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这些会议文集结合了会议的材料 – 研究论文和科学工作者的论文报告。 它考察了职业化人格的技术和社会学问题。一些文章涉及人格职业化研究问题的理论和方法论方法和原则。
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These Conference Proceedings combine materials of the conference – research papers and thesis reports of scientific workers. They examine technical, juridical and sociological aspects of research issues. Some articles deal with theoretical and methodological approaches and principles of research questions of personality professionalization.

Authors are responsible for the accuracy of cited publications, facts, figures, quotations, statistics, proper names and other information.

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攻击性言语行为实现特征研究在教学实践中的应用
INTRODUCTION OF THE STUDY OF THE FEATURES OF REALIZING AGGRESSIVE SPEECH ACTS INTO TEACHING PRACTICES

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摘要：本文探讨如何将攻击性言语行为研究融入教学实践，并开发一门面向教育工作者和学生的专门课程。该课程将研究置于情感语言学的跨学科领域，探讨情感内容如何在语言中以言语和非言语的方式编码和表达。本文从心理学和语言学的角度回顾了攻击性行为的不同定义和分类，强调言语攻击性是一种多维现象，既涉及明确的语言标记，也涉及隐含的交际意图。“识别课堂中的言语攻击”特别课程强调其教育意义，旨在提供一门综合性的课程，将理论基础与实践诊断和干预技巧相结合，包括对真实言语案例的分析、冲突降级策略以及伦理考量。该课程旨在提升参与者识别、解读和建设性地管理言语攻击性行为的能力，从而营造一个更安全、更具支持性的沟通环境。本研究强调了让未来教师掌握有效应对和缓解攻击性沟通的必要技能的重要性，这有助于取得积极的教育成果并促进学生的心理健康。

关键词：情绪语言学、攻击性行为、言语攻击、特殊课程、教育环境。

Abstract. *This article explores the integration of the study of aggressive speech acts into teaching practice through the development of a specialized course aimed at educators and students. It situates the research within the interdisciplinary field of linguistics of emotions, examining how emotional content is encoded and expressed verbally and nonverbally in language. The article reviews diverse definitions and classifications of aggression from psychological and linguistic perspectives, highlighting verbal aggression as a multidimensional phenomenon involving both explicit linguistic markers and implicit communicative intents. Emphasizing the educational significance, the proposed special course “Recognizing Speech Aggression in the Classroom” offers a comprehensive curriculum that combines theoretical foundations with practical diagnostic and intervention techniques, including analysis of real-life speech cases, conflict de-escalation strategies, and*

ethical considerations. The course aims to enhance participants' competence in identifying, interpreting, and constructively managing speech aggression, thereby fostering a safer and more supportive communicative environment. This study underlines the importance of equipping future teachers with the skills necessary to navigate and mitigate aggressive communication effectively, contributing to positive educational outcomes and emotional well-being.

Keywords: *linguistics of emotions, aggressive behavior, verbal aggression, special course, educational environment.*

The field of the linguistics of emotions encompasses a wide range of issues related to the study of how emotions are manifested, encoded, and conveyed in language and speech. The linguistics of emotions (emotiology) emerged at the intersection of linguistics and psychology and has become an interdisciplinary domain combining approaches from linguistics, cognitive and social sciences, cultural studies, and even biology.

Key directions in the linguistics of emotions include investigating the typology and classification of emotional signs in language, such as words, expressions, and constructions that carry emotional information; studying the influence of emotional thinking on the formation of linguistic worldviews and the specifics of national-cultural expression of emotions; analyzing the communication of emotions in various speech and discursive manifestations; and conducting comparative studies of emotional lexicons across languages to identify ethnocultural differences in verbalizing feelings and emotional states [4].

Special attention is given to analyzing the emotional space of language, its categorical structure, and the specifics of emotional expression across different linguistic personalities and cultures. The linguistics of emotions considers both verbal (lexical and grammatical) means of expressing emotions and nonverbal ones, including intonation, facial expressions, and gestures.

Within contemporary theories of aggressive behavior, existing definitions of aggression can be divided into two main groups. The first focuses on evaluating the behavior itself, viewing aggression as any action that causes harm to another subject. The second group emphasizes the intentionality of actions: according to one definition, aggression is any form of behavior aimed at insulting or harming another living being that does not wish such treatment [3].

Y.M. Antonyan offers a classification of aggression into two types: "cruel" and "non-cruel" aggression [1]. His approach is morally neutral, treating aggression not only as a destructive and useless form of violence but also as a form of survival. According to Antonyan, aggressive acts are not always cruel in nature, although all cruelty is aggressive.

In contrast, L.M. Semenyuk adopts a stricter position, defining aggression as intentional destructive behavior that violates norms of human coexistence and causes harm—often physical or psychological, such as fear or depression—to the objects of attack [6]. Typical manifestations of aggression for Semenyuk are associated with uncontrollable anger and impulsivity. He emphasizes that aggression is not an innate biological reaction but a form of behavior shaped and maintained within social relationships and interactions. In his interpretation, aggression appears as motivated external actions that violate norms and rules of coexistence, causing pain and suffering.

However, aggression can also be considered not only as a behavioral phenomenon. N.D. Levitov highlights its psychological nature, distinguishing three components: cognitive, emotional, and volitional [5]. V.V. Boyko views aggression as a result of the transformation of excessive (primarily negative) emotional states [2].

In the scientific literature of the last two decades, both in Russia and abroad, the terms "verbal aggression" and "speech aggression" are widely used. Researchers such as A. Bass, R. Baron and D. Richardson, V.I. Zhelvis, K.E. Izard, N.D. Levitov, A.K. Mikhalskaya, K.F. Sedov, L.M. Semenyuk, I.A. Furmanov, E. Fromm, and others actively employ these concepts. Usually, "speech aggression" and verbal aggression denote the same phenomenon and are used interchangeably as Russian and Latinized variants, often to avoid tautology in texts.

Defining a universal, scientifically substantiated, and comprehensive concept of speech aggression that accounts for all diverse forms and manifestations is extremely challenging. Attempts to formulate precise definitions largely belong to foreign scholars, whose analyses help clarify the characteristics of this phenomenon.

Particular attention is given to A. Bass's definition, who regards verbal aggression as the expression of negative feelings both through form (e.g., quarrel, shout, scream) and content of verbal responses (threat, curse, abuse) [7]. This definition was chosen as foundational because it highlights two key components of speech aggression:

- the external, formal (explicit) level: studying how aggression is formalized in speech—features of intonation, voice timbre, tempo and volume, specific diction and suggestion traits, as well as the set of lexical and syntactic constructions manifesting verbal aggression;
- the internal, semantic (implicit) level: analyzing the topic of utterances, their meaning, and communicative goals pursued by the speaker.

The introduction of studying the features of aggressive speech acts into teaching practice as a specialized course is an urgent task aimed at forming students' skills in recognizing, analyzing, and constructively responding to manifestations of aggression in speech.

Incorporating study of aggressive speech acts through a special course will prepare students for real communicative situations, increase their emotional and speech literacy, and improve their ability to handle conflicts with respect and professionalism.

An example of a course program: “Recognizing Speech Aggression in the Classroom”.

Course Goal: To train educators and students in identifying, analyzing, and constructively responding to speech aggression in an educational environment to create a safe and supportive atmosphere.

