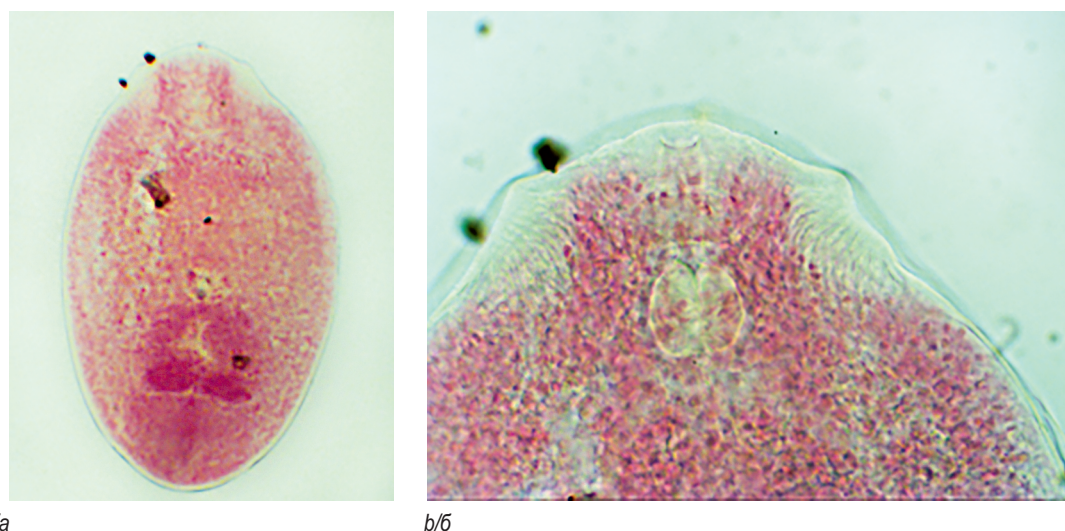


Fig. 1. Metacercaria of *Diplostomum* sp. from the eye of a perch, Lake Veroyarvi, Leningrad Region; stained with acetic carmine: a — general morphology, $\times 10$ objective; b — anterior end of the body, $\times 40$ objective (photo by Makarov D.V. — here and below)

Рис. 1. Метациркария *Diplostomum* sp. из глаза окуня обыкновенного, озеро Вероярви, Ленинградская область; окраска — уксуснокислый кармин: а — общая морфология, объектив $\times 10$; б — передний конец тела, объектив $\times 40$ (фото Макарова Д.В. — здесь и далее)

is possible during observation *in vivo* and in unstained preparations (Fig. 2).

According to literature sources [10], representatives of the family *Diplostomidae* are the most common fish parasites that cause trematodosis. These trematodes are characterized by complex life cycles, including development with a change of three hosts: two intermediate and one definitive. Mature *Diplostomidae* parasitize in the digestive system of birds, while metacercariae (one of the larval stages) live in the body of fish or amphibians. The development of parthenites of these trematodes occurs inside the body of the mollusc [13].

Parasitism of the genera *Diplostomum* and *Tylodelphys* of the family *Diplostomidae* in the eyes of fish has a negative effect on functioning of the visual organ and modifies feeding behavior [21, 26]. It is known that the presence of metacercariae of various species of the genus *Diplostomum* in the eye lens leads to development of parasitic cataracts (diplostomosis) in fish. Metacercariae parasitism in the eyes of young fish is especially dangerous. This parasite causes significant harm to fish farming.

Unlike the metacercariae of *Diplostomum*, the metacercariae of species of the genus *Tylodelphys* are localized in the vitreous body and have significant mobility. Parasitism of *Tylodelphys* metacercariae in the vitreous body does not result in the development of parasitic cataracts in fish. However, due to ability to actively move inside the eye, *Tylodelphys* metacercariae can change the behavior of their intermediate hosts depending on the day time, which is important for implementation of



Fig. 2. Metacercaria of *Diplostomum* sp. from the eye of a perch, Lake Veroyarvi, unstained preparation, $\times 10$ objective

Рис. 2. Метациркария *Diplostomum* sp. из глаза окуня, озеро Вероярви, неокрашенный препарат, объектив $\times 10$

the parasite's life cycle [26]. Infected fish lose an ability to orient themselves normally in space and become easy prey for the final host.

In our study, the work was carried out in field conditions, which allowed us to study the eyes of fish with live larvae. In the vitreous body, mobile metacercariae were found, which was recorded during video filming (Fig. 3 — frame from the video record).

Results of the study indicate a high level of infected fish of the family *Percidae* with larvae of trematodes of the family *Diplostomidae* and are consistent with data obtained

during the study of other reservoirs of the Leningrad Region in 2005–2023 [8, 10]. Despite the large number of larvae in the eyes, they were not found in brain of fish. However, according to literary data, the brain is one of the most affected organs after the eyes [18, 19, 24]. Metacercariae parasitism in the eyes of fish (especially young fish) can cause their death. However, representatives of the genera *Diplostomum* and *Tylodelphys* do not pose any danger to humans.

Numerous (several dozen) metacercariae of the family *Strigeidae* were found in the connective tissue membrane of the swim bladder (Fig. 4, a) of three individuals of *Perca fluviatilis*, in parenchyma of the ovary (Fig. 4, b) of one fish, and in mesentery of two individuals. The larvae of trematodes of the family *Strigeidae* are often enclosed

in thick-walled capsules of complex structure, with a cartilaginous or gelatinous consistency. Mechanical extraction of metacercariae from such capsules for the purpose of research is difficult [3].

The life cycle of most trematodes of the family *Strigeidae* includes three hosts: a definitive host and two intermediate hosts [14]. The first intermediate hosts are gastropods, the second are various invertebrates (molluscs, some annelids) and vertebrates including fish. The final hosts are vertebrates, mainly birds. Sexually mature individuals of these trematodes live in their bodies. Some representatives of the family, for example, *Alaria* spp., include a fourth (reservoir) host and an additional stage, mesocercaria, in the life cycle [4]. In this case, the reservoir host may be a human [17, 20, 22]. The representatives of the family *Strigeidae* that we found and identified have no medical significance, but the presence of parasites of the families *Diplostomidae* and *Strigeidae* may affect the ichthyopathological condition of fish, the organoleptic properties of fish raw materials and, accordingly, the quality of fish products for human nutrition.

According to the literature, metacercariae of trematodes of the *Paracoenogonimus ovatus* spp. of the family *Cyathocotylidae* [11], the *Metorchis bilis* spp. of the family *Opisthorchiidae* [7] and *Clinostomum complanatum* spp. of the family *Clinostomidae* [6] are found in the fish body of the family *Percidae*, which are pathogenic for humans. In our study, larvae of these species were not detected.

The first intermediate hosts of the trematode *Paracoenogonimus ovatus* are molluscs of the genus *Viviparus*, the second are various species of fish, and the final hosts are predatory and fish-eating birds, as well as some mammals,

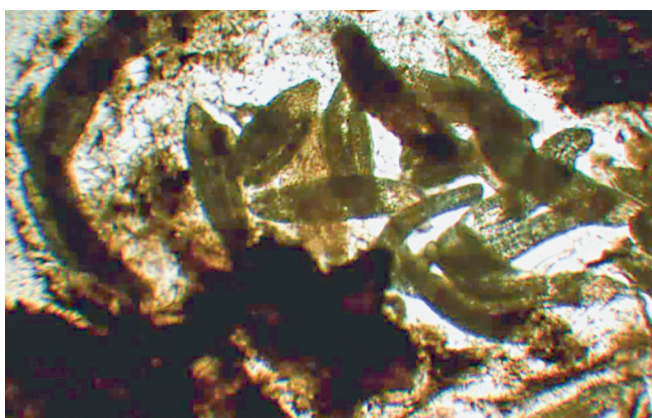
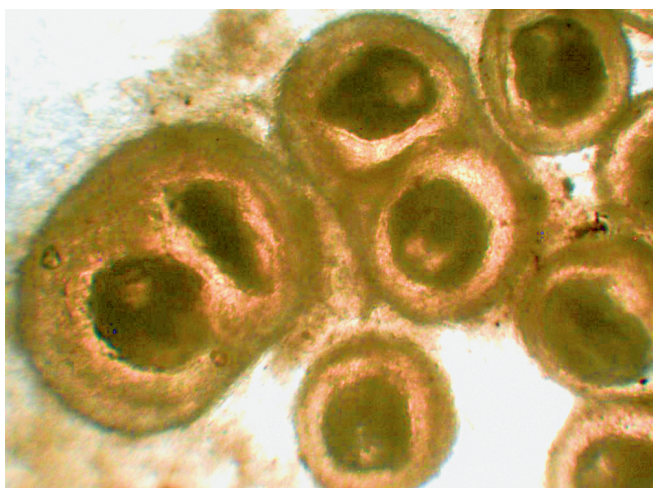
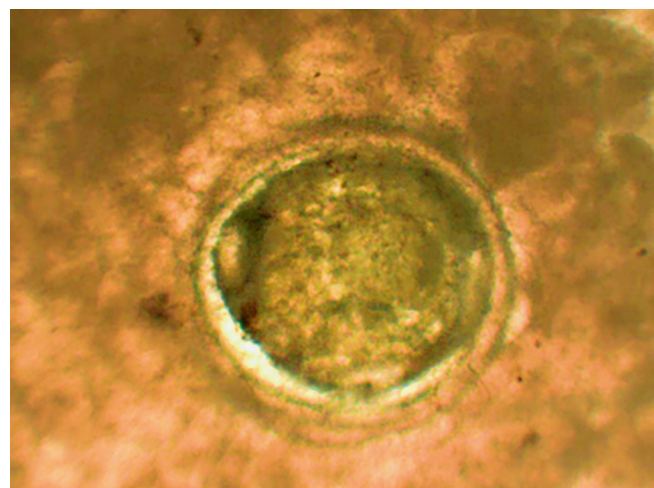


Fig. 3. Metacercariae of *Tylodelphys* sp. from the vitreous body of the eye of a perch (still from a video recording)

Рис. 3. Метациркаррии *Tylodelphys* sp. из стекловидного тела глаза окуня обыкновенного (кадр из видеозаписи)



a/a



b/b

Fig. 4. Metacercariae of the *Strigeidae* family in the tissues of the internal organs of the perch: a — from the wall of the swim bladder in the connective tissue membrane; b — from the ovarian tissue

Рис. 4. Метациркаррии семейства *Strigeidae* в тканях внутренних органов окуня обыкновенного: а — из стенки плавательного пузыря в соединительнотканной оболочке; б — из ткани яичника

including humans [25]. The first intermediate hosts of the *Metorchis bilis* spp. are molluscs of the family *Bithyniidae*, the second intermediate hosts are fish (mainly the family *Cyprinidae*), the final hosts are vertebrates that feed on fish (birds, mammals), and humans can also act as a final host [23]. The larvae of the *Clinostomum complanatum* spp. are found in fish of the family *Percidae*. The first intermediate host of the parasite are freshwater gastropods (pond snails of the genus *Lymnaea*, etc.). The final hosts are many species of fish-eating birds (herons, etc.), in which sexually mature helminths are localized in the pharynx, and in some cases, mammals and humans [6].

CONCLUSION

1. In tissues and organs of fish of the family *Percidae* from Lake Veroyarvi in the Vsevolzhsky district of the Leningrad region, trematode larvae of the families *Diplostomidae* and *Strigeidae* were found.

2. The most common parasites of a perch are representatives of the family *Diplostomidae*, found in 14 out of 15 individuals.

3. The study did not identify any trematode species that are dangerous to humans.

ADDITIONAL INFORMATION

Author contribution. Thereby, all authors made a substantial contribution to the conception of the study, acquisition, analysis, interpretation of data for the work, drafting and revising the article, final approval of the version to be published and agree to be accountable for all aspects of the study.

Competing interests. The authors declare that they have no competing interests.

Funding source. This study was not supported by any external sources of funding.

Experiments with animals were carried out in accordance with international rules (Directive 2010/63/EU of the European Parliament and of the Council of the European Union of September 22, 2010 on the protection of animals used for scientific purposes).

ДОПОЛНИТЕЛЬНАЯ ИНФОРМАЦИЯ

Вклад авторов. Все авторы внесли существенный вклад в разработку концепции, проведение исследования и подготовку статьи, прочли и одобрили финальную версию перед публикацией.

Конфликт интересов. Авторы декларируют отсутствие явных и потенциальных конфликтов интересов, связанных с публикацией настоящей статьи.

Источник финансирования. Авторы заявляют об отсутствии внешнего финансирования при проведении исследования.

Эксперименты с животными проводили в соответствии с международными правилами (Директивой 2010/63/EU Европейского парламента и Совета Европейского союза от 22 сентября 2010 года по охране животных, используемых в научных целях).

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UDC 612.141
DOI: 10.56871/RBR.2024.74.45.011

A NEW MINIMALLY INVASIVE METHOD FOR MEASURING BLOOD PRESSURE IN THE CAUDAL VENTRAL ARTERY IN RATS — EVALUATION

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For citation: Belyanina EV, Ovsepyan AA, Pchelintseva EO, Garanova VN, Lykov MV. A new minimally invasive method for measuring blood pressure in the caudal ventral artery in rats — evaluation. Russian Biomedical Research. 2024;9(4):68–73. DOI: <https://doi.org/10.56871/RBR.2024.74.45.011>

Received: 14.10.2024

Revised: 25.11.2024

Accepted: 17.12.2024

Abstract. Introduction. Blood pressure is an important hemodynamic indicator characterizing the state of the cardiovascular system, which plays an important role in the experimental modeling of pathological conditions associated with impaired hemodynamics (for example, blood loss or hemorrhagic shock) in biological test systems. In modern practice, invasive and non-invasive blood pressure measurement methods are used in conducting research. However, if the objectives of the study include the registration of blood pressure in modeling pathological conditions associated with impaired hemodynamic processes, such as hemorrhagic shock, then with existing methods of measuring blood pressure, obtaining accurate, reliable data is often difficult. **The aim of the study** was to develop a minimally invasive, continuous method for recording blood pressure in the caudal artery in rats, both under anesthesia and without it, including without the use of anticoagulants; comparative analysis of various blood pressure measurement techniques in intact animals, in experimental modeling of hemorrhagic shock. **Materials and methods.** 110 male rats, Sprague Dawley, weighing 360 ± 20 g were involved in the work. During the experiment, a minimally invasive method of blood pressure registration was developed, surgical modeling of hemorrhagic shock was performed, and a comparative analysis of various blood pressure measurement methods was carried out. **The results of the study.** It was found that the developed method can be considered accurate and low-traumatic, allowing fast, continuous blood pressure measurements in real time, both under general anesthesia and without it, without the use of anticoagulants. The accuracy of measurements does not depend on the nature, complexity of the experimental study and the general hemodynamic picture of the animal.

Keywords: blood pressure, caudal ventral artery, hemorrhagic shock, heparinized saline solution, biological test system

НОВЫЙ МАЛОИНВАЗИВНЫЙ МЕТОД ИЗМЕРЕНИЯ АРТЕРИАЛЬНОГО ДАВЛЕНИЯ В ХВОСТОВОЙ ВЕНТРАЛЬНОЙ АРТЕРИИ У КРЫС — ОЦЕНКА

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Для цитирования: Белянина Е.В., Овсепян А.А., Пчелинцева Е.О., Гаранова В.Н., Лыков М.В. Новый малоинвазивный метод измерения артериального давления в хвостовой вентральной артерии у крыс — оценка. Российские биомедицинские исследования. 2024;9(4):68–73. DOI: <https://doi.org/10.56871/RBR.2024.74.45.011>

Поступила: 14.10.2024

Одобрена: 25.11.2024

Принята к печати: 17.12.2024



Резюме. Введение. Артериальное давление (АД) — важный гемодинамический показатель, характеризующий состояние сердечно-сосудистой системы, выполняющий важную роль при экспериментальном моделировании патологических состояний, связанных с нарушением гемодинамики (например, кровопотери или геморрагического шока) в биологических тест-системах. В современной практике при проведении исследований применяются инвазивные и неинвазивные методы измерения АД. Однако если в задачи исследования входит регистрация АД при моделировании патологических состояний, связанных с нарушением процессов гемодинамики, таких как геморрагический шок, то с существующими методами измерения АД получение точных, достоверных данных зачастую бывает затруднительно. **Цель исследования** — разработка малоинвазивного, непрерывного метода регистрации АД в хвостовой артерии у крыс, как под анестезией, так и без нее, в том числе без использования антикоагулянтов; сравнительный анализ различных методик измерения АД у интактных животных, при экспериментальном моделировании геморрагического шока. **Материалы и методы.** К работе привлечено 110 самцов крыс, Sprague Dawley, весом 360 ± 20 г. В процессе эксперимента разработан малоинвазивный метод регистрации АД, выполнено хирургическое моделирование геморрагического шока, проведен сравнительный анализ различных методик измерения АД. **Результаты исследования.** Установлено, что разработанный метод можно считать точным и малотравматичным, позволяющим выполнять быстрые, непрерывные измерения АД в режиме реального времени, как под общей анестезией, так и без нее, без использования антикоагулянтов. Точность измерений не зависит от характера, сложности экспериментального исследования и общей гемодинамической картины животного.

Ключевые слова: артериальное давление, хвостовая вентральная артерия, геморрагический шок, гепаринизированный физиологический раствор, биологическая тест-система

INTRODUCTION

According to generally accepted methods, invasive measurement of arterial pressure (AP) in rats is carried out directly in isolated vessels (aorta, femoral or carotid arteries) or in the heart cavity using “liquid” and “non-liquid” methods [2, 3, 4].

The “liquid” method of recording blood pressure is based on the placement of a catheter or cannula into a “dedicated” vessel, connected via a liquid line filled with heparinized saline to a pressure recording sensor. This system allows for the most accurate measurement of arterial pressure, however, under certain conditions (catheter flushing), heparinized saline solution can enter the animal’s body, which in some cases is unacceptable or critical for experimental research [1–7].

To measure blood pressure using the “non-liquid” method, a micro pressure sensor is used. It consists of a sensitive sensor part connected to the main unit of the pressure measurement system, which allows for quick measurements without introducing anticoagulants into the animal’s body [2, 3].

When registering blood pressure using invasive methods, surgical isolation of a vessel is required.

In turn, among non-invasive methods of measuring blood pressure, the most widely used is the electroplethysmographic (cuff) method associated with the caudal artery (tail-cuff) of rats. This method is based on the same principle as the measurement of blood pressure in humans by the Riva–Rocci method [1–3]. Compared to invasive methods,

the Riva–Rocci method does not require anesthesia for animals, including reuse, although it is less accurate. For example, in the hemorrhagic shock (HS) model, with exsusion of more than 40% of the circulating blood volume (CBV), blood pressure is not recorded by this method).

Thus, in preclinical practice, the task of finding and developing a minimally invasive method for recording arterial pressure in the body of rats remains relevant.

AIM

The aim of our study is to develop a minimally invasive, continuous method for recording blood pressure in the caudal artery in rats, both with and without anesthesia, without use of anticoagulants. To provide a comparative analysis of various methods for measuring blood pressure in intact animals (without anesthesia and with injection anesthesia), including experimental modelling of HS.

MATERIALS AND METHODS

Animals. 110 male rats, Sprague Dawley, weighing 360 ± 20 g, SPF category, obtained from the Scientific and Production Enterprise “Nursery of Laboratory Animals” of the branch of the Institute of Bioorganic Chemistry of the Russian Academy of Sciences, Pushchino, were used as biological test systems in the experiment. The maintenance, care of animals and experimental modelling were carried out in accordance with international European bioethical standards, Russian ethical standards for the maintenance

and handling of laboratory animals, and the norms and rules of the "Policy for Working with Animals of JSC GENERIUM".

Equipment. To record arterial pressure in rats, modules and sensors of the MP150WSW electrophysiological research apparatus (BIOPAC Systems Inc., USA) were used:

- 1) minimally invasive and non-liquid methods — MPMS100 unit and TSD175A micro pressure sensor;
- 2) cuff method — NIBP200A2 module and RXTCUF-SENSOR pressure sensor;
- 3) liquid method — DA100C module and TSD104A invasive pressure sensor.

Study design. The experiment consisted of four stages.

Stage I — The development of a minimally invasive method for recording blood pressure in the caudal artery in rats (n=10).

Stage II — A comparative analysis of various methods for recording blood pressure in rats without anesthesia: 1) minimally invasive method (n=10); 2) cuff method (n=10).

Stage III — A comparative analysis of various methods of recording blood pressure in rats with anesthesia (n=40): 1) minimally invasive method (n=10); 2) cuff method (n=10); 3) liquid method (n=10); 4) non-liquid method (n=10).

Stage IV — A comparative analysis of various methods of recording blood pressure in rats in the HS model (n=40): 1) minimally invasive method (n=10); 2) cuff method (n=10); 3) liquid method (n=10); 4) non-liquid method (n=10).

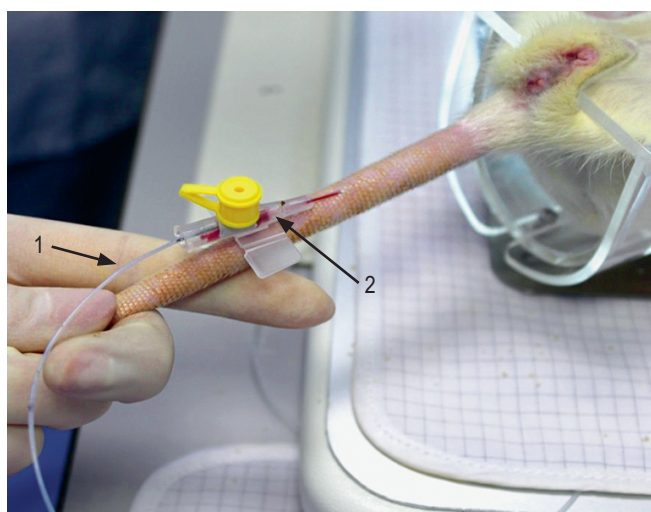
Stage I — the development of a minimally invasive method for recording blood pressure in the caudal artery of rats

The development of this method for recording arterial pressure in rats is based on the technique of catheterization of the caudal artery and placement of a micro pressure sensor in the vessel.

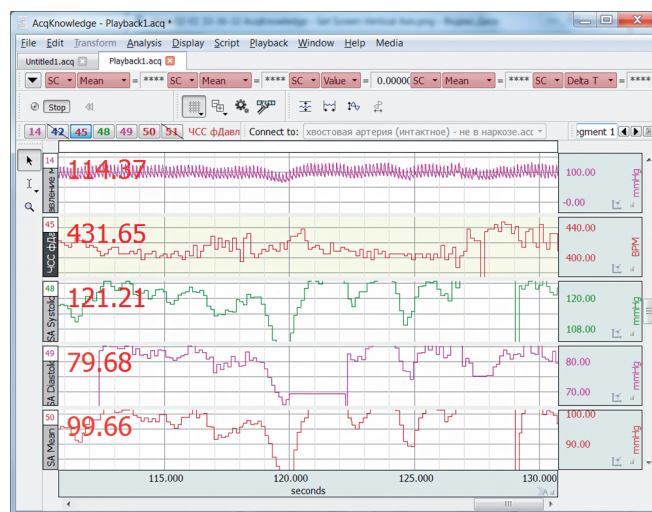
To insert a microsensor, an animal was placed in the spinal position on a heated operating panel (Medi-heat V500DVsta (PecoServices LTD, UK)) and the caudal artery was visualized by gently massaging the tail. Next, the caudal artery was catheterized using a peripheral intravenous catheter (G24/26 intravenous catheter (HELMFLON®ptfe, Germany)). The catheter was inserted into the vessel at an acute angle (~10–15°); when inserted correctly, blood appeared in the catheter port. In this case, the artery was clamped proximal to the puncture site to stop bleeding. Then the needle was removed from the catheter, a pressure microsensor was inserted into the lumen of the catheter, after which the clamp was removed from the artery and blood pressure was recorded (Fig. 1).

Stage II — a comparative analysis of various methods for recording blood pressure in rats without anesthesia

Recording of blood pressure in the study without anesthesia was carried out in rats using both a minimally inva-



a/a



b/6

Fig. 1. Minimally invasive method of recording blood pressure in the caudal artery in an intact animal without anesthesia: **a** — technique of placing a catheter and a pressure sensor into the caudal artery (1 — intravenous catheter; 2 — micro pressure sensor TSD175A); **b** — schedule of blood pressure registration (1 — systolic blood pressure, mmHg; 2 — diastolic blood pressure, mmHg; 3 — average blood pressure, mmHg)

Рис. 1. Малоинвазивный метод регистрации артериального давления (АД) в хвостовой артерии у интактного животного без анестезии: **a** — техника постановки катетера и микродатчика давления в хвостовую артерию (1 — внутривенный катетер; 2 — микродатчик давления TSD175A); **б** — график регистрации АД (1 — АД систолическое, мм рт.ст.; 2 — АД диастолическое, мм рт.ст.; 3 — АД среднее, мм рт.ст.)

sive method and a cuff method in the caudal artery area of the middle third of a tail.

Stage III — comparative analysis of various methods for recording blood pressure in rats under anesthesia.

Liquid, non-liquid, and minimally invasive methods were used to measure blood pressure in rats under anesthesia.

Injectable zoletil-xylazine anesthesia was used for general anesthesia when preparing an animal for work.

Femoral artery catheterization was performed when recording blood pressure using non-liquid and liquid methods.

Stage IV — comparative analysis of various methods for recording blood pressure in rats in the HS model

When recording blood pressure in rats in a HS model, the researchers performed experimental modelling of hemorrhagic shock using the «fixed volume» method without introducing heparinized saline into the body. To perform exfusion, arteriosection of the femoral artery was performed with subsequent controlled exfusion. The exfusion was 2.8–3.0% of the animal’s weight, which corresponded to 40–50% of the total circulating blood volume. Ringer–Locke solution was used for reperfusion. Blood pressure was measured: 1) before exfusion; 2) during exfusion; 3) in the time interval from exfusion to reperfusion; 4) during reperfusion; 5) 10 minutes after reperfusion.

Minimally invasive, cuff, non-liquid and liquid methods were used to record blood pressure.

In the HS model, exfusion and measurement of blood pressure by non-liquid and liquid methods were performed in one femoral artery, since additional isolation of the second femoral artery resulted in trauma to the animal and significantly increased labor costs and time.

Thus, in these variants of blood pressure measurement, its monitoring was possible only during the periods: 1) during exfusion (in our case, at 5, 10, 15 and 20 minutes, which corresponded to 40, 70, 90 and 100% of the calculated exfusion volume); 2) in the time interval from exfusion to reperfusion; 3) during and after reperfusion.

Blood pressure recording using the minimally invasive and cuff method during the HS modeling was performed continuously.

Statistical processing. The data obtained during the work were checked for normal distribution. Statistical analysis included calculation of the mean value, standard deviation. To compare values, a parametric indicator was used — Student’s t-test, since the sample corresponded to the law of normal distribution. Differences were considered statistically significant at $p < 0.05$. Statistical data processing was performed using IBM SPSS Statistics (23 v (IBM SPSS Statistics 23) (IBM Corp., USA)).