Course Structure:

Module 1. Introduction to Speech Aggression

- Concepts, types, and forms of speech aggression
- The significance of speech aggression in education
- General signs of aggressive speech acts

Module 2. Theoretical Foundations of Recognizing Speech Aggression

- Linguistic means of expressing aggression: lexicon, syntax, intonation
- Verbal and nonverbal aggression: differences and interaction
- The role of context and nonverbal signals in recognizing aggression

Module 3. Practical Methods of Diagnosing Aggressive Speech in the Classroom

- Observation and analysis methods: audio/video recording, notes
- Analysis of specific speech situations: school practice cases
- Using emotionality descriptors for detecting aggression

Module 4. Handling Speech Aggression in the Educational Environment

- Strategies for preventing and de-escalating conflicts
- Effective responses to students’ aggressive utterances
- Speech techniques for constructive interaction and strengthening positive communication

Module 5. Ethical and Psychological Aspects

- Ethical communication standards and the teacher’s role as a speech culture model
- Psychological foundations of aggression and emotional self-regulation
- Supporting the emotional climate in the classroom

Module 6. Final Practicum and Evaluation

- Role plays and simulations of speech conflicts
- Analysis of video fragments with aggressive speech and group discussion
- Development of personal strategies for managing speech aggression

Training Format:

- Lectures and interactive seminars
- Group discussions and case studies

- Practical training and role-playing games
- Homework assignments analyzing real situations

Expected Outcomes:

- Increased competence in identifying and interpreting speech aggression
- Improved skills for constructive responses to aggressive speech
- Creation of a learning environment with elevated trust and mutual understanding.

Thus, a comprehensive approach to introducing the study of aggressive speech acts into teaching practice as a dedicated special course will contribute to preparing competent professionals capable of effectively recognizing and managing speech aggression in various communication spheres.

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基于能力的父母身份在当今的数字化教育环境中如何发挥作用?
HOW DOES COMPETENCY-BASED PARENTHOOD ACT IN THE DIGITAL EDUCATIONAL ENVIRONMENT TODAY?

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摘要：俄罗斯教育环境的数字化扩展促使我们反思学校和家庭如何能够并且应该充分利用数字工具（包括技术、资源和服务），以促进符合儿童利益的有效且有意义的互动，因为对儿童而言，数字空间是自然而然的现实。本文探讨了教育环境中基于能力的育儿模式的发展，展示了教育参与者之间为了儿童的利益和利益而进行对话互动这一理念的有效性。作者将远程育儿支持描述为一种软实力机制，鼓励父母积累能够胜任抚养和教育子女的育儿经验。他们概述了最受欢迎的数字资源，并阐明了其在家长与专业人士互动中的教学本质。文章论证了协同活动方法在数字教育环境中的重要作用，该方法可作为有子女家庭社会和心理教育支持的目标指南。

关键词：基于能力的育儿模式，数字教育环境，协同活动方法，有子女家庭，育儿支持。

Abstract. *The digital expansion of the Russian educational environment requires a reflection on how schools and families can and should best utilize digital tools, including technologies, resources, and services, to foster competent and meaningful interactions in the interests of children, for whom the digital space is a natural reality. This article explores the development of competency-based parenthood in the educational environment, demonstrating the productivity of the idea of dialogic interaction between educational actors in the interests and on behalf of children. The authors characterize remote parenting support as a soft power mechanism that encourages parents to develop parenting experiences that are competent in raising and educating children. They characterize the most popular digital resources and define their pedagogical essence in the interactions between parents and professionals. The significant role of the co-event approach in the digital educational environment is substantiated, which serves as a target*

guideline in the social and psychological-pedagogical support of families with children.

Keywords*: competency-based parenthood, digital educational environment, co-event approach, families with children, parenting support.*

1. Today, educators' reflections on the realities of current education stimulate the development of pedagogical visions for the near and distant future of education. This necessitates expanding the research field in the study of traditional educational objects and emerging pedagogical phenomena. The problem associated with the contradictions and paradoxes of modern parenthood is becoming increasingly clear to pedagogical science and practice. Its experience is developing in a context where many cultural and educational values, knowledge, and worldviews are diversifying; new models, practices, and norms for the upbringing and education of the younger generation are being created. It's important to acknowledge that modern parenting is diverse. But motherhood and fatherhood must remain significant individual and social values for humanity to avoid a "dead end" in the evolution of family and society [4].

Materials and methods

Analytical method: analysis of theoretical sources; generalization of research concepts defining parenting support in the digital educational environment; study of the pedagogical experience of 125 Russian and international educational practices focused on parental involvement in the digital educational environment.

A critical analysis facilitated a qualitative assessment of digital tools for parents of school-aged children, including digital technologies, services, and resources used in practices to provide remote support for various types of parenthood (motherhood and fatherhood).

Specification as a method for exploring the role of a co-event approach in the discourse of family, childhood, and parenting, which generates new knowledge about the experience of parenting as a competency-based approach.

Results and its discussion

1. Competency-based parenthood (motherhood and fatherhood) is today emerging as a new pedagogical phenomenon that requires both the conceptualization of the concept itself in accordance with current pedagogical discourse and pedagogical understanding of the prospects for developing the experience of parenting as a competence-based one in the educational environment. It is obvious that for the sustainable development of present and future generations in a complex and uncertain world, supporting adults in their social role as parents (mothers and fathers) and developing their parenting experience as a competent one is an urgent reality.

The phenomenon of competence-based parenthood appears valuable and significant in its discursive and co-eventual meanings in the context of strategic directions of public and family education in the Russian Federation, practical tasks of state policies in the sphere of family, childhood and education, approved in accordance with the fundamental documents and national projects "Education", "Decade of Childhood", "Youth and Children" in force in the country [5; 7]. This phenomenon of competency-based parenthood expresses a specific way of being, presented as an experience of understanding the Other. We are already seeing its manifestations today in process-oriented parents who strive to expand their opportunities and methods of interaction with school and the parent community, actively using available services and resources to develop their own parenting experience and parenting competencies for the benefit of their children's education and upbringing. Such parents understand their socializing mission in the upbringing and education of the child, therefore their message to the education system is clearly formulated: to be recognized as competent in parenthood [1].

2. A study of Russian and international best practices in education allowed us to characterize remote support as a soft power mechanism. It provides parents with digital tools for developing their parenting competencies in raising and educating their children. Transforming online communication into real-life interactions is the message of modern competency-based parenthood, allowing every parent to demonstrate parenting competencies and / or acquire new ones [2].

We identified digital technologies and resources that are in demand among parents. Through these tools, they "connect" the digital educational community to develop their own parenting competencies in raising and educating their children. This defines the technosocial nature of modern parenthood as competency-based and determines the specifics of its remote support in the educational environment. The technosocial nature of parenting expands as children mature and becomes more stable. Parents actively engage in social media, creating contacts, groups, chats, and forums. For them, digital technologies become a channel of communication with the school. Families have the opportunity to consult and exchange information, gaining and significantly expanding their parenting experience as competent participants in communication and participation in the school educational community. From this perspective, we can say that remote support for families with children is becoming supranational in nature. This is reflected in a general trend common to different socio-linguistic cultures at the national and regional levels.

In this article, we present popular digital technologies and services that provide remote support for families with children in the educational environment within the "school-family" context.

An *educational institution's website* serves an informational and educational function, creates a school information environment, and ensures the openness and accessibility of education systems. Providing feedback is the most important function of a website in remote support for families with children. For example, school websites actively offer services such as parent chats and message boards for homework assistance, as well as video conferencing and streaming video, allowing parents to "connect" to the educational environment. This ensures their engagement and understanding of their child's progress at school.

Digital workshops, the emergence of which is driven by the significant evolution of digital technologies in children's school education, are highlighting a number of issues within families. Among these, we identify the problem of digital inequality between different generations of adults – parents, grandparents, and between adults and their children – as the most crucial in creating a unified digital environment. This inequality increases social differentiation within the local educational community and creates a greater barrier to the social integration of certain categories of parents. Digital workshops provide information literacy training for parents, based on the principles of collaborative learning technology. This engages parents, teachers, and children, transforming digital technologies into a tool for shared learning and leisure.

Parent community online platforms are an important and sought-after digital tool for facilitating the personal integration of modern parents into the educational environment. We studied over 125 parent community online platforms in Russian and international educational environment. We concluded that parents themselves are most often the initiators of their creation. For them, such platforms offer online tools for mutual remote support in their parenting experiences without the involvement of professionals. We note their focus on interfamily solidarity, mutual exchange, and collaboration as a motivating factor in the creation of online platforms by parents. Today, we can confirm that such online platforms have demonstrated greater potential during the period of self-isolation, facilitating the maintenance of connections and horizontal interactions between families and schools [3]. Parents are highly active online. Parent forums, chats, and blogs feature diverse topics, and information is constantly updated. This demonstrates the demand for these digital tools, which provide mutual support in their parenting experiences as competent parents.

3. The digital educational environment serves as an interactive territory where "...co-existence is that which develops and evolves. Accordingly, the very process of development consists of the emergence, transformation, and replacement of certain forms of togetherness, unity, and co-existence with other forms – more complex and of a higher level of development..." [6, p. 174]. The experience of engaging families with children in co-event projects in the digital educational envi-

ronment is axiologically significant, it dynamically develops. This facilitates and ensures the social and educational integration of competency-based parenthood into the local educational community. Thus, the following events have already become traditional: online meetings with children "Visiting a Fairy Tale"; the online family competition "Friendly Family" with the hashtag #FriendlyFamily on VKontakte; and online campaigns with a variety of themes. These events have an educational and outreach focus on preserving family values, developing family creativity, uniting the older and younger generations, and stimulating co-event community among parents, children, and teachers through digital tools.

Conclusion.

Competence-based parenthood as a pedagogical phenomenon represents a new quality of parenting in the present and future, and defines the scenario of interaction between parents and the school, and between older and younger generations.

Remote support for modern parenting is not implemented in tandem with the expansion of digital technologies, but alongside them, ensuring interaction between the two key actors – family and school – for the benefit of children's well-being. Today, such support for families with children is an innovative direction in the educational environment manifested both in the methods of its implementation in this digital word and in the digital tools provided to parents. The parent "connects" with the child, "rediscovering" their school-age child in the digital space, which changes the vector of parental trust and strengthens the parent-child relationship.

Today, we are witnessing a significant growth in online content authored by parents motivated to engage with educational institutions in the interests of co-education and co-scholarship of their children. We believe that parental online communication represents a developing area of co-event community in the digital environment, which holds promise for developing the parenting experience as a competency-based one and its axiologically significant mission in education.

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为工业实践提供教育和方法支持，确保未来工业培训硕士的持续专业和教育教育的连续性

DEVELOPMENT OF EDUCATIONAL AND METHODOLOGICAL SUPPORT FOR INDUSTRIAL PRACTICES, ENSURING THE CONTINUITY OF CONTINUOUS PROFESSIONAL AND PEDAGOGICAL EDUCATION OF FUTURE MASTERS OF INDUSTRIAL TRAINING

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摘要：在劳动力市场瞬息万变、职业教育质量要求日益提高的背景下，工业培训专家的培养尤为重要。培训效果在很大程度上取决于工业实习的组织质量和内容，这应确保其在持续职业教育和师范教育框架内的连续性。本文重点探讨工业实习的教育和方法支持，旨在培养未来工业培训专家的研究能力、方法论能力和专业能力。本文探讨了此类支持的理论基础、设计原则、内容和实施技术，并重点关注不同职业培训层次（中等职业教育（SVE）和高等教育（HE））之间的连续性。

关键词：教育和方法支持；工业实践；工业培训硕士；连续性；技能；能力。

Abstract. *In a dynamically changing labor market and increasing demands on the quality of vocational education, the training of industrial training specialists is particularly relevant. The effectiveness of their training is largely determined by the quality of the organization and content of industrial internships, which should ensure continuity within the framework of continuous professional and pedagogical education. This article focuses on the development of educational and methodological support for industrial internships aimed at developing the research, methodological, and professional competencies of future industrial training specialists. The theoretical foundations, design principles, content, and*

implementation technologies for such support, focused on continuity between different levels of professional training (secondary vocational education (SVE) and higher education (HE), are considered.

Keywords: *educational and methodological support; industrial practice; industrial training master; continuity; skills; competencies.*

The modern vocational education system faces the challenge of training qualified teachers capable of not only imparting industrial skills but also conducting methodological, organizational, and research work. The industrial training master plays a key role in this process, serving as a link between production and educational institutions, as well as a mentor for future skilled workers and specialists.

The quality of training for industrial training specialists directly depends on the effectiveness of their industrial training. Traditional approaches to practical training, often limited to simply completing industrial assignments, do not always contribute to the development of the necessary pedagogical, methodological, and research competencies in future specialists. Ensuring continuity between the various levels of professional and pedagogical education is particularly important – from college students studying a vocational profession and the fundamentals of pedagogy to university students pursuing higher pedagogical education and deepening their competencies.

The purpose of this article is to develop educational and methodological support for industrial internships, which will contribute to the formation of a comprehensive system of continuous professional and pedagogical education of future masters of industrial training, ensuring continuity at different stages of their training.

The development of professional and pedagogical competencies of future industrial training masters is a complex, multifaceted process that relies on a number of fundamental theoretical concepts.

The concepts of continuous education (B.S. Gershunsky, A.M. Novikov) emphasize the importance of a holistic approach to personal development throughout the entire educational journey. The competency-based approach (I.A. Zimnyaya, A.V. Khutorskoy) envisions developing in future specialists a set of knowledge, skills, abilities, and personal qualities that enable them to effectively solve professional problems. For industrial training instructors, this means not only mastering industrial skills but also the ability to teach, organize, motivate, and develop students.

The use of a systems approach (V.G. Afanasyev, Y.K. Babansky) allows us to consider the process of training a master of industrial training as a unified system, where all components (specialized training, pedagogical training, industrial internship, and research) are interconnected and interdependent. An integrative

approach (V.P. Bespalko) emphasizes the unification of various activities (educational, industrial, and research) to achieve a synergistic effect.

Various models of teacher professional development (K.M. Ushakov, I.M. Podlasy) identify stages in the development of personality and professional identity. For a vocational training master, it is important to progress from mastering a vocational profession to understanding their role as a mentor and organizer of the educational process, which requires specialized pedagogical support at each stage.

An approach based on activity theory (A.N. Leontiev) assumes that competencies are developed through the active performance of professional actions. Student-centered learning (I.S. Yakimanskaya) emphasizes the individual characteristics of the student, their needs, and motivation. For a vocational training instructor, this means the ability to create individualized educational trajectories for their future students.

The educational and methodological support (EMS) for industrial internships for future industrial training masters should be comprehensive, consistent, and results-oriented. In our opinion, the development of the EMS should be based on the following principles.

The principle of continuity When developing a teaching and methodological organization, the goal is to ensure a logical connection between the knowledge and skills acquired in previous stages of education (for example, in college) and the tasks solved in subsequent stages (at a university). The teaching and methodological organization should take into account that students may have different levels of preparation (both industrial and pedagogical).

The principle of systematicity implies that the educational and methodological organization should represent a holistic system, where all elements (practice programs, methodological guidelines, assessment materials) are interconnected and aimed at achieving common goals.

The principle of integration The program combines specialized (technological) and pedagogical training within the framework of industrial internships. The internship objectives should stimulate not only the improvement of industrial skills but also the development of pedagogical, methodological, and research competencies.