RESULTS AND DISCUSSION

During the experiment, a minimally invasive method for recording arterial pressure in the caudal artery of rats was developed, and a comparative analysis of blood pressure with existing methods for recording arterial pressure in intact animals without anesthesia, with anesthesia, and in the HS model was conducted.

Comparative analysis of various methods of recording blood pressure in rats with and without anesthesia. No statistically significant differences were found when recording blood pressure in animals with and without anesthesia (Table 1).

Comparative analysis of various methods of recording blood pressure in dynamics during experimental modelling of HS. The use of the cuff method in the HS model was difficult, since when exfoliating more than 40% of the calculated volume, the equipment did not record blood pressure.

The use of the non-liquid method allowed reliable and accurate measurement of BP throughout the experiment, but at certain periods: 1) during exfusion (in our case, at 5, 10, 15 and 20 minutes, which corresponded to 40, 70, 90 and 100% of the calculated exfusion volume); 2) in the time interval from exfusion to reperfusion; 3) during and after reperfusion. To conduct continuous recording of BP

Table 1

Indicators of average blood pressure in animals without anesthesia and under anesthesia

Таблица 1

Показатели среднего артериального давления у животных без анестезии и под анестезией

Методы регистрации артериального давления / Blood pressure registration methods	Среднее артериальное давление, мм рт.ст., $x \pm \text{ст. откл.}$ / Average blood pressure, mmHg, $x \pm \text{standard deviation}$	
	без анестезии / without anesthesia	с анестезией / under anesthesia
Малоинвазивный метод / Minimally invasive method	92,0 $\pm$ 7,1	76,5 $\pm$ 2,7
Манжеточный метод / The cuff method	91,3 $\pm$ 6,7	72,0 $\pm$ 2,7
Жидкостный метод / The liquid method	–	76,3 $\pm$ 2,0
Безжидкостный метод / The non-liquid method	–	81,5 $\pm$ 2,2

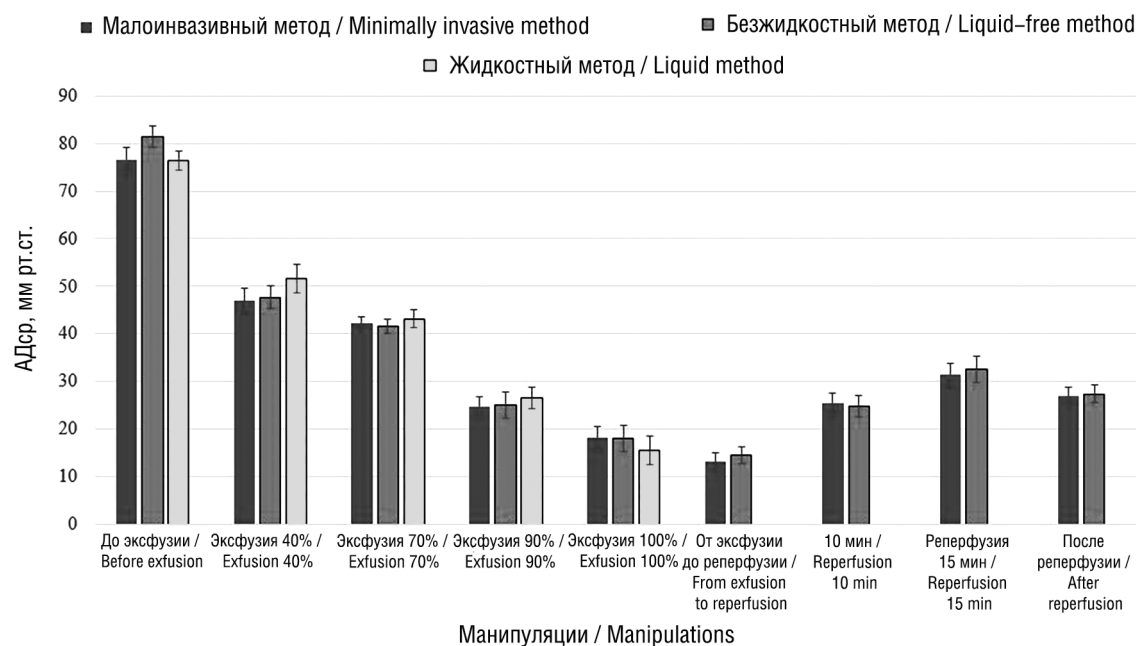


Fig. 2. Parameters of the mean pressure in rats in the CS model during registration by various method

Рис. 2. Параметры АДср у крыс в модели ГШ при регистрации различными методами

Table 2

Parameters of mean blood pressure in rats in a hemorrhagic shock model

Таблица 2

Параметры среднего артериального давления у крыс в модели геморрагического шока

Манипуляции / Manipulations	Время, мин / Time, min	%	АДср, мм рт.ст., $\bar{x} \pm \text{откл.}$ Методы измерения АД / Average blood pressure, mmHg, $\bar{x} \pm \text{standard deviation}$. Blood pressure measurement methods		
			малоинвазивный метод / minimally invasive method	жидкостный метод / the liquid method	безжидкостный метод / the non-liquid method
До эксфузии / Before exfusion	—	—	76,5 $\pm$ 2,7	76,3 $\pm$ 2,0	81,5 $\pm$ 2,2
Эксфузия / Exfusion	5	40	46,9 $\pm$ 2,6	51,6 $\pm$ 2,9	47,7 $\pm$ 2,4
	10	70	42,3 $\pm$ 1,3	43,1 $\pm$ 1,9	41,6 $\pm$ 1,5
	15	90	24,7 $\pm$ 2,1	26,5 $\pm$ 2,2	25,1 $\pm$ 2,8
	20	100	18,0 $\pm$ 2,4	18,5 $\pm$ 2,9	18,0 $\pm$ 2,7
От эксфузии до реперфузии / From exfusion to reperfusion	30	—	13,2 $\pm$ 1,7	—	14,5 $\pm$ 1,7
Реперфузия / Reperfusion	10	—	25,3 $\pm$ 2,3	—	24,8 $\pm$ 2,2
	15	—	31,2 $\pm$ 2,4	—	32,5 $\pm$ 2,7
После реперфузии / After reperfusion	10	—	26,9 $\pm$ 1,8	—	27,4 $\pm$ 1,9

Примечание: % — процент от расчетного объема эксфузии.

Note: % is a percentage of the estimated volume of exfusion.

using this method, additional surgical intervention was required to isolate another femoral artery.

Recording of blood pressure using the liquid method was only possible during the exfusion period, since as the volume of exfusion increased and blood viscosity increased, thrombosis of the catheter occurred, which led to data distortion.

When recording BP using a minimally invasive method, continuous monitoring of BP parameters was performed during the experiment, and correct data were obtained throughout all stages of the work on the HS model.

The parameters of middle BP in rats in the HS model when recorded using various methods are shown in Figure 2 and Table 2.

CONCLUSION

Thus, the developed minimally invasive method of recording blood pressure, in comparison with generally accepted methods, has the following characteristics.

1. It is minimally invasive, continuous, does not require surgical intervention;
2. It allows measurements to be taken on animals, both with and without general anesthesia;
3. It allows recording blood pressure without the use of anticoagulants;
4. It allows real-time blood pressure measurements, regardless of the animal's overall hemodynamic picture.

ADDITIONAL INFORMATION

Author contribution. Thereby, all authors made a substantial contribution to the conception of the study, acquisition, analysis, interpretation of data for the work, drafting and revising the article, final approval of the version to be published and agree to be accountable for all aspects of the study.

Competing interests. The authors declare that they have no competing interests.

Funding source. This study was not supported by any external sources of funding.

Experiments with animals were carried out in accordance with international rules (Directive 2010/63/EU of the European Parliament and of the Council of the European Union of September 22, 2010 on the protection of animals used for scientific purposes).

ДОПОЛНИТЕЛЬНАЯ ИНФОРМАЦИЯ

Вклад авторов. Все авторы внесли существенный вклад в разработку концепции, проведение исследования и подготовку статьи, прочли и одобрили финальную версию перед публикацией.

Конфликт интересов. Авторы декларируют отсутствие явных и потенциальных конфликтов интересов, связанных с публикацией настоящей статьи.

Источник финансирования. Авторы заявляют об отсутствии внешнего финансирования при проведении исследования.

Эксперименты с животными проводили в соответствии с международными правилами (Директивой

2010/63/EU Европейского парламента и Совета Европейского союза от 22 сентября 2010 года по охране животных, используемых в научных целях).

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UDC 611.018+591.86+612.741+616-003.93
DOI: 10.56871/RBR.2024.37.29.012

COMPARATIVE FEATURES OF DIFFERENT TYPES OF MUSCLE TISSUE

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For citation: Skvortsova MYu, Petyalina MV, Apraksina NK, Kozhukhar VG. Comparative features of different types of muscle tissue. Russian Biomedical Research. 2024;9(4):74–85. DOI: <https://doi.org/10.56871/RBR.2024.37.29.012>

Received: 23.09.2024

Revised: 06.11.2024

Accepted: 17.12.2024

Abstract. Muscle tissues are widespread in the human organism. Since their main feature is ability to contractility, their sarcoplasm (cytoplasm) contains a well-developed contractile apparatus, which can have its specific characteristics in different muscle tissues. Muscle tissues differ from each other not only in their localization and structural characteristics, but also in their origin, as well as their ability to regenerate. There are two main classifications of muscle tissues: morphological one taking into account the peculiarities of the structure of the contractile apparatus, and histogenetic one taking into account the origin of tissue. According to the morphofunctional classification, muscle tissues are divided into striated (cross-striated) and smooth. In turn, striated tissues are divided into skeletal and cardiac. The main tissue element of skeletal muscle tissue is myosymplast, which is formed during embryogenesis as a result of the fusion of myoblast cells. The main tissue element of cardiac muscle tissue are cells — cardiomyocytes, which during embryogenesis connect with each other to form fibers. The main tissue element of smooth muscle tissue are cells — smooth myocytes, which during embryonic development can migrate from different rudiments. Muscle tissue of internal organs and vessels has a mesenchymal origin, the muscles of the iris of the eyeball are neural, myoepithelial cells of glands are ectodermal. Despite the fact that the structure and origin of the muscle tissues are well studied, in recent years a lot of information has appeared from the field of molecular biology concerning their development in embryogenesis. In addition the issues of regenerative capabilities of different types of muscle tissues remain debatable. Skeletal muscle tissue shows the greatest regenerative abilities. Its regeneration is provided by satellite cells (myosatellitocytes), which isolate themselves on the surface of skeletal muscle fiber during intrauterine development, without fusing with it and preserving regenerative abilities due to the protein Pax7 expressed by myoblasts that are the precursors of myosatellitocytes. Until now, there is no unambiguous data on the regenerative capabilities of cardiomyocytes. There is controversial information in the literature about the possible role of cells c-kit+ as cardiac stem cells. However, they cannot provide full-fledged regeneration due to their small quantity in the myocardium. Smooth myocytes of blood vessels and internal organs are capable of reparative regeneration, which is provided by cells entering mitosis when smooth muscle tissue is damaged. But the question remains not fully clarified, which cells are capable of performing this function. Clarification of issues related to the regeneration of various types of muscle tissue may be of great importance for practical medicine.

Keywords: muscle tissues, structural and functional unit, the unit of contractility, muscle contraction, ultrastructural features, the motor unit, regenerative ability, histogenetic classification



СРАВНИТЕЛЬНЫЕ ОСОБЕННОСТИ РАЗЛИЧНЫХ ВИДОВ МЫШЕЧНЫХ ТКАНЕЙ

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Для цитирования: Скворцова М.Ю., Петялина М.В., Апраксина Н.К., Кожухарь В.Г. Сравнительные особенности различных видов мышечных тканей. Российские биомедицинские исследования. 2024;9(4):74–85. DOI: <https://doi.org/10.56871/RBR.2024.37.29.012>

Поступила: 23.09.2024

Одобрена: 06.11.2024

Принята к печати: 17.12.2024

Резюме. Мышечные ткани широко распространены в организме человека. Поскольку главной их особенностью является способность к сократимости, в их саркоплазме (цитоплазме) находится хорошо развитый сократительный аппарат, который в разных мышечных тканях может иметь свои особенности. Мышечные ткани отличаются друг от друга не только своей локализацией и морфологическими характеристиками, но и происхождением, а также способностью к регенерации. Существуют две основные классификации мышечных тканей: морфологическая, учитывающая особенности строения сократительного аппарата, и гистогенетическая, учитывающая происхождение. В соответствии с морфофункциональной классификацией мышечные ткани делятся на исчерченные (поперечно-полосатые) и гладкие. В свою очередь, исчерченные подразделяются на скелетную и сердечную. Главным тканевым элементом скелетной мышечной ткани является миосимпласт, который в ходе эмбриогенеза образуется в результате слияния клеток миобластов. Главным тканевым элементом сердечной мышечной ткани являются клетки — кардиомиоциты, в ходе эмбриогенеза соединяющиеся друг с другом с формированием волокон. Главным тканевым элементом гладкой мышечной ткани являются клетки — гладкие миоциты, которые в ходе эмбрионального развития могут выселяться из разных зачатков. Мышечная ткань внутренних органов и сосудов имеет мезенхимальное происхождение, мышцы радужной оболочки глазного яблока — нейральное, миоэпителиальные клетки желез — эктодермальное. Несмотря на то что строение и происхождение мышечных тканей хорошо изучено, в последние годы появилось много информации в области молекулярной биологии, касающейся их развития именно в эмбриогенезе. Кроме того, дискуссионными остаются вопросы регенеративных возможностей различных видов мышечных тканей. Наибольшие регенеративные способности проявляет скелетная мышечная ткань. Регенерацию ее обеспечивают клетки-сателлиты (миосателлитциты), которые обособляются на поверхности скелетного мышечного волокна в процессе внутриутробного развития, не сливаясь с ним и сохраняя регенеративный потенциал за счет белка Pax7, экспрессируемого миобластами — предшественниками миосателлитцитов. До настоящего времени не имеется однозначных данных о регенеративных возможностях кардиомиоцитов. В литературе имеется спорная информация о возможной роли клеток c-kit⁺ в качестве кардиальных стволовых клеток. Однако они не могут обеспечить полноценную регенерацию, вследствие их незначительного количества в миокарде. Гладкие миоциты сосудов и внутренних органов способны к репаративной регенерации, которая обеспечивается клетками, вступающими в митоз при повреждении гладкой мышечной ткани. Но остается не до конца выясненным вопрос, какие именно клетки способны выполнять эту функцию. Уточнение вопросов, связанных с регенерацией различных видов мышечных тканей, может иметь большое значение для практической медицины.