The principle of variability When constructing the educational and methodological unit, it provides for the possibility of adaptation to various professional training profiles and also takes into account the specifics of specific production sites.

The principle of phased development suggests that the content and objectives of the internship should gradually become more complex, reflecting the stages of development of the future master of industrial training.

The principle of interactivity consists of using active forms and methods of work that promote the involvement of students in independent activities and reflection.

Educational and methodological support should include the following components:

1. Industrial internship programs – a program for secondary vocational education, which will focus on mastering a working profession, primary pedagogical skills (assistance in training, observation of the process), developing an understanding of the role of a master of industrial training, and a program for higher education, which, in turn, will focus on in-depth mastery of pedagogical and methodological aspects, the development of research competencies, and the conduct of independent methodological developments and pedagogical experiments.

2. A common framework program that defines common goals, objectives, principles and evaluation criteria, ensuring continuity between levels.

3. Methodological guidelines and recommendations for students (step-by-step instructions for completing internship tasks, reporting requirements, examples of document preparation), for internship supervisors from the educational institution (goals, objectives, content, forms of control, evaluation criteria) and for internship supervisors from the enterprise (procedure for interaction, rights and responsibilities, forms of mentoring).

4. Assessment materials – criteria for assessing competencies (industrial, pedagogical, research), reporting forms (reports, practice diaries, reflective essays, presentations, portfolios), assessment tools (questionnaires, assessment sheets, checklists).

5. Information and methodological materials – a list of recommended literature, regulatory documents, sample documents (practical diary, report, individual assignment), digital resources (video materials, simulators, electronic textbooks).

The content of the educational method should be differentiated depending on the stage of the student's preparation.

During the secondary vocational education stage, students master a vocational profession and gain a first understanding of teaching. The objectives of the internship are to: deepen and consolidate industrial skills in the chosen profession; become familiar with the organization of work at the enterprise; develop basic mentoring skills (assist in teaching younger students, observe a foreman at work); and develop an understanding of the role of an industrial training teacher. The objectives of the industrial internship during the college stage are: performing work operations at the qualification level; participating in product quality control; observing the training process on the job; and maintaining a diary of the internship, recording both industrial and initial pedagogical observations.

The content of educational and methodological support at the stage of secondary vocational education includes:

- an internship program that clearly outlines production tasks, descriptions of work stages, and requirements for the workplace; modules on the fundamentals of pedagogy and mentoring have been added (for example, “Psychology of Professional Training,” “Fundamentals of Ethics for a Master of Industrial Training”);
- methodological guidelines consisting of instructions on labor protection, requirements for maintaining a practice diary (with sections for recording industrial observations and primary pedagogical observations);
- assessment materials containing criteria for assessing production skills, reporting form (practice report, diary).

At the higher education stage, students already have an understanding of the production process and the fundamentals of pedagogy, and they will deepen their professional and pedagogical competencies.

The objectives of the industrial practice at this stage are: developing competencies in the field of organization and methods of vocational training; developing skills in pedagogical analysis and lesson design; developing research skills in the field of professional pedagogy; preparation for independent teaching. The objectives of the internship may include: conducting lessons or master classes under the guidance of an experienced teacher; developing fragments of work programs for academic disciplines or modules; conducting mini-research (for example, analyzing the effectiveness of a specific methodological technique, studying the motives of students); participating in the development of teaching and methodological materials (didactic games, presentations, tests); maintaining a reflective diary of the internship, analyzing pedagogical situations.

The content of educational and methodological support at the stage of higher education should include:

- An internship program reflecting tasks related to methodological and pedagogical activities, research projects; in-depth modules on professional pedagogy, methods of teaching technological disciplines, and the psychology of professional training.
- methodological guidelines in the form of manuals for developing educational activities, conducting pedagogical experiments, analyzing pedagogical situations, and preparing research papers.
- assessment materials, such as criteria for assessing methodological developments, the quality of teaching sessions, and the results of pedagogical experiments; reporting forms (practice reports, methodological developments, research work).

To ensure the continuity and effectiveness of the educational and methodological training of industrial practices, the following technologies can be used.

Digital platforms and electronic educational resources. The creation of a unified digital platform where students of all levels can access internship programs,

teaching materials, interact with supervisors, and share experiences. The use of electronic internship diaries, online testing systems, and interactive simulators.

Project-oriented approach. Incorporating project tasks into the curriculum that require students to apply both industrial and pedagogical knowledge. For example, the project "Developing a Training Module on New Technology" and "Creating a Virtual Workshop on Occupational Safety."

Mentoring and mentoring. Establishing a mentoring system where senior-year students (Hons) act as mentors for junior-year students (SPO) during their internships. Experienced industrial training instructors and university professors act as internship supervisors, providing methodological and advisory support.

Case technologies and simulation games. Using real or simulated pedagogical and industrial situations (cases) to practice analytical skills, decision-making, and activity planning. Simulation games allow you to simulate the process of conducting a lesson, managing a group of students, and resolving conflicts.

Research seminars and workshops. Regular seminars are held where students present their practical research findings, discuss problems, and share experiences. Master classes by experienced educators and industry professionals showcase cutting-edge methods and technologies.

Evaluative-reflexive procedures. Implementation of a regular assessment system (self-assessment, peer assessment, assessment by the internship supervisor) with an emphasis on reflective learning. Students are encouraged to analyze their experiences, identify strengths and weaknesses, and formulate goals for further development.

Developing educational and methodological support for industrial training focused on the continuity of continuous professional and pedagogical education is a crucial task for training highly qualified industrial training specialists. This approach allows future teachers to systematically develop not only strong industrial skills but also essential pedagogical, methodological, and research competencies. The integration of specialized and pedagogical training, the use of modern technologies and active learning methods, and close collaboration between educational institutions and industry serve as the foundation for creating an effective system for training specialists in demand in the labor market and capable of innovatively developing vocational education.

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小学儿童创造性教育环境中的焦虑矫正
ANXIETY CORRECTION IN A CREATIVE EDUCATIONAL ENVIRONMENT IN PRIMARY SCHOOL CHILDREN

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摘要：本文探讨了小学儿童焦虑症的治疗问题。如果满足本文所讨论的以下条件，这一过程将会更加成功：教师通过组织创造性的教育环境，掌握一定的理论知识，了解如何应对儿童焦虑；组织一个专注于通过艺术疗法减轻焦虑的创造性教育环境；以及组织一个与家长互动的过程，以在创造性的教育环境中减轻儿童的焦虑。

关键词：治疗，焦虑，创造性的教育环境，小学年龄，敏感期，艺术疗法。

Abstract. *This article examines the problem of anxiety treatment in primary school-aged children. This process will be more successful if the following conditions, discussed in this article, are met: teachers will acquire certain theoretical knowledge on working with children's anxiety through the organization of a creative educational environment; a creative educational environment focused on reducing anxiety through art therapy will be organized; and a process of interaction with parents will be organized to reduce children's anxiety in a creative educational environment.*

Keywords: *treatment, anxiety, creative educational environment, primary school age, sensitive period, art therapy.*

In modern society, high levels of emotional stress can be observed across generations. Minors are the most susceptible group in this context. While adjusting to school, many students experience intense psycho-emotional stress, which manifests itself in increased anxiety, emotional vulnerability, and social withdrawal.

In this regard, developing a system of psychological and pedagogical support focused on preserving the child's mental well-being is particularly important. A key objective is the timely identification and prevention of anxiety before it becomes ingrained as stable personality traits [11].

The phenomenon of anxiety has been comprehensively explored in the scientific works of Russian and foreign scholars (A. Adler, A.M. Prikhozhan, K. Rogers, K. Horney, Z. Freud, and others). This issue is particularly significant in today's world, where rapid technological advances are combined with insufficient consideration of the individual's psychological state.