Ключевые слова: мышечные ткани, структурно-функциональная единица, единица сократимости, мышечное сокращение, ультраструктурные особенности, двигательная единица, регенеративная способность, гистогенетическая классификация

INTRODUCTION

Muscle tissues are united by a common function — the ability to contract and the associated morphological feature (the presence of certain organelles in the cytoplasm that ensure contractility). At the same time, muscle tissues differ in the features of their contractile apparatus, origin and ability to regenerate (Fig. 1).

According to the morphofunctional classification, muscle tissues are divided into striated and smooth. Striated muscle tissues include skeletal and cardiac muscle tissues. Smooth tissues include muscle tissues of internal organs and blood vessels, muscles of the iris of the eyeball and myoepithelial cells of a number of exocrine glands.

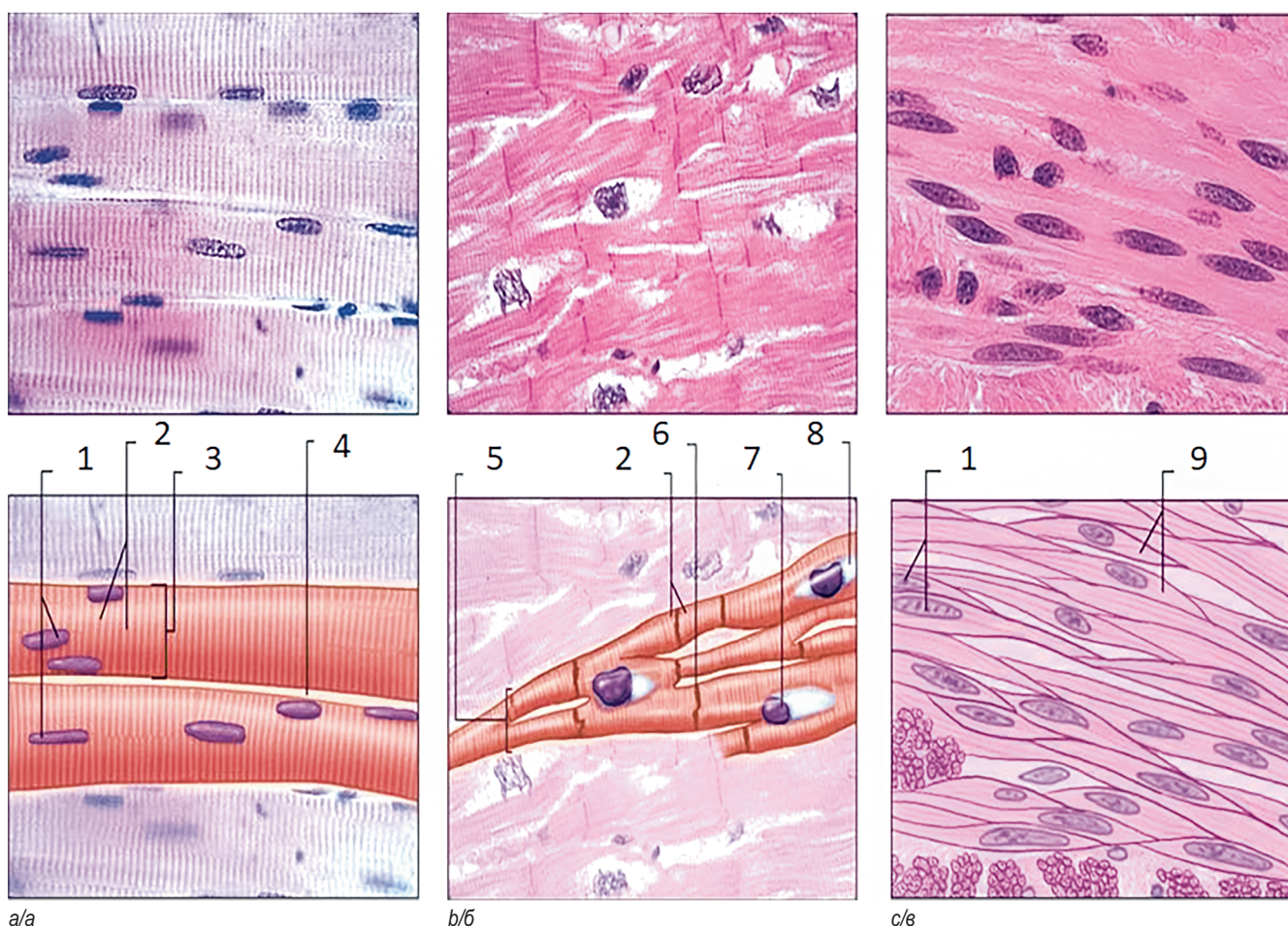


Fig. 1. The three types of muscle tissue: *a* — skeletal muscle tissue; *b* — cardiac muscle tissue; *c* — smooth muscle tissue. 1 — nuclei; 2 — striations; 3 — muscle fiber; 4 — connective tissue; 5 — anastomosis; 6 — intercalated disc; 7 — nucleus; 8 — glycogen; 9 — muscle cells [18]

Рис. 1. Три типа мышечных тканей: *а* — скелетная мышечная ткань; *б* — сердечная мышечная ткань; *в* — гладкая мышечная ткань. 1 — ядра; 2 — поперечная исчерченность; 3 — мышечное волокно; 4 — соединительная ткань; 5 — анастомоз; 6 — вставочный диск; 7 — ядро; 8 — гликоген; 9 — мышечные клетки [18]

SKELETAL MUSCLE TISSUE

Such tissue is widespread in the human body, not only muscles attached to bones, but also some organs such as the esophagus, pharynx and tongue. According to the histogenetic classification, such tissue belongs to the somatic type.

Development

The source of development of this muscle tissue is the myotomes of somites. Myotome cells migrate to the sites of skeletal muscle formation. Such cells express molecular markers Pax3 and Pax7, characteristic of myoblasts and myosatellite cells [3, 7]. Migration is controlled by the genes Pax3, Met. Then myogenic cells actively proliferate under the influence of growth factors. At this stage, myogenesis is blocked by the myogenesis repressor MyoR [17].

From the 5th week of intrauterine development, myoblasts fuse to form muscle tubes, in which myofilaments are formed, from which myofibrils are assembled. After the fusion of myoblasts, DNA synthesis and nuclear division cease. Myosimplasts grow by adding new myoblasts [7]. The nuclei are initially located in the center of the muscle tube, but as the number of myofibrils increases, they shift to the periphery. In this way, relatively mature muscle fibers are formed (Fig. 2).

This occurs from the 20th week of intrauterine development. Myoblasts are isolated on the surface of muscle fibers at the G1 stage. These are myosatellite cells. *In vivo* studies on mice it has shown that the survival and proliferation of myosatellite cells is encoded by the Pax7 protein. It also prevents their fusion into muscle fiber, preserving regenerative potential [9]. *In vitro* studies also confirm the important role of this protein in myoblast survival processes [21, 22].

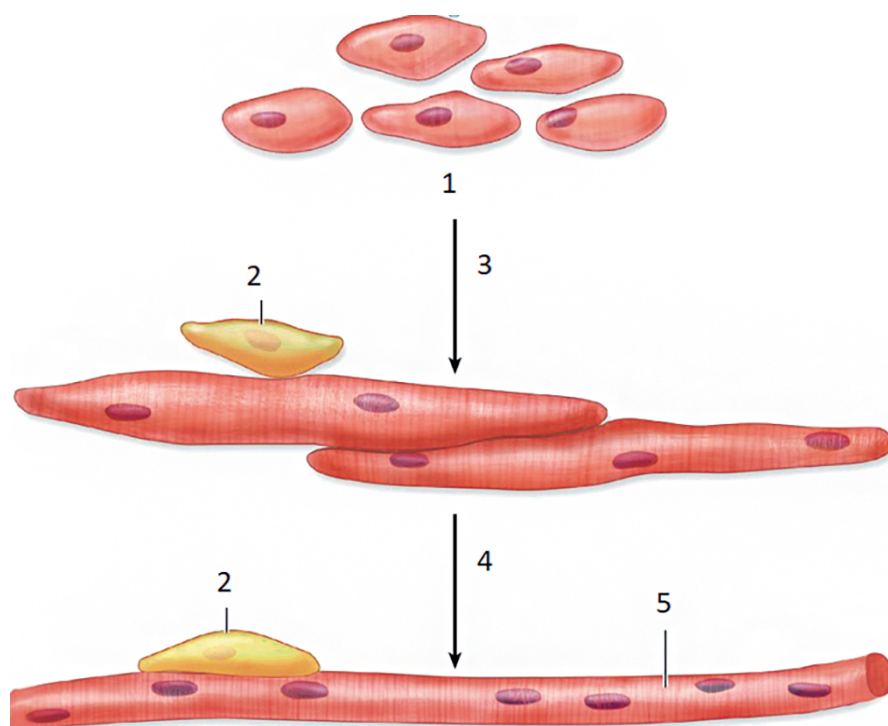
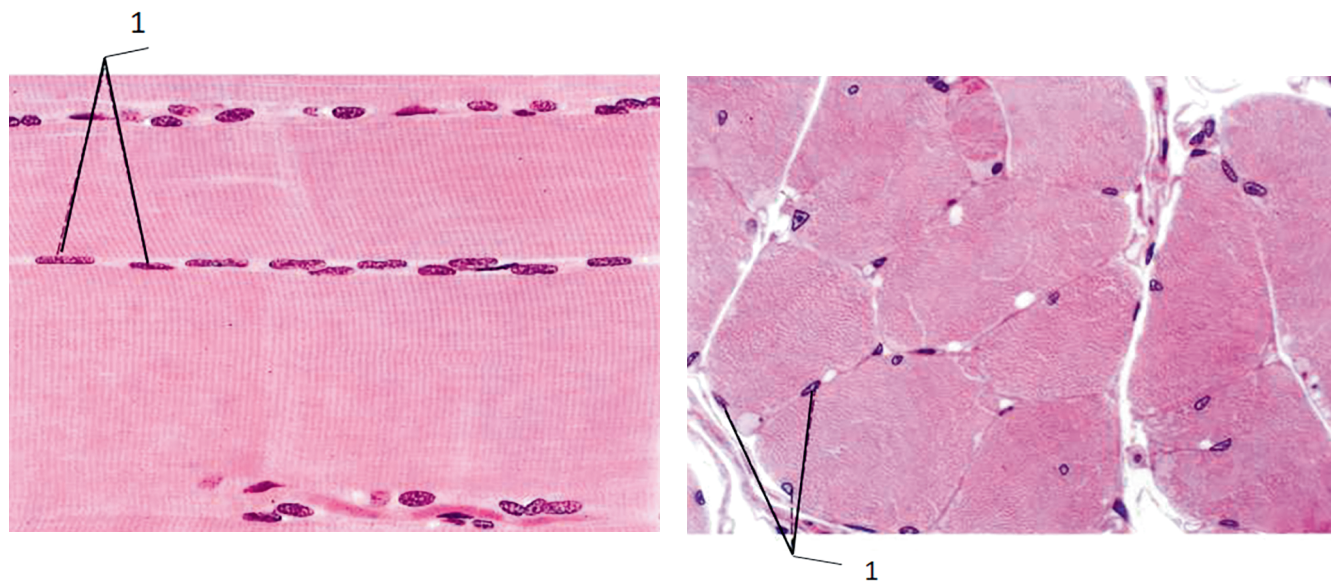


Fig. 2. Development of skeletal muscle tissue: 1 — myoblasts; 2 — myosatellitocite; 3 — myoblast fusion to form myotubules; 4 — differentiation; 5 — muscle fiber [24]

Рис. 2. Развитие скелетной мышечной ткани: 1 — миобласты; 2 — миосателлитоцит; 3 — слияние миобластов с образованием миотубул; 4 — дифференцировка; 5 — мышечное волокно [24]



a/a

b/б

Fig. 3. Skeletal muscle tissue at longitudinal (a) and cross (b) section. 1 — nuclei [4]

Рис. 3. Скелетная мышечная ткань в продольном (а) и поперечном (б) разрезе. 1 — ядра [4]

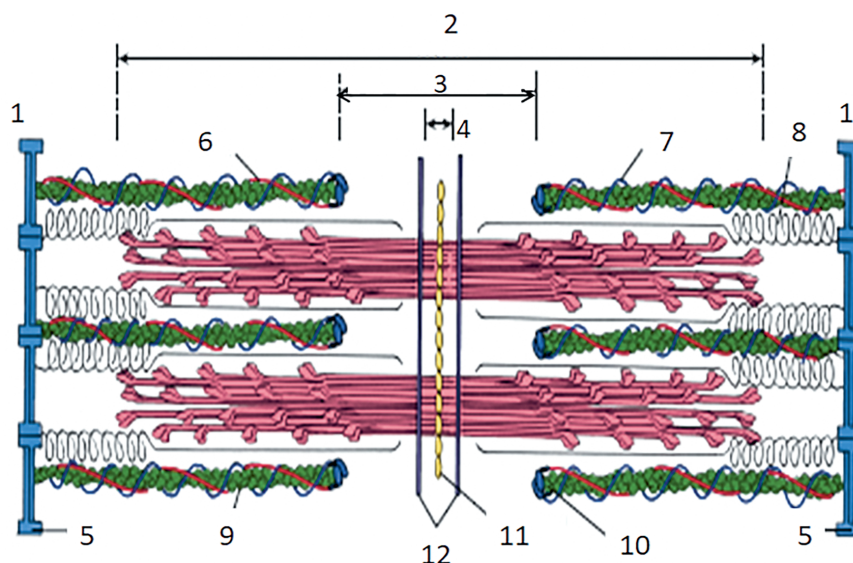


Fig. 4. Molecular structure of a sarcomere: 1 — Z-line; 2 — A-band; 3 — H-band; 4 — M-line; 5 — α -actinin; 6 — tropomyosin; 7 — nebulin; 8 — titin; 9 — actin; 10 — tropomodulin; 11 — myomesin; 12 — C-protein [23]

Рис. 4. Молекулярная структура саркомера: 1 — Z-линия; 2 — А-диск; 3 — Н-полоска; 4 — М-линия; 5 — α -актинин; 6 — тропомиозин; 7 — небулин; 8 — титин; 9 — актин; 10 — тропомодулин; 11 — миомезин; 12 — С-белок [23]

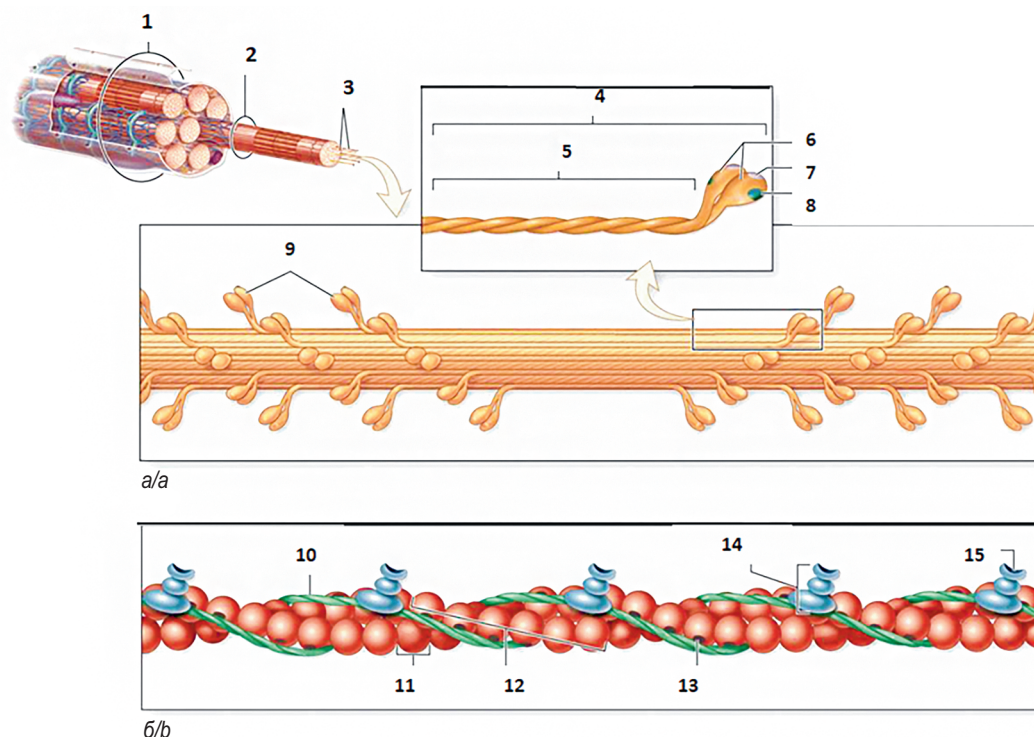


Fig. 5. Molecules composing myosin (thick — a) and actin (thin — b) filaments. 1 — muscle fiber; 2 — myofibril; 3 — myofilaments; 4 — myosin molecule; 5 — tail; 6 — heads; 7 — actin-binding site; 8 — ATPase-binding site; 9 — myosin heads; 10 — tropomyosin; 11 — G-actin; 12 — F-actin; 13 — myosin-binding site; 14 — troponin; 15 — Ca^{2+} -binding site [18]

Рис. 5. Молекулы, образующие миозиновые (толстые — а) и актиновые (тонкие — б) филаменты. 1 — мышечное волокно; 2 — миофибрилла; 3 — миофиламенты; 4 — молекула миозина; 5 — хвост; 6 — головки; 7 — актинсвязывающий участок; 8 — АТФ-связывающий участок; 9 — миозиновые головки; 10 — тропомиозин; 11 — G-актин; 12 — F-актин; 13 — миозинсвязывающий сайт; 14 — тропонин; 15 — Ca^{2+} -связывающий участок [18]

Myotubules are formed by myoblasts at the G0 stage, which have irreversibly left the cell cycle [17].

The development of skeletal muscle tissue is associated with the development of nervous tissue. During ontogenesis, it is not individual muscle fibers that develop, but motor units, represented by a motor neuron and the muscle fibers innervated by it. Thus, the development of muscle fibers is associated with the development of motor neurons [15].

Features of the structure of skeletal muscle tissue

The structural and functional unit of such tissue is the myosymplast. The cytoplasm of muscle fibers is called sarcoplasm, the plasmalemma is called sarcolemma. Each skeletal muscle fiber is represented by a myosymplast and is surrounded by a basal membrane. Between the basal membrane and the sarcolemma are myosatellite cells (Fig. 3).

The sarcoplasm of the myosymplast is characterized by a well-developed contractile apparatus. It is represented by myofibrils consisting of orderly arranged actin and myosin myofilaments. The myofibrils are located very close to each other. Each one is characterized by transverse striation associated with the alternation of isotropic (I) and anisotropic (A) disks. The disks of each myofibril are localized strictly opposite the same disks of neighboring myofibrils, due to which transverse striation of the entire muscle fiber is revealed. Anisotropic disks are represented by myosin filaments and, in an uncontracted muscle fiber, by small fragments of actin filaments. During contraction, actin filaments penetrate deeper into the spaces between the myosin filaments. Isotropic disks are represented by free fragments of actin filaments. Actin filaments consist of F-actin chains, which are two helical polymers of G-actin, resembling a twisted pearl necklace. Each groove of the F-actin helix contains tightly adjacent thread-like molecules of tropomyosin. Each tropomyosin molecule is associated with troponin, a polypeptide consisting of three subunits: troponin T, troponin I, and troponin C. Troponin I, when bound to actin, inhibits the zone in it through which actin interacts with myosin [5, 10]. In the middle of each isotropic disk is a Z-line (telophragm), which contains proteins, desmin and vimentin. The space between two telophragms is called a sarcomere. The sarcomere is considered a unit of contractility, since its length changes during muscle contraction (Fig. 4). Actin filaments are attached to the telophragm by α -actinin and nebulin. The free end of the actin filaments is coated with the protein tropomodulin.

Myosin filaments consist of 200–300 mirror-image myosin molecules. In such a molecule, heavy and light meromyosin (heavy and light parts) are distinguished. Heavy meromyosin includes two fragments: S1, represented by globular heads, and S2, represented by a linear elastic component. The S1

fragment has ATPase activity, which requires contact between the myosin heads and the active centers of the actin filaments. The terminal part of the myosin tail filament is formed by light meromyosin. Myosin has two hinge regions that allow the molecule to change conformation. One hinge region is located at the border of heavy and light meromyosins, the other is in the neck region, near the head. Light meromyosin provides aggregation of myosin molecules, while heavy meromyosin has actin-binding regions and has ATPase activity [1, 25]. Myosin molecules are assembled into aggregates in such a way that half of the heads face one end and half face the other. Myosin filaments are attached to the Z-lines by the elastic protein titin. The M-line runs through the middle of the anisotropic disk, in which the myosin filaments are linked to each other by myomesin and C-protein (Fig. 4, 5).

In addition to myofibrils, mitochondria and sarcoplasmic reticulum are well developed in the sarcoplasm.

The sarcoplasmic reticulum is a modified smooth endoplasmic reticulum that stores calcium due to the presence of the calcium-binding protein calsequestrin. The membrane of the sarcoplasmic reticulum contains integral proteins that act as calcium pumps. It surrounds each sarcomere. The sarcoplasmic reticulum is represented by anastomosing membrane tubules ending in terminal cisterns located next to the T-tubules. T-tubules are invaginations of the sarcolemma located between two terminal cisterns. Together they form a triad. Depolarization waves pass through the T-tubules to the myofibrils. Dihydropyridine receptors of T-tubules register changes in membrane potential and activate ryanodine receptors of the sarcoplasmic reticulum, followed by the release of calcium ions from the sarcoplasmic reticulum into the sarcoplasm [17].

Muscle contraction mechanism

Muscle contraction is described by the sliding filament theory. Calcium ions released from the sarcoplasmic reticulum cisterns into the sarcoplasm bind to troponin C, which causes conformational changes in the troponin-tropomyosin complex, resulting in the opening of active zones (myosin-binding zones) on actin molecules. Myosin heads attach to these zones, then the myosin heads deflect and pull actin filaments along with them, which penetrate deeper into the spaces between the myosin filaments. During this process, ATP bound to the S1 fragment of the myosin molecule is hydrolyzed. Relaxation of the muscle fiber occurs when the calcium pump pumps calcium ions from the cytosol into the sarcoplasmic reticulum system. A decrease in the calcium concentration in the cytoplasm stimulates the return of troponin C to its previous conformational state, and the tropomyosin molecule itself to its original position, closing the active center of the actin molecule [5].

Muscle fibers are characterized by different contraction speeds. This may be related to their ultrastructural features, in particular, the number of mitochondria, the density of blood capillaries, and the amount of myoglobin. Myoglobin is an oxygen-binding protein that gives muscle fibers a red-dish tint, so muscle fibers containing a large amount of myoglobin are called red. Red fibers are capable of remaining in a contracted state for a long time. During prolonged muscle contraction, the lumen of blood vessels may be compressed and the transport of oxygen from the blood may be disrupted. In this case, the oxygen bound by myoglobin is consumed. Fibers containing significantly less myoglobin are called white. They exhibit the ability to contract quickly. In addition, there are intermediate fibers that have the characteristics of red and white muscle fibers.

Red muscle fibers, in addition to a large amount of myoglobin, are characterized by a large number of mitochondria and a low glycogen content. White muscle fibers are characterized by a low myoglobin content, fewer mitochondria and a high glycogen content. Intermediate fibers are characterized by a large amount of myoglobin and mitochondria and an average glycogen content [14]. Each muscle has its own unique ratio of muscle fibers.

Regeneration

Regeneration of skeletal muscle tissue is carried out by satellite cells. The amount of transferrin increases significantly in regenerating skeletal muscle. It is assumed that transferrin and transferrin-dependent growth factor activate the proliferation of myosatellite cells. There is evidence that

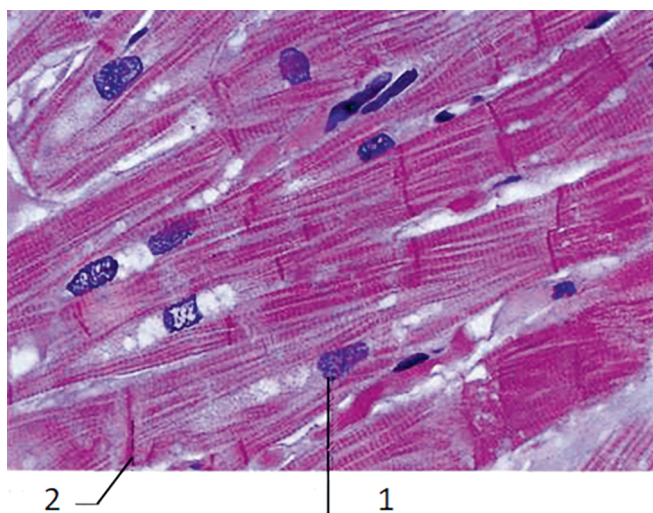
satellite cells themselves are capable of secreting insulin-like growth factor [7]. Animal experiments have shown that the basic fibroblast growth factor, AB and BB isoforms of platelet-derived growth factor, and beta-transforming growth factor enhance the mitotic activity of satellite cells, and insulin-like growth factors stimulate not only proliferation, but also their differentiation. The action of growth factors in various combinations is a potential mechanism for regulating the activity of myosatellite cells and can be used in medical practice [7].

CARDIAC MUSCLE TISSUE

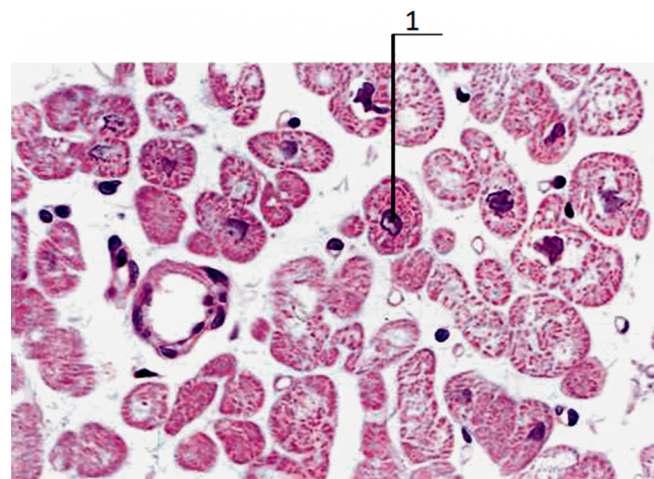
According to histogenetic classification, it belongs to the coelomic type.