Primary school age is characterized by a highly flexible nervous system and receptiveness to educational influences. This sensitive stage of development offers significant potential for the development of the basic components of mental functioning, as it is during this period that the foundation for subsequent personal development is laid. Consequently, interventions aimed at reducing anxiety at this age are particularly effective. Creating a creatively rich educational environment is an important prerequisite for achieving positive results.

It should be emphasized that the design of a creative educational environment as a tool for reducing anxiety in primary school students remains understudied in modern scientific literature.

A wide range of methodological tools for the correction of anxiety states is available in modern psychological and pedagogical practice. Of particular interest is art therapy, which not only helps alleviate fears and anxieties but also activates students' personal resources.

Developing a creatively enriched educational environment is a prerequisite for the implementation of a variety of activities in primary school students. According to research by G.G. Kravtsova, E.V. Zvorygina, and S.L. Novoselova, a developmental space acts as a catalyst for a child's mental development [2]. Organizing an educational environment that prioritizes creative practices creates optimal conditions for reducing emotional tension and harmonious personal development.

The concept of a creative educational environment has received various interpretations in scientific research. A.N. Tubelsky interprets this concept as a "school life structure" – a specific organization of the educational process that forms a unique atmosphere, stylistic features and spiritual component of school existence [9].

V.A. Yasvin defines a creative environment as a system of targeted pedagogical influences and conditions that facilitate the development of personality in accordance with given parameters, as well as providing opportunities for self-realization inherent in the social and subject environment. From his perspective, the educational environment should stimulate the development and expression of creative potential [12].

L.S. Vygotsky emphasized the importance of awakening in schoolchildren a desire to embody aesthetic ideals in all spheres of life [2]. His concept enriches the understanding of the creative environment as a space for the cultural development of the individual.

Based on a synthesis of existing scientific approaches, it is possible to formulate an integrative definition: a creative educational environment is a specially organized environment that facilitates the development of individual characteristics, the development of creative potential, and the spiritual enrichment of the child.

An essential characteristic of the creative process is its spontaneous nature and the unpredictability of its results. Although direct management of creative activity is impossible, an educational institution can create favorable psychological and pedagogical conditions that increase the likelihood of students expressing creative initiative. This is a fundamental goal of modern education: creating an environment that stimulates and develops creativity as a mechanism for personal growth.

An effective tool for constructing such an environment is art therapy, a practice founded by artist Adrian Hill in the 1930s [5]. Broadly defined, art therapy encompasses a variety of forms of creative expression, including visual arts, dramatization, and choreography. Contemporary practice has been supplemented by specialized modalities: drama therapy, which utilizes theatrical improvisation; bibliotherapy, based on literary creativity; fairy tale therapy, which utilizes the metaphorical resources of folklore; and music therapy, which utilizes the therapeutic potential of sound vibrations. Synthetic forms, such as art drama, which integrate various artistic media, are particularly valuable [10].

Art therapy represents a unique form of psychological and pedagogical interaction, implemented in a creatively organized space [8]. The methodological substantiation of this approach is presented in the research of scholars such as T. Bronskaya, D. Woods, K. Drucker, E. Kramer, and others.

Contemporary research in the field of art therapy has identified the system-forming characteristics of this process:

Metaphoricality: creative activity serves as a symbolic language for expressing complex internal experiences through artistic images;

Developmental potential: focus on actualizing the individual's internal resources and stimulating creative abilities;

Three-component structure: a system of relationships uniting the specialist, the participant, and the creative product being created [6].

Art therapy support is implemented through successive stages [4]:

Organizational stage, including the establishment of psychological safety and preparation of materials

Phase of establishing contact and initial creative activity

Period of in-depth work with artistic content

Final stage with reflection and integration of the acquired experience

Modern art therapy tools include a variety of methodological approaches:

Art therapy utilizes the potential of visual creativity to address emotional disturbances and difficulties with social adaptation. Artistic practice promotes self-knowledge and the transformation of negative experiences.

Fairytale therapy utilizes metaphorical narratives to expand consciousness and optimize interaction with the social environment.

Music therapy utilizes acoustic stimulation and musical improvisation as therapeutic tools, activating imaginative thinking and the emotional sphere.

Dance movement therapy aims to integrate psycho-emotional and physical states through bodily expression, demonstrating particular effectiveness in addressing communication difficulties.

Photographic therapy methods involve the creation, selection, and subsequent analysis of images, followed by their creative transformation and verbal comprehension [7]. The use of art therapy technologies creates a protected space for children, allowing them to express feelings and experiences through creativity. A fundamental condition for effectiveness is the creation of an atmosphere of psychological safety that fosters liberation and experimentation with forms of self-expression that might otherwise be subject to social stigma. This approach provides a cathartic effect, facilitating the transformation of negative emotional states.

Primary school-age students typically project deep-seated experiences onto artistic images: anxiety, conflict, and traumatic experiences. Verbalizing such experiences often presents significant difficulties, making nonverbal channels of expression particularly valuable when working with this age group.

Art therapy promotes the development of communication skills and the formation of productive models of interaction with peers. This method allows for indirect work with personal issues, promoting adequate self-esteem and a positive perception of reality. A key advantage is the emphasis not on the artistic merits of the created works, but on their therapeutic potential.

Key advantages of the art therapy approach:

- accessibility for participants with varying levels of experience;
- activation of creativity;
- deep involvement in the process;
- positive psycho-emotional impact.

Our study prioritizes visual arts as the most appropriate medium for the characteristics of childhood. The study of children's visual arts has a solid scientific tradition, represented by the works of international (A. Clark, E.Kh. Knudsen, S. Levinstein) and Russian researchers (L.S. Vygotsky, V.S. Mukhina, N.P. Sakulina).

The age period between 6 and 10 years is characterized by significant changes in mental development, including the formation of self-awareness and voluntary

behavioral regulation. Visual arts contribute significantly to this process, stimulating the right hemisphere of the brain and developing imaginative thinking. The creation of graphic images involves complex intellectual work transforming thought into visual representation, facilitating the visualization of internal conflicts and their subsequent resolution.

Children's cognitive development in primary school age is characterized by a faster-paced development than their verbal abilities—they absorb the surrounding reality more intensively than their verbal apparatus develops. Visual arts become an effective means of representing thoughts and emotional experiences in a form accessible to the child [2].

Numerous studies interpret children's visual arts as a specific form of communication, a natural developmental need. Graphic images allow children to identify their current needs and internal contradictions. The process of drawing itself has a psychotherapeutic effect, creating a relaxing atmosphere free from anxiety and excessive tension.

The development of communicative skills requires a systematic expansion of the arsenal of psychological tools and mediation techniques necessary for the development of higher mental functions. The accumulation of emotional experience and behavioral patterns helps develop the child's ability to self-regulate in stressful situations. This contributes to an adequate level of aspiration and stable self-esteem.

A promising approach is to address childhood anxiety and fears through psychological mediation. According to research (V.I. Garbuzov, V.V. Lebedinsky, and others), ignoring anxiety can lead to disruptions in personal development. Uncontrolled anxiety leads to maladjustment and loss of self-confidence.

Terminological peculiarities in the scientific literature should be taken into account: followers of the cultural-historical school use the concepts of "mediation" and "mediation" interchangeably or differentiated—in a broad sense, including environmental determinants, and in a narrow sense, cultural tools and signs. In the context of our study, the term "mediation" was adopted, emphasizing children's use of cultural means.