Development

Myocardial precursor cells are detected in the epiblast on the 16th day of intrauterine development. They are localized in the cranial end of the primitive streak as part of the presumptive material of the mesoderm. From there, they migrate to the middle leaflet and are subsequently located in the visceral leaflet of the splanchnotome, where they form the myoepicardial plate. It consists of two cell clusters: the primary heart field (PHF), which gives rise to the myocardium of the atria, left ventricle and part of the right ventricle, and the secondary heart field (SHF), which forms part of the right ventricle, the cardiac conus and the arterial trunk. The transcription factor NKX2.5 is key to heart development. Expression of the NKX2.5 gene is stimulated by bone



a/a



b/b

Fig. 6. Cardiac muscle tissue. Longitudinal (a) and cross (b) section of myocardium. 1 — nucleus; 2 — intercalated disc [4]

Рис 6. Сердечная мышечная ткань. Мышечные волокна на продольном (а) и поперечном (б) разрезе. 1 — ядро; 2 — вставочный диск [4]



Fig. 7. Intercalated disc at high magnification (1:40 000): 1 — *macula adherens* (desmosome); 2 — *zonula adherens* [4]

Рис. 7. Вставочный диск при большом увеличении (1:40 000): 1 — десмосомы; 2 — опоясывающие десмосомы [4]

morphogenetic proteins BMP2 and BMP4 (produced in adjacent endoderm cells and acting in a paracrine manner). In addition, these morphogenetic proteins stimulate the production of fibroblast growth factor FGF8, which, in turn, is important for the expression of genes for specific cardiac proteins [11]

Features of the structure of cardiac muscle tissue

The cardiomyocyte acts as a structural and functional unit of cardiac muscle tissue. Cardiomyocytes are connected to each other, forming fibers. Unlike skeletal muscle tissue, there is a division into cells inside the cardiac muscle fiber (Fig. 6).

The contact sites between adjacent cardiomyocytes are called intercalated discs. Electron micrographs show that the intercalated disc area is uneven, because cardiomyocytes form numerous interdigitations connected by connections such as desmosomes, encircling desmosomes, and gap junctions (Fig. 7). The latter provide ionic communication between cells, thereby facilitating their combined contraction. Cardiac muscle fibers actively branch and anastomose.

There are different types of cardiomyocytes — contractile, atypical, secretory. In this lecture we will talk only about contractile cardiomyocytes. Typical (contractile) cardiomyocytes are cylindrical cells of different sizes, depending on their localization (atrial or ventricular); binuclear ones are often found among them. The nucleus, unlike skeletal muscle fibers, occupies a central position. Cardiomyocytes are covered with a basal membrane located on top of the sarcolemma.

The contractile apparatus and the mechanism of muscle contraction are similar to those in skeletal muscle fibers, but the transverse striation in cardiac muscle fibers is less pronounced than in skeletal ones, which is due to the presence of intercellular boundaries within the cardiac muscle fiber and interdigitations of cardiomyocytes, due to which isotropic and anisotropic disks of neighboring cells can shift relative to each other. The sarcoplasmic reticulum is less developed than in skeletal muscle fiber, and it deposits calcium ions less actively. T-tubules are well developed in ventricular cardiomyocytes and poorly developed in atrial cardiomyocytes.

There are differences between atrial and ventricular cardiomyocytes. Ventricular ones are thicker and longer, they have more mitochondria and myofibrils, the sarcoplasmic reticulum and T-tubules are better developed. In atrial cardiomyocytes, T-tubules are less pronounced, and in some cells, caveolae (small invaginations of the sarcolemma) are found instead of them. But gap junctions are more common between atrial cardiomyocytes.

Regeneration

The proliferative capacity of cardiomyocytes is expressed only during the period of intrauterine development and in the first days after birth. Experiments on rats have shown that in the first 4 days of postnatal life, a considerable part of cardiomyocytes divides by mitosis — 60%, during the next few days — only 6-7% [6]. In vivo studies have shown that in the first 3 days after birth, the number of cardiomyocytes increases by 68%, but then this figure drops sharply [6]. Some authors believe that mitosis slows down in the G0-G1 phase, others — in the G2-M phase [6]. For a long time, it was believed that cardiac muscle tissue is completely devoid of the ability to regenerate. Later, it was established that local progenitor cells are present in all tissues, including the myocardium. However, information on the existence and functioning of stem cells in the organs of the cardiovascular system is still limited [18, 19, 21]. Recent data indicate the presence of a cellular regenerative pool in the myocardium. One type of such cells are undifferentiated stem cells c-kit+. Committed GATA-4+ cells show an early cardiomyogenic orientation and belong to the cardiomyoblastic cellular form [24]. However, there is also an opposite point of view, where the cardiomyogenic role of these cells is questioned, since they were found in granulation tissue, which was subsequently transformed into scar tissue [20]. But even if we consider c-kit+ cells as regional cardiac stem cells, they cannot ensure full myocardial regeneration, since their content in the myocardium is insignificant and cannot cover the deficit of lost cardiomyocytes after injury [12].

SMOOTH MUSCLE

Such tissue may have different origins depending on its localization: smooth muscle tissue of vessels and internal organs differentiates from mesenchyme and, according to histogenetic classification, belongs to the visceral type. Myoepitheliocytes of glands have an ectodermal origin, this muscle tissue belongs to the epidermal type. Muscle tissue of the iris of the eyeball belongs to the neural type, since it differentiates from cells of the neural rudiment (neural crests).

Visceral muscle tissue

Development

The source of development of visceral smooth muscle tissue is the mesenchyme emanating from the visceral leaf of the splanchnotome. In the dynamics of specific differentiation, smooth myocytes (leiomyocytes) go through the stages of premyoblast, myoblast, differentiating and differentiated myocytes. In the process of differentiation, the contractile apparatus develops: the volume density of filaments and dense bodies increases, the number of vesicles, while the total volume occupied by the components of the contractile apparatus increases due to a decrease in the volume occupied by other organelles. In addition, intercellular communications and neuromuscular connections develop. The processes of specific differentiation do not block DNA synthesis and cell proliferation for a long time. In the embryonic period, there is practically no growth of smooth myocytes, which is explained by their high proliferative activity. At the postnatal stage of histogenesis, the processes of reproduction and differentiation become incompatible under conditions of increasing functional load, which leads to the exit of the overwhelming majority of leiomyocytes from the reproductive cycle [8].

Structural features

The smooth myocyte acts as a structural and functional unit of smooth muscle tissue. Smooth myocytes are spindle-shaped cells with an oval, relatively large nucleus, located almost close to each other; between them there are various connections, the most common of which are gap junctions, which ensure the transfer of excitation between cells and their combined contraction. Smooth myocytes can vary in size: the smallest are located in the walls of small vessels, the largest form the myometrium. Each smooth myocyte is surrounded by a sarcolemma and a basal membrane (Fig. 8).

There are two types of smooth myocytes: secretory and contractile. The main function of secretory myocytes is protein synthesis, which is why their cytoplasm has well-

developed synthesis organelles (rough endoplasmic reticulum, Golgi apparatus), while their contractile apparatus is poorly developed. Contractile smooth myocytes specialize in the contractility function and therefore have a well-developed contractile apparatus and numerous mitochondria. Unlike striated muscle fibers, the contractile apparatus here is represented by actin and myosin myofilaments that do not form myofibrils. Actin filaments are located mainly along the long axis of the cell, but can also be located obliquely. Their ends are fastened to each other and to the sarcolemma by dense bodies — cross-linking proteins and contain α -actinin. The same protein is located at the junction of actin filaments with the telophragm in skeletal muscle fibers. Actin filaments consist of smooth muscle α -actin and tropomyosin. Unlike striated muscle fibers, they do not contain troponin. Myosin in a relaxed smooth myocyte is in a monomeric form. When a smooth myocyte is stimulated by a nerve impulse or by the action of neurotransmitters, hormones and some bioactive substances, calcium channels open and the concentration of calcium ions in the cytoplasm increases. The result is the binding of calcium to calmodulin, the resulting complex activates myosin light chain kinase, an enzyme that catalyzes the phosphorylation of myosin light chains and the subsequent assembly of myosin filaments, which is a trigger for the formation of bonds between actin and myosin filaments [8].

The sarcoplasmic reticulum is expressed here less strongly than in striated muscle fibers and is represented by narrow tubes. The sarcolemma forms small invaginations, caveolae, as analogs of T-tubes. The flow of calcium ions into the sarcolemma from the sarcoplasmic reticulum entails both the polymerization of myosin and its interaction with actin, which is ensured by the same mechanisms as in

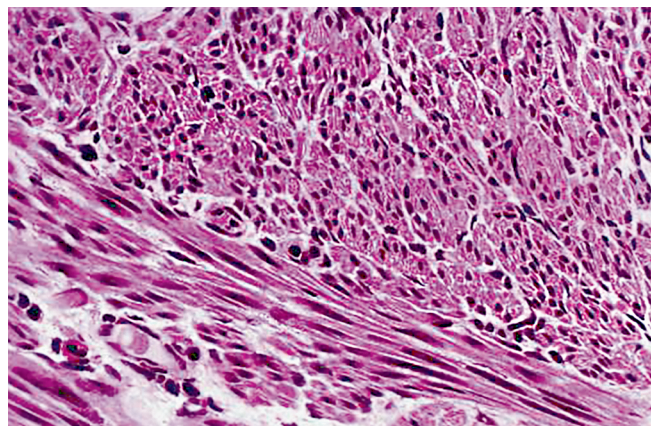


Fig. 8. Longitudinal and cross sections of smooth muscle tissue [4]

Рис. 8. Продольный и поперечный срезы гладкой мышечной ткани [4]



Fig. 9. Smooth muscle cell relaxed (a) and constructed (b) [23]

Рис. 9. Гладкий миоцит в расслабленном (а) и в сокращенном состоянии (б) [23]

striated muscle fibers (the formation of contacts between myosin heads and active centers). Then the actin filaments are drawn in between the myosin ones, the dense bodies come together, the force is transmitted to the plasma membrane, the cell shortens and twists in a spiral, the areas of the sarcolemma to which the actin filaments are attached are drawn in, and the areas located between them bulge, so the surface of the contracted smooth myocyte is uneven (Fig. 9). Muscle relaxation occurs when the initial calcium concentration inside the cell is restored by its removal by calcium pumps. Myosin light chain kinase is inactivated by detaching from calmodulin, and myosin is dephosphorylated.

Regeneration

Smooth myocytes are rarely found in the intact definitive muscle tissue of vessels and internal organs during the division process. Proliferative activity of smooth muscle tissue is manifested in the case of its damage or with an increase in the functional load. The mechanism of regeneration of muscle tissue of vessels and internal organs has not been fully elucidated. There is evidence that these tissues contain poorly differentiated cells that can differentiate into cells capable of entering the mitotic cycle. In addition, in the case of stimulation, for example as a result of injury, cambial elements capable of entering the mitotic cycle are activated. Under the influence of damaging factors, myocytes can transform from a contractile to a synthetic (secretory) phenotype [2].

Muscle tissue of the epidermal type

This tissue is represented by myoepithelial cells, which are found in the terminal sections and small excretory ducts of the salivary, sweat and mammary glands. The cells have processes that cover the secretory cells. The contractile apparatus of myoepithelial cells is similar to that of the smooth myocyte system of the visceral type. Contraction of myoepithelial cells promotes the release of secretion from the terminal section into the excretory duct. Numerous studies have shown that myoepithelial cells develop from the same rudiment (ectoderm) as the epithelium of the glands in which they are found [13, 16]. There is no

unambiguous data in the literature regarding the regeneration of myoepithelial cells. It is possible that it is carried out due to poorly differentiated epithelial cells of the terminal sections of the glands.

Muscle tissue of the neural type

The structural and functional unit of this muscle tissue is a smooth myocyte, which has a similar structure to a leiomyocyte. A feature of neural myocytes is the inclusion of melanin in the sarcoplasm. The source of the development of contractile elements of the muscle that constricts and dilates the pupil of the eye of mammals and humans are cells emanating from the edges of the optic cup. A few studies have shown low regenerative activity of this muscle tissue or its absence [7].

CONCLUSION

The tissue type of muscle tissues is distinguished by a functional feature — they are specialized in contractile function. At the same time, representatives of this type have different origins, are represented by different tissue elements, have a number of differences in structure and different regeneration abilities. Despite the fact that muscle tissues have been well studied, controversial issues still remain unresolved, primarily concerning their ability to regenerate. Actively developing molecular biology will help shed light on the solution of these issues. Knowledge of the sources of development, structural features and functioning of muscle tissues, as well as the processes of their proliferation and differentiation is of great importance for making a correct diagnosis and choosing the right treatment tactics.

ADDITIONAL INFORMATION

Author contribution. Thereby, all authors made a substantial contribution to the conception of the study, acquisition, analysis, interpretation of data for the work, drafting and revising the article, final approval of the version to be published and agree to be accountable for all aspects of the study.

Competing interests. The authors declare that they have no competing interests.

Funding source. This study was not supported by any external sources of funding.

ДОПОЛНИТЕЛЬНАЯ ИНФОРМАЦИЯ

Вклад авторов. Все авторы внесли существенный вклад в разработку концепции, проведение исследования и подготовку статьи, прочли и одобрили финальную версию перед публикацией.

Конфликт интересов. Авторы декларируют отсутствие явных и потенциальных конфликтов интересов, связанных с публикацией настоящей статьи.

Источник финансирования. Авторы заявляют об отсутствии внешнего финансирования при проведении исследования.