Within the cultural-historical paradigm, L.S. Vygotsky identified three basic types of sign-symbolic activity: substitution, modeling, and experimentation [4]. Primary school age is characterized by the dominance of modeling as a priority method of cognition, with a gradual transition to the stage of experimentation. Children experiencing persistent conflicts with reality develop a need for the compensatory function of imagination. The specificity of children's thinking is manifested in the use of special symbols that explicate complex contents through specific images. This determines the importance of visual representations obtained through the process of perception for the genesis of mental operations [7].

The semiotic and symbolic function of a primary school student's emotional imagination is capable of not only mitigating anxiety but also profoundly transforming frightening images through a creative reinterpretation of reality.

A theoretical and methodological understanding of the cultural-historical paradigm, the concept of higher mental functions, and psychological tools of mediation allows us to conclude that the development of a system of mental self-regulation tools, including the organization of emotional states (in particular, fear) and behavioral patterns, leads to the development of the ability to self-regulate in various situations. The child acquires the ability to predict the long-term consequences of their reactions and manage behavior under emotional stress through collaboration with adults and the process of enterization.

The study confirms the effectiveness of a cultural-historical approach in remedial and developmental work with primary school-aged children. The developed system of psychological and pedagogical support, based on the principles of semiotic-symbolic mediation, has demonstrated its effectiveness in overcoming anxiety and fears through art therapy techniques.

The fundamental conditions for the effectiveness of the remedial process are:

- integration of individual and group work formats;
- active involvement of parents in the remedial and developmental process;
- use of a variety of mediation methods (play techniques, visual arts, fairy tale therapy);
- creation of conditions for the assimilation of cultural means of self-regulation.

The study results demonstrate that the systematic use of psychological mediation tools not only facilitates the overcoming of emotional difficulties but also the development of stable self-regulation mechanisms, which ultimately lays the foundation for the child's successful socio-psychological adaptation in the educational environment. A promising direction for further research could be the development of differentiated correctional programs taking into account the typological characteristics of children's development.

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基于项目的学习框架下的高校学生跨文化对话
INTERCUTURAL DIALOGUE AMONG THE STUDENTS OF HIGHER EDUCATION IN THE FRAMEWORK OF PROJECT-BASED LEARNING

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摘要：本文探讨了通过国际项目活动在俄罗斯高校学生中教授英语的问题。本文介绍了“品味美国”教育项目，该项目由富布赖特国际交流项目毕业生小额资助框架实施。该项目包括一场烹饪“秀”和国际交流项目校友见面会。该项目旨在拓宽学生对美国文化和美食的了解，并通过基于项目的外语学习活动，证明跨文化对话的成功。项目参与者包括车里雅宾斯克国际设计与服务学院、车里雅宾斯克南乌拉尔国立人文师范大学和夏威夷大学马诺阿分校的学生。

关键词：跨文化交流、项目活动、教育项目、基于项目的学习、国家研究、传统、测验、在线形式、富布赖特国际交流项目。

Abstract. *The article discusses the problem of teaching English to students of higher education in Russia through international project activity. The article is devoted to the description of the educational project “Taste America”, implemented within the framework of small grants for graduates of the international Fulbright exchange program. This project is a culinary “show” and a meeting of the alumni of international exchange programs. The aim of the project is to broaden the outlook of American culture and cuisine, in particular and to prove the success of intercultural dialogue through project-based activities in studying a foreign language. The project participants were students of Chelyabinsk International Institute of Design and Service, Chelyabinsk South Ural State Humanitarian Pedagogical University, the University of Hawai’i at Manoa.*

Keywords: *intercultural communication, project activity, educational project, project-based learning, country studies, traditions, quiz, online format, Fulbrigh international exchange program.*

Intercultural dialogue plays a key role in developing foreign language communication skills in higher education. Intercultural communication is essential for the students who study language as their major as well those who learn it as part of their general education. Over the past decade, project-based learning has increasingly become an integral part of foreign language teaching. The purpose of this article is to summarize and describe the experience gained as a result of the implementation of the international educational project "Taste America", the goal of which was to expand linguocultural knowledge about the country of the studied language.

Having summarized our experience over the past ten years, we noted that the project-based method is widely represented by both foreign (Andy Blunden, Ali Shahan Kuru and others) [2; 8]. and domestic scholars (M.V. Vasilizhenko [4], T.A. Maksimova [9], N.A. Popova [11], G.A. Korchagina [5] and others).

According to «The Glossary of Education Reform», «when engaged in project-based learning, students will typically be assigned a project or series of projects that require them to use diverse skills—such as researching, writing, interviewing, collaborating, or public speaking—to produce various work products, such as research papers, scientific studies, public-policy proposals, multimedia presentations, video documentaries, art installations, or musical and theatrical performances, for example» [3].

In this regard, foreign teachers also often use the terms "research-based learning" or "learning by doing": «For this reason, project-based learning may be called *inquiry-based learning* or *learning by doing*, since the learning process is integral to the knowledge and skills students acquire. Students also typically learn about topics or produce work that integrates multiple academic subjects and skill areas» [3].

According to O.S. Kudinova and L.G. Skulmovskaya, «implemented in various areas, project-based learning at a university contributes, among other things, to students' acquisition of the required competencies in terms of project-based and innovative skills, and can also serve as the basis for innovation in the university's areas of specialization» [6]. L.A. Fedoseeva and A.A. Zhidkov state: «student project-based learning can be viewed as a didactic system, and the project method as an element of this system and an educational technology that provides not only for the integration of knowledge, but also the use of updated knowledge and the acquisition of new knowledge» [15].

The implementation of project activities in higher education has the following directions:

1) Project-based activities carried out directly by the university's faculty and administrative staff and aimed at implementing and improving the educational process, ensuring the university's competitiveness through the development and

implementation of mini- and macro-projects, the implementation of grant-funded research, etc.;

2) Project-based activities of students, carried out within the framework of educational activities and aimed at both developing specific competencies and developing the ability to engage in project-based activities as such;

3) Joint participation of university faculty and students in the implementation of grants, engaging proactive students in project-based activities [3].

We are interested in the third area, as collaborative activities between teachers and students offer an effective creative means of interaction, motivating students to acquire new knowledge and skills. Moreover, as I.V. Kuzina notes, participation in the project and preparation for it «allows students to actively engage in social relations, fosters the development of a new social position, enables them to acquire skills in planning and organizing their activities, discover and realize their creative potential, and develop their individuality» [7].

The goal of our project is to develop intercultural communication skills with native English speakers through project-based activities and to update students' knowledge of the culture and culinary traditions of the United States. The "Taste America" project simultaneously addressed several objectives: developing students' linguistic competence, expanding their cultural and regional perspectives, gaining experience in international exchange and collaboration, and motivating them to further improve their language skills.

The project was organized by the authors of this article, Fulbright Exchange Program alumni of various years: E.N. Abramova (FFDP, 2013-2014, Montclair State University, N.J.) and E.S. Sedova (SIR, 2016-2017, University of Hawai'i at Manoa).

This project was implemented online on the ZOOM platform. Participants included 40 people from different parts of the world (Russia, USA, Japan, Turkey): 4th- and 5th-year philology students from the Pedagogical Institute (13 people), a master's student in the philology department of the Pedagogical Institute from Turkey, 1st- and 2nd-year students in the linguistics department of the International Institute of Design and Service (15 people), students from the University of Hawaii at Manoa in Honolulu (3 people), a master's student in history from Ohio State University, a professor at Honolulu Pacific University (USA), an independent researcher from Japan (Doctor of Biological Sciences), and alumni of the Fulbright exchange program (5 people).

To achieve this goal, the project included two aspects:

1. *Cultural* (in the form of a presentation, culinary master class, and quiz). The main objective was to provide an understanding of American culinary traditions, whose cuisine features a blend of other cultures; introduce participants to the main dishes typical of each American state; and conduct a quiz aimed at systematizing acquired knowledge and expanding their regional horizons.