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ПРАВИЛА ДЛЯ АВТОРОВ

Утв. приказом и.о. ректора
ФГБОУ ВО СПбГПМУ Минздрава России от 05.04.24

НАСТОЯЩИЕ ПРАВИЛА ДЛЯ АВТОРОВ ЯВЛЯЮТСЯ ИЗДАТЕЛЬСКИМ ДОГОВОРом

Условия настоящего Договора (далее «Договор») являются публичной офертой в соответствии с п. 2 ст. 437 Гражданского кодекса Российской Федерации. Данный Договор определяет взаимоотношения между редакцией журнала «**Russian Biomedical Research**» (далее по тексту «Журнал»), зарегистрированного Федеральной службой по надзору в сфере связи, информационных технологий и массовых коммуникаций (РОСКОМНАДЗОР), свидетельство: ПИ № ФС77-74228 от 02 ноября 2018 г. (ранее ПИ № ТУ78-01869 от 17 мая 2016 г.), именуемой в дальнейшем «Редакция» и являющейся структурным подразделением ФГБОУ ВО СПбГПМУ Минздрава России, и автором и/или авторским коллективом (или иным правообладателем), именуемым в дальнейшем «Автор», принявшим публичное предложение (оферту) о заключении Договора.

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Размещение публикаций возможно только после получения положительной рецензии.

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Перед заполнением анкеты авторам рекомендуется подготовить все необходимые для ввода данные, а также выбрать автора (в случае коллектива авторов статьи), **ОТВЕТСТВЕННОГО ЗА ПЕРЕПИСКУ**. Для успешного заполнения анкеты необходимо иметь всю указанную информацию и на русском, и на английском языках.

Все названия на английском языке, включая названия статьи, названия учреждений, их подразделений должны приводиться с прописных букв (например: Sex Differences In Aging, Life Span And Spontaneous Tumorigenesis; Bulletin of Experimental Biology and Medicine; Saint Petersburg State Pediatric Medical University) и непременно в соответствии с официальными наименованиями без самодеятельности.

Анкетные данные всех авторов — Имя Отчество Фамилия (полностью), ученая степень, звание, должность, место работы (кафедра, отделение), название учреждения, адрес учреждения, e-mail, ORCID, SPIN-код, телефон, ФИО автора, ответственного за переписку, и т.д. — заполняются в соответствующих полях формы заявки. Резюме, ключевые слова и название статьи также заполняются онлайн.

Статья должна соответствовать правилам оформления статей к публикации (см. ниже).

К каждой статье прилагается файл Экспертного заключения (ЭЗ). Для авторов СПбГПМУ ЭЗ может только подписываться авторами статьи, печать необязательна. Для авторов других учреждений ЭЗ оформляется обязательно полностью, с печатями (круглая печать учреждения) и подписями руководителей и комиссий данного учреждения. Заполненный, подписанный и «опечатанный» бланк ЭЗ для отправки онлайн предварительно сканируется или фотографируется. Образец ЭЗ можно скачать (https://gpmu.org/science/pediatricsmagazine/Russian_Biomedical_Research, Бланк экспертного заключения).

Отправленные анкетные данные авторов, статья, ЭЗ поступают на E-mail автору-отправителю (для подтверждения и проверки отправки) и на E-mail редакции scrcenter@mail.ru техническому редактору журнала «Russian Biomedical Research», с которым осуществляется вся дальнейшая работа по подготовке статьи в печать. Все вопросы по отправке статей можно адресовать на электронный

адрес srccenter@mail.ru техническому редактору журнала «Russian Biomedical Research» Марии Александровне Пахомовой.

Рукопись считается поступившей в Редакцию, если она представлена комплектно и оформлена в соответствии с описанными требованиями. Предварительное рассмотрение рукописи, не заказанной Редакцией, не является фактом заключения между сторонами издательского Договора.

При представлении рукописи в Журнал Авторы несут ответственность за раскрытие своих финансовых и других конфликтных интересов, способных оказать влияние на их работу. В рукописи должны быть упомянуты все лица и организации, оказавшие финансовую поддержку (в виде грантов, оборудования, лекарств или всего этого вместе), а также другое финансовое или личное участие.

В конце каждой статьи обязательно указываются вклад авторов в написание статьи, источники финансирования (если имеются), отсутствие конфликта интересов, наличие согласия на публикацию со стороны пациентов.

Правила оформления статей к публикации

Статья предоставляется в электронной форме (файл MS Word версии не старше 2003, т.е. с расширением doc), шрифт — 14, интервал — полуторный.

Файл статьи называется по Фамилии первого автора, например, Иванов.doc или Petrov.doc. Никаких других слов в названии не должно быть!

Ориентировочные размеры статьи, включая указатель литературы, таблицы и резюме, — 10–12 страниц текста через полтора интервала или 20–25 тысяч знаков с пробелами. Рекомендуемый размер обзора — 18–20 страниц «машинописного» текста или 35–40 тысяч знаков с пробелами. Примерное число литературных ссылок для экспериментальной статьи — 20, для обзоров и проблемных статей — 50.

Файл статьи должен содержать НА РУССКОМ И АНГЛИЙСКОМ ЯЗЫКАХ:

- Заглавие (Title) должно быть кратким (не более 120 знаков), точно отражающим содержание статьи.
- Сведения об авторах (публикуются). Для каждого автора указываются: фамилия, имя и отчество, место работы, почтовый адрес места работы, e-mail, ORCID, SPIN-код. Фамилии авторов рекомендуется транслитерировать так же, как в предыдущих публикациях, или по системе BGN (Board of Geographic Names), см. сайт <http://www.translit.ru>.
- Резюме (Abstract) (1500–2000 знаков, или 200–250 слов) помещают перед текстом статьи. Резюме не требуется при публикации рецензий, отчетов о конференциях, информационных писем.

Авторское резюме к статье является основным источником информации в отечественных и зарубежных информационных системах и базах данных, индексирующих журнал. Резюме доступно на сайте журнала «Russian Biomedical Research» и индексируется сетевыми поисковыми системами. Из аннотации должна быть понятна суть исследования, нужно ли обращаться к полному тексту статьи для получения

более подробной, интересующей его информации. Резюме должно излагать только существенные факты работы.

Рекомендуемая структура как аннотации, так и самой статьи IMRAD (для оригинальных исследований структура обязательна): введение (Introduction), материалы и методы (Materials and methods), результаты (Results), обсуждение (Discussion), выводы (Conclusion). Предмет, тему, цель работы нужно указывать, если они не ясны из заглавия статьи; метод или методологию проведения работы целесообразно описывать, если они отличаются новизной или представляют интерес с точки зрения данной работы. **Объем текста авторского резюме** определяется содержанием публикации (объемом сведений, их научной ценностью и/или практическим значением) и должен быть в пределах **200–250 слов (1500–2000 знаков)**.

- Ключевые слова (Keywords) от 3 до 10 ключевых слов или словосочетаний из 2–4 слов, которые будут способствовать правильному перекрестному индексированию статьи, помещаются под резюме с подзаголовком «Ключевые слова». Используйте термины из списка медицинских предметных заголовков (Medical Subject Headings), приведенного в Index Medicus (если в этом списке еще отсутствуют подходящие обозначения для недавно введенных терминов, выберите наиболее близкие из имеющихся). Ключевые слова разделяются запятой.
- Текст статьи может быть написан либо на русском, либо на английском языке, также возможна публикация статьи с полным переводом. На русском и английском языках необходимо предоставить все рисунки и таблицы (заголовки, все надписи, а также текст таблиц должны иметь перевод). В разделе «Методика» обязательно указываются сведения о статистической обработке экспериментального или клинического материала. Единицы измерения даются в соответствии с Международной системой единиц — СИ. Фамилии иностранных авторов, цитируемые в тексте рукописи, приводятся в оригинальной транскрипции. Таблицы и рисунки приводятся непосредственно в теле статьи, каждый из которых имеет номер и название с обязательными ссылками на них в тексте статьи — в контексте предложения (например: «...как показано на рисунке 1...») или в конце предложения в круглых скобках (например: «...выявлена положительная корреляционная связь умеренной степени ($r=0,41$) между уровнем ТТГ матери и новорожденного (рис. 2)»; просьба учитывать, что в печатной версии журнала рисунки будут воспроизводиться в черно-белом варианте).
- Список литературы обязательно приводится в порядке упоминания.

Текст статьи должен быть подготовлен в строгом соответствии с настоящими правилами и тщательно выверен автором. В случае обнаружения значительного количества опечаток, небрежностей, пунктуационных и орфографических ошибок, нерасшифрованных сокращений, отсутствия основных компонентов, переводов заголовков таблиц, подрисовочных подписей, надписей на рисунках,

текста таблиц и других технических дефектов оформления статей редакция возвращает статью автору для доработки. Небольшие погрешности редакция может исправить сама без согласования с автором. Редакция оставляет за собой право осуществления литературного и технического редактирования статей.

Сокращений, кроме общеупотребительных, следует избегать. Сокращения в названии статьи, названиях таблиц и рисунков, в выводах недопустимы. Если аббревиатуры используются, то все они должны быть непременно расшифрованы полностью при первом их упоминании в тексте (например: «Наряду с данными о РОН (резидуально-органической недостаточности), обуславливающей развитие ГКС (гиперкинетического синдрома), расширен диапазон исследований по эндогенной природе данного синдрома».

Все цитирования производятся следующим образом:

ФИО автора, год издания и прочая информация не упоминаются в тексте. Вместо этого указывается ссылка на источник литературы в виде номера в квадратных скобках (пример: «Ряд исследователей отмечает различные нарушения речевых функций при эпилепсии в детском возрасте [17, 21, 22].»), который включен в расставленный в порядке упоминания (1, 2, 3 и т.д.) список источников в конце статьи.

Все ссылки должны иметь соответствующий источник в списке, а каждый источник в списке — ссылку в тексте.

В виде исключения в тексте могут приводиться ФИО конкретных авторов в формате И.О. Фамилия, год и даже название источника, но при этом все равно обязательна ссылка (в квадратных скобках в конце предложения) на источник, включенный в список литературы. (Например: «В 1892 году великий Эраст Гамильтонский описал в своем бессмертном труде «Об открытии третьего уха у человека» третье (непарное) ухо» [34].)

Литература (References)

Учитывая требования международных систем цитирования, список литературы приводится не только в обычном виде, но также и дополнительно в переведенном на английский язык (References).

В статье приводятся ссылки на все упоминаемые в тексте источники.

Фамилии и инициалы авторов в приставном списке приводятся в порядке упоминания.

В описании указываются все авторы публикации.

Библиографические ссылки в тексте статьи даются в квадратных скобках.

Ссылки на неопубликованные работы не допускаются.

Список литературы комплектуется в следующем порядке:
Нормативные акты

Приказы, нормативные акты, методические письма и прочие законные акты, патенты, полезные модели не вносятся в список литературы, оформляются в виде сносок. Сноска — примечание, помещаемое внизу страницы (постраничная сноска). Знак сноски ставят цифрой после фрагмента основного текста, где есть упоминание об этих источниках. Рекомендуется сквозная нумерация сносок по тексту.

Интернет-ресурс

1. Интернет-ресурс, где есть название источника, автор, вносится в список литературы (в порядке алфавита) с указанием даты обращения (см. ниже пример оформления).

2. Если есть только ссылка на сайт, оформляется подстрочное примечание (сноска), с указанием даты обращения.

Щеглов И. Насколько велика роль микрофлоры в биологии вида-хозяина? Живые системы: научный электронный журнал. Доступен по: http://www.biorf.ru/catalog.aspx?cat_id=396&id_po=3576 (дата обращения: 02.07.2012).

Kealy M. A., Small R. E., Liamputtong P. Recovery after caesarean birth: a qualitative study of women's accounts in Victoria, Australia. BMC Pregnancy and Childbirth. 2010. Available at: <http://www.biomedcentral.com/1471-2393/10/47/> (accessed: 11.09.2013).

Примеры оформления литературы

Книга:

Юрьев В.К., Моисеева К.Е., Глущенко В.А. Основы общественного здоровья и здравоохранения. Учебник. СПб.: СпецЛит; 2019.

Никифоров О.Н., ред. Санкт-Петербург в 2021 году. СПб.: Петростат; 2022.

Brandenburg J.H., Ponti G.S., Worring A.F. eds. Vocal cord injection with autogenous fat. 3 rd ed. NY: Mosby; 1998.

Domeika M. Diagnosis of genital chlamydial infection in humans as well as in cattle. Uppsala; 1994.

Глава из книги:

Тутельян В.А., Никитюк Д.Б., Шарафетдинов Х.Х. Здоровое питание — основа здорового образа жизни и профилактики хронических неинфекционных заболеваний. В кн.: Здоровье молодежи: новые вызовы и перспективы. Т. 3. М.; 2019: 203–227.

Статья из журнала:

Карсанов А.М., Полунина Н.В., Гогичаев Т.К. Безопасность пациентов в хирургии. Часть 2: Программа менеджмента качества хирургического лечения. Медицинские технологии. Оценка и выбор. 2019;1(35):56–65. DOI: 10.31556/2219-0678.2019.35.1.056-065.

Brandenburg J.H., Ponti G.S., Worring A.F. Vocal cord injection with autogenous fat: a long-term magnetic resonance. Laryngoscope. 1996;106(2,pt 1):174–80.

Deb S., Campbell B.K., Pincott-Allen C. et al. Quantifying effect of combined oral contraceptive pill on functional ovarian reserve as measured by serum anti-Müllerian hormone and small antral follicle count using three-dimensional ultrasound. Ultrasound Obstet Gynecol. 2012;39(5):574–580.

Тезисы докладов, материалы научных конференций:

Марковская И.Н., Завьялова А.Н., Кузнецова Ю.В. Микробный пейзаж пациента первого года жизни с дисфагией, длительно находящегося в ОРИТ. XXX Конгресс детских гастроэнтерологов России и стран СНГ: тез. докл. М.; 2023: 29–31.