2. *Linguistic*. This aspect involves live interaction with native speakers, which is associated with improving students' communicative and linguistic-cultural competencies and engages them in intercultural interaction.

The cultural aspect included meeting the organizers, who shared stories of their unforgettable experiences working and studying at American universities, living in another country, their traditions, and more.

The presentation included photographs reflecting their academic, scientific, and cultural experience. One piece of the presentation also covered American cuisine and its diversity across the states.

To address the cultural aspect, a culinary masterclass on making a traditional brownie dessert was held. All participants were able to watch the dessert preparation process on-line. Browny was chosen for the masterclass because it is easy to make and is considerred one of the most popular American desserts, beloved by many around the world.

A key component of this part of the project was the history of the brownie dessert presented in English by the first-year students of the Faculty of Linguistics. This form of work helps develop communicative and linguistic competencies in the target language. The ability and willingness to communicate in a foreign language with native speakers are an integral part of the language component, which requires knowledge of English grammar, vocabulary, and phonetics for successful communication. Public presentation in a foreign language takes up a significant portion of the educational process at the university, especially for students of the humanities.

As O.S. Soboleva and T.P. Savitskaya noted, «a presentation in a foreign language, as one of the forms of prepared monologue speech, is the result of complex educational activity» [12, p. 3]. Any monologue is characterized by a strict structure, logic, and consistency of presentation. It should be noted that the problem of teaching monologue speech is one of the most pressing issues in foreign language teaching methods. The problem of teaching speaking (monologue speech) is one of the priorities in the Federal State Educational Standard [14].

The first part of the project also included a "Taste America" quiz. The participants learned a lot about drinks, main dishes, and desserts of American cuisine. The quiz consisted of 30 questions, ranging from simple to those requiring a specific knowledge of American culture. Since the target audience was Russian-speaking students, the quiz was in Russian. For invited guests, the information on the slides was with English subtiteles.

The quiz covered various aspects of American life. Questions were presented in four sections.

1. Questions about American holidays: «For which holiday do Americans prepare pumpkin pie, roasted vegetables, cranberry sauce, mashed sweet potatoes, stuffed turkey, and gravy?»; «What dish is prepared for Fat Tuesday?».

2. Questions reflecting the influence of other cultures on American cuisine: «What is the name of the Mexican dish popular in America, consisting of a soft wheat tortilla wrapped with a variety of fillings?»; «What Italian dish is worth trying in New York City?»; «What is the name of the type of sandwich brought from Germany, consisting of a chopped fried patty served inside a split bun?» [10].

3. Questions about traditional American dishes and desserts: «What is the national dessert served over pancakes, waffles, and ice cream?»; «Every year on July 4th, an annual eating contest is held at Coney Island in New York City.»; «What is a popular confection made with sugar or corn syrup?"».

4. Questions about specific food facts: «In what year did the world first taste Coca-Cola?»; «In what year did the first McDonald's restaurant open?».

Thus, the quiz questions were aimed not only at identifying the knowledge of the participants and students as a target audience in particular, but also contained additional regional information, since each question was also accompanied by additional comments.

It's interesting to note that our American guests also learned a lot, as few people know that the average American eats nearly one and a half kilograms of nut butter per year; that the very first McDonald's restaurant was called "McDonald's Famous Barbeque"; that Coca-Cola was originally advertised as a cure for opium and morphine addiction, and others.

One cannot but agree with the statement of N.I. Khruleva that "a quiz has great potential for creating favorable conditions for revealing the personal potential of students, increasing learning motivation and a positive attitude towards the subject, developing the ability to collaborate, demonstrate ingenuity, and erudition" [16].

The linguistic aspect focused on a "dialogue of cultures." Students had the opportunity to interact with the students and scholars from the United States and Japan, as well as with Fulbright alumni. Everyone expressed hope that similar and future joint projects are important and necessary for sharing experiences, broadening understanding of traditions and cultures across countries, and, of course, for establishing friendly relations between Russia and the United States.

We believe the discussion with the American guests was highly productive and useful. American students gave short presentations about their experiences studying at summer schools and their live in Russia, including the dishes they tried, what they learned, and more. Honolulu Pacific University Professor Kurt Pauli also gave a master class, demonstrating the process of making a popular coconut drink. The Russian guests had the opportunity to ask questions both in their native language and in English, resulting in an engaging intercultural dialogue and culinary exchange.

Alumni of international exchange programs shared their experiences working at universities abroad. The experience gained during their international internships undoubtedly proved useful to the graduates in Russia.

Upon completion of the project, student participants were asked to complete a Google Form survey to determine how effective this interactive format was for the students, how engaging they found the project, and whether they were able to build on the skills they acquired during their university studies. Participants were asked to indicate "yes," "no," or "don't know" next to each question. This neutral response format reflects each participant's actual assessment, avoiding mathematical reflection on a point scale. Here are some of the survey questions:

- I enjoyed participating in the "Taste America" project.
- I learned a lot about the country of the target language and literature.
- I understood native English speakers.
- I expanded my understanding of American culture and traditions.
- I expanded my vocabulary.
- I enjoyed the brownie-making master class.
- I enjoyed the "Taste America" quiz.

Thus, the survey demonstrated a positive response from the participants of the project. Questions related to the implementation of the cultural aspect of the project received a 100% student satisfaction rating. Questions related to the implementation of the linguistic aspect of the project also demonstrated the effectiveness of this type of interactive work. Thus, 85% of respondents noted that the project helped to develop their communication skills, 80% of respondents emphasized the importance of the intercultural dialogue, and 60% of respondents noted that they enlarged their vocabulary.

The "Taste America" project was successfully implemented, generated genuine interest from all participants, and allows for the simultaneous resolution of several educational and developmental objectives.

Thus, the project activity contributed to the establishment of successful intercultural dialogue, which is conceived as «a process involving an open and polite exchange of views between individuals and groups with different ethnic, cultural, religious and linguistic backgrounds and heritages, based on mutual understanding and respect. It requires freedom and the ability to express oneself, as well as a willingness and ability to listen to the views of others <…> It promotes equality, human dignity and a sense of common purpose. It aims to develop a deeper understanding of different worldviews and behaviors, increase the level of cooperation and involvement (or freedom of choice), create conditions for personal development, and promote tolerance and respect for others" [1, p. 17]. Of course, an important component here is mutual understanding aimed at uniting people of different cultures. As S. G. Ter-Minasova notes, «mutual understanding in all its

aspects—linguistic, sociocultural, axiological (awareness and appreciation of the values of another culture, a dialogue partner), and many others—is the foundation and goal of dialogue among cultures» [11, p. 18].

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关于为学生创建有氧运动项目的问题
ON THE QUESTION OF CREATING AEROBIC PROGRAMS FOR SCHOOLCHILDREN

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摘要：本文提出了针对综合学校学生制定有氧运动项目的指标。这些指标基于基本有氧运动步骤的心血管负荷的客观数据。这些指标的模式可用于设计体育课中的有氧运动项目。

关键词：有氧运动，基本有氧运动步骤，有氧运动。

Abstract. *This article presents indicators for developing aerobic programs for students in comprehensive schools. These indicators are based on objective data on the cardiovascular load of basic aerobic steps. The identified patterns allow them to be used to design aerobic programs in physical education classes.*

Keywords: *aerobics, basic aerobic steps, cardio.*

Introduction. Currently, considerable attention is being paid to the development of educational content for students in comprehensive schools. However, the literature describes aerobic programs for health and sports aerobics [2-4]. It should be noted that the content of aerobic programs for school physical education lessons has its own specific characteristics, corresponding to the solution of educational, health, and developmental objectives. Therefore, the problem of finding and substantiating criteria for designing the content of aerobic exercise programs for students in comprehensive schools remains relevant.