Салов И.А., Маринушкин Д.Н. Акушерская тактика при внутриутробной гибели плода. В кн.: Материалы IV Российского форума «Мать и дитя». Ч. 1. М.; 2000: 516–519.

Авторефераты:

Авилов А.Ю. Девиации полоролевой идентичности мужчин с умственной отсталостью в условиях психоневрологического интерната. Автореф. дис. ... канд. психол. наук. СПб.; 2021.

Описание интернет-ресурса:

Естественное движение населения. Москва: Росстат. Доступен по: <https://rosstat.gov.ru/folder/12781> (дата обращения: 23.10.2023).

World Health Organization. Prevalence and incidence of selected sexually transmitted infections — 2008. Geneva: World Health Organization; 2012. Available at: https://aefsg.ch/wp-content/uploads/who-9789241503839_eng.pdf (accessed^ 11.04.2024)

Перевод и транслитерация

В зависимости от ситуации следует либо проводить транслитерацию (писать исходные неанглоязычные слова буквами романского алфавита), либо указывать перевод неанглоязычной информации о первоисточниках в References.

Если цитируемая статья написана **на латинице** (на английском, немецком, испанском, итальянском, финском, датском и других языках, использующих романский алфавит), ссылку на нее следует привести на оригинальном языке опубликования. Пример (статья в норвежском журнале на норвежском языке):

Ellingsen A.E., Wilhelmsen I. Sykdomsangst blant medisinerstudenter. Tidsskr Nor Laegeforen. 2002;122(8):785–787. (In Norwegian).

Если статья написана **не на латинице** (на кириллице, в том числе на русском), нужно привести официальный перевод или выполнить транслитерацию в романский алфавит. Для книг необходимо в этом случае привести транслитерацию на латиницу. В конце описания в скобках указать язык издания.

Ссылка на источник литературы в References может состоять одновременно и из транслитерированных элементов (например, ФИО авторов, названия журналов), и из переводных (название публикации).

Стандарт транслитерации. При транслитерации рекомендуется использовать стандарт BSI (British Standard Institute, UK). Для транслитерации текста в соответствии со стандартом BSI можно воспользоваться ссылкой <http://ru.translit.ru/?account=bsi>.

ФИО авторов, редакторов. Фамилии и инициалы всех авторов на латинице следует приводить в ссылке так, как они даны в оригинальной публикации. Если в оригинальной публикации уже были приведены на латинице ФИО авторов, в ссылке на статью следует указывать именно этот вариант (независимо от использованной системы транслитерации в первоисточнике). Если в официальных источниках (на сайте журнала, в базах данных, в том числе в eLIBRARY) ФИО авторов на латинице не приведены, следует транслитерировать их самостоятельно по стандарту BSI.

Название публикации. Если у цитируемой Вами работы существует официальный перевод на английский язык или англоязычный вариант названия (его следует искать на сайте журнала, в базах данных, в том числе в eLIBRARY), следует указать именно его. Если в официальных источниках название публикации на латинице не приведено, следует выполнить транслитерацию в романский алфавит по стандарту BSI.

Название издания (журнала). Некоторые неанглоязычные научные издания (журналы) имеют кроме названия на родном языке официальное «параллельное» название на английском (например, у журнала «Сахарный диабет» есть официальное англоязычное название «Diabetes Mellitus»). Таким образом, для списка References в ссылке на статью из русскоязычного журнала следует

указать либо транслитерированное название журнала, либо переводное. Переводное название журнала можно взять либо с официального сайта журнала (или использовать данные о правильном написании англоязычного названия из цитируемой статьи), либо проверить его наличие в базе данных, например в CAS Source Index, библиотеке WorldCat или каталоге Web of Science (ISI), каталоге названий базы данных MedLine (NLM Catalog). В случае, когда у журнала нет официального названия на английском языке, в References нужно приводить транслитерацию по системе BSI. Не следует самостоятельно переводить названия журналов.

Место издания. Место издания в ссылках всегда следует указывать на английском языке и полностью — не в транслитерации и без сокращений. То есть Moscow, а не «Moskva» и не «М.:», Saint Petersburg, а не «Sankt Peterburg» и не «SPb».

Название издательства/издателя. В отличие от места издания, название издательства для ссылок в References следует только транслитерировать (за исключением крайне редких случаев наличия у издателя параллельного официального англоязычного названия).

Примеры перевода русскоязычных источников литературы для англоязычного блока статьи*Книга:*

Yuriev V.K., Moiseeva K.E., Glushchenko V.A. Fundamentals of public health and healthcare. Textbook. Saint Petersburg: SpetsLit; 2019. (In Russian).

Nikiforov O.N., ed. Saint Petersburg in 2021. Saint Petersburg: Petrostat; 2022. (In Russian).

Глава из книги:

Tutelyan V.A., Nikityuk D.B., Sharafetdinov Kh.Kh. Healthy nutrition is the basis of a healthy lifestyle and the prevention of chronic non-communicable diseases. In: Youth health: new challenges and prospects. T. 3. Moscow; 2019: 203–227. (In Russian).

Статья из журнала:

Karsanov A.M., Polunina N.V., Gogichaev T.K. Patient safety in surgery. Part 2: Quality management program for surgical treatment. Medical technologies. Evaluation and selection. 2019;1(35):56–65. DOI: 10.31556/2219-0678.2019.35.1.056-065. (In Russian).

Тезисы докладов, материалы научных конференций:

Markovskaya I.N., Zavyalova A.N., Kuznetsova Yu.V. Microbial landscape of a patient in the first year of life with dysphagia who has been in the ICU for a long time. XXX Congress of pediatric gastroenterologists of Russia and the CIS countries: abstract. report. Moscow; 2023: 29–31.

Salov I.A., Marinushkin D.N. Obstetric tactics in intrauterine fetal death. In: Materialy IV Rossiyskogo foruma “Mat’ i ditya”. Part 1: Moscow; 2000; 516–519. (In Russian).

Авторефераты:

Avilov A.Yu. Deviations of gender role identity of men with mental retardation in a psychoneurological boarding school. PhD thesis. Saint Petersburg; 2021. (In Russian).

Описание интернет-ресурса:

Natural population movement. Moscow: Rosstat. Available at: <https://rosstat.gov.ru/folder/12781> (accessed: 10/23/2023). (In Russian).

Kealy M.A., Small R.E., Liamputtong P. Recovery after caesarean birth: a qualitative study of women’s accounts in Victoria,

Australia. BMC Pregnancy and Childbirth. 2010. Available at: <http://www.biomedcentral.com/1471-2393/10/47/> (accessed: 11.09.2013).

Пример списка литературы (References):

ЛИТЕРАТУРА

1. Криворученко В.К. Жестокое обращение с ребенком. Проявление и меры предотвращения. Информационный гуманитарный портал Знание. Понимание. Умение. 2012; 3. Доступен по: http://www.zpu-journal.ru/e-zpu/2012/3/Krivoruchenko_Child-Abuse (дата обращения: 27.12.2023).
2. Jacobi G., Dettmeyer R., Banaschak S., Brosig B., Herrmann B. Child abuse and neglect: diagnosis and management. Dtsch Arztebl Int. 2010;107(13):231-239. DOI: 10.3238/arztebl.2010.0231.

REFERENCES

1. Krivoruchenko V.K. Child abuse. Manifestation and prevention measures. Informationsnyy gumanitarnyy portal Znaniye. Ponimaniye. Umeniye. 2012; 3. Available at: http://www.zpu-journal.ru/e-zpu/2012/3/Krivoruchenko_Child-Abuse (accessed: 27.12.2023) (In Russian).
2. Jacobi G., Dettmeyer R., Banaschak S., Brosig B., Herrmann B. Child abuse and neglect: diagnosis and management. Dtsch Arztebl Int. 2010;107(13):231-239. DOI: 10.3238/arztebl.2010.0231.

Для всех статей необходимо указывать индекс DOI в конце библиографического описания, а также EDN при его наличии.

Примеры:

Саттаров А.Э., Карелина Н.Р. Особенности ростовых процессов у мальчиков и юношей различных пропорций и телосложения, проживающих в южной части Кыргызстана. Педиатр. 2018;9(5):47–52. DOI: 10.17816/PED9547-52. EDN: YRAEPZ.

Voropaeva E.E., Khaidukova Yu.V., Kazachkova E.A., et al. Perinatal outcomes and morphological examination of placentas in pregnant women with critical lung lesions in new COVID-19 coronavirus infection. Ural Medical Journal. 2023;22(2):109–121. DOI: 10.52420/2071-5943-2023-22-2-109-121. EDN: CXRCMN. (In Russian).

ОТВЕТСТВЕННОСТЬ ЗА ПРАВИЛЬНОСТЬ БИБЛИОГРАФИЧЕСКИХ ДАННЫХ НЕСЕТ АВТОР.

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Редакция отбирает, готовит к публикации и публикует переданные Авторами материалы. Авторское право на конкретную статью принадлежит авторам статьи. Авторский гонорар за публикации статей в Журнале не выплачивается. Автор передает, а Редакция принимает авторские материалы на следующих условиях:

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Заключением Договора со стороны Редакции является опубликование рукописи данного Автора в журнале «Russian Biomedical Research» и размещение его текста в сети Интернет. Заключением Договора со стороны Автора, т.е. полным и безоговорочным принятием Автором условий Договора, является передача Автором рукописи и экспертного заключения.

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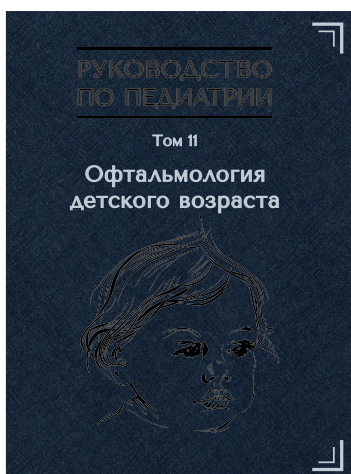
Сайты журнала: http://www.gpmu.org/science/pediatrics-magazine/Russian_Biomedical_Research, <https://ojs3.gpmu.org/index.php/biomedical-research>



ИЗДАТЕЛЬСТВО ПЕДИАТРИЧЕСКОГО УНИВЕРСИТЕТА ПРЕДСТАВЛЯЕТ

Руководство по педиатрии. ОФТАЛЬМОЛОГИЯ ДЕТСКОГО ВОЗРАСТА

Редакционная коллегия тома: Д.О. Иванов, В.В. Бржеский



Том 11 «Руководства по педиатрии» отражает современный уровень развития офтальмологии детского возраста. Книга содержит актуальную информацию о современных методах диагностики и лечения заболеваний глаз у детей. Отдельные разделы посвящены клиническим рекомендациям по основным синдромам и заболеваниям.

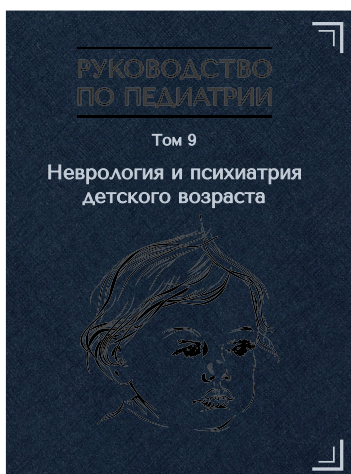
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ИЗДАТЕЛЬСТВО ПЕДИАТРИЧЕСКОГО УНИВЕРСИТЕТА ПРЕДСТАВЛЯЕТ

ОРТОПЕДИЧЕСКАЯ СТОМАТОЛОГИЯ. ПРОТЕЗИРОВАНИЕ НЕСЪЁМНЫМИ КОНСТРУКЦИЯМИ ЗУБНЫХ ПРОТЕЗОВ

М. Ф. Сухарев, С. Б. Фиццев, М. Г. Рожкова



Учебник соответствует программе Министерства здравоохранения Российской Федерации по ортопедической стоматологии, предназначен и будет полезным для преподавателей курсов и стоматологических кафедр, студентов стоматологических факультетов, ординаторов, аспирантов, врачей-стоматологов.

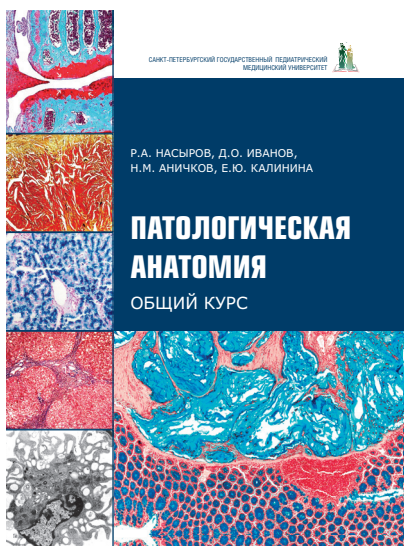
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Р.А. Насыров, Д.О. Иванов, Н.М. Аничков, Е.Ю. Калинина



В общем курсе патологической анатомии (клинической патоморфологии) рассмотрены вопросы общей патологической анатомии: методы исследования в патоморфологии, повреждение и гибель клеток и тканей, в том числе старение; нарушения кровообращения и иных сред организма, воспаление, репарация и регенерация, заживление ран, иммунная патология, адаптация, патология роста клеток и их дифференцировки, опухоли, генетические заболевания, учение о диагнозе в патологической анатомии, патология и факторы окружающей среды, патология, вызванная питанием, констатация смерти и др.

Учебник рассчитан на студентов-медиков всех факультетов, а также на врачей, интересующихся вопросами общей патологической анатомии.

Твердый переплет, цветные иллюстрации, 280 страниц.

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