Methods and organization of the study. To streamline the approach to designing aerobic programs for schoolchildren, this study used basic aerobic steps, which, according to the classification of the FIG – International Gymnastics Fed-

eration, include: step (March), run (Jog), jump (Skip), knee lift (Kick), jump - stance legs apart - legs together (Jumping Jack) and lunge (Lunge).

The choice of these exercises as basic ones for physical education lessons at school is based on the following premises [3]:

- Basic aerobic steps form the basis of most aerobic exercise technique;
- Basic aerobic steps most fully satisfy the pedagogical requirements of accessibility and activity and allow for the simultaneous solution of several types of lesson tasks, from educational to health-improving;
- These tools have several design options, which allows you to change the composition of aerobic exercises in physical education classes.

To validate the technology for creating aerobic programs for schoolchildren, a model experiment was conducted with 32 girls and 52 boys in grades 10-11 of a comprehensive school to assess the cardiovascular load of each of the selected basic aerobic steps. In this case, the cardiovascular load was defined as the heart rate (HR) per minute [1], which was assessed using a Polar 387 cardiotester.

Research results and discussion. The indicators of cardio load during the performance of basic aerobic steps (BAS - hereinafter) are presented in Table 1.

An analysis of the magnitude of cardio load allows us to identify a number of patterns in the changes in this indicator in schoolchildren:

1. Basic aerobic steps can be arranged in order of increasing average cardio load:

- for young men, the ranking sequence looks like this: “step”, “run”, “swing”, “jump”, “knee lift”, “jump - stand with legs apart - legs together” and “lunge”;
- For girls, the ranking sequence looks different: “step”, “run”, “jump - stand with legs apart - legs together”, “knee lift”, “lunge”, “leap” and “swing”.

Table 1.

Comparison of cardio load indicators during basic aerobic exercises in young men and women

Item No.	Name BAU	Young men X+ σ n=52	Girls X+ σ n=32	Student’s cytherium	Level of significance, p
1.	Step	117.7+12.5	121.8+12.2	1.49	>0.05
2.	Running	121.0+13.7	127.0+13.0	2.01	<0.05
3.	Leap	134.0+12.7	146.0+12.8	4.20	<0.05
4.	Knee lift	137.4+12.6	140.1+12.2	0.97	>0.05
5.	Max	128.0+13.4	146.0+12.9	6.34	<0.05
6.	Jump - stand with legs apart - legs together	137.6+12.0	136.9+12.3	0.26	>0.05
7.	Lunge	145.0+12.4	144.0+12.5	0.36	>0.05

2. The amount of cardio load does not differ significantly when performing certain basic aerobic steps:

- for young men, these are the exercises “jump”, “knee lift”, and “jump - stand with legs apart - legs together”;
- For girls, these are the exercises “lunge” and “swing”, “jump”.

From a methodological perspective, it can be said that the exercises listed above have similar effects on the body of schoolchildren and can be considered identical. From a technological perspective, this means they can be used to create a variety of aerobic exercise combinations in specific parts of the lesson based on the principle of interchangeability.

3. Cardiovascular load indicators for the basic aerobic steps “run,” “jump,” and “swing” are significantly higher in girls than in boys. From a technical perspective, this finding can be interpreted as suggesting that boys of this age need to perform a greater number of repetitions of these basic aerobic exercises than girls to achieve a similar training effect. For the remaining basic aerobic steps, the cardiovascular load values differ insignificantly, i.e., within the margin of error.

The obtained patterns open up the possibility of using the following parameters of basic aerobic steps for constructing aerobic programs in physical education classes at school:

- basic aerobic exercise rank,
- indicators of cardio load of basic aerobic exercise,
- number of repetitions of basic aerobic exercise,
- number of modifications of basic aerobic exercise,
- number of combinations of basic aerobic exercises.

The proposed indicators have a specific numerical value that each physical education teacher can use to design aerobic programs for high school students, as well as to monitor the amount of workload that high school students receive in physical education lessons.

Conclusions.

1. Analysis of cardio load revealed a number of patterns in changes in this indicator in schoolchildren:

- Basic aerobic steps can be arranged in order of increasing average cardio load;

- the cardio load indicators when performing the basic aerobic steps “run”, “jump” and “swing” are significantly higher in girls compared to the same indicator in boys ($p<0.05$);

- the cardio load indicators when performing the basic aerobic steps “step”, “knee lift”, “jump - stand legs apart - legs together” and “lunge” do not have reliable differences ($p> 0.05$).

2. For the design of aerobic programs in physical education classes at school, the following parameters of basic aerobic steps are used:

- basic aerobic exercise rank,
- indicators of cardio load of basic aerobic exercise,
- number of repetitions of basic aerobic exercise,
- number of modifications of basic aerobic exercise,
- number of combinations of basic aerobic exercises.

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将核电专业人才的高级培训项目纳入传统大学的教育计划

INTEGRATION OF ADVANCED TRAINING PROGRAMS FOR NPP SPECIALISTS INTO THE EDUCATIONAL PROGRAMS OF CLASSICAL UNIVERSITIES

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摘要：分析大学与核电站的互动，为学生提供相关方法和实践经验。关于现代教育技术，强调应急预报和监测方法的创新性，以提高毕业生的效率。

关键词：人才培养，核工业，核能，教育课程，工程培训。

Abstract. *The interaction of universities with NPPs is analyzed to provide students with relevant methods and practical experience. About modern educational technologies. The originality of emergency forecasting and monitoring methods is emphasized to improve the efficiency of graduates.*

Keywords: *personnel training, nuclear industry, nuclear energy, educational courses, engineering training.*

Introduction

The modern development of Russia's nuclear energy sector dictates the need for a comprehensive approach to training personnel capable of ensuring the safe and efficient operation of nuclear facilities. The State Atomic Energy Corporation "Rosatom" is implementing large-scale projects for the construction of nuclear power units both in Russia and abroad, which indicates the high demand for domestic technologies on the international stage. Currently, contracts are being implemented for the construction of 22 power units in seven countries, and the share

of foreign projects in the corporation's revenue structure is 50%, confirming the strategic importance of international cooperation. In the long term, it is planned to increase the share of nuclear generation in Russia's energy balance to 25% by 2042, which will require the commissioning of 42 new power units. In this regard, the importance of educational initiatives aimed at training specialists with competencies in the design, operation, and safety of nuclear installations is growing. The integration of modern educational technologies, including digital simulators and simulation modeling methods, is becoming a key element in forming a personnel reserve for the nuclear industry.

The effective implementation of strategic plans for the development of nuclear energy requires targeted training of personnel with the necessary professional competencies. According to forecast data, in the coming years, more than 370,000 specialists will need to be trained, possessing deep knowledge in the fields of nuclear physics, nuclear energy, radiation safety, and materials science [1]. Solving this task requires a systematic approach to integrating higher education programs and additional professional education (APE), as well as developing modern methods for training engineering personnel.

However, staffing the industry is complicated by negative demographic trends. Since 2016, Russia has recorded a steady natural population decline, which leads to a reduction in the potential contingent of students in technical fields [2]. In the context of a projected labor shortage, which, according to the Russian Ministry of Labor, may reach 2.4 million people by 2030, the nuclear industry faces the need to improve educational strategies and increase the attractiveness of engineering and technical professions among young people. The development of continuous education systems, project-based learning, and interaction between universities and industrial enterprises is becoming a key tool for forming a sustainable personnel reserve and providing the industry with competent specialists.

One of the key challenges in training engineering personnel for the nuclear industry remains the mismatch between the competency level of university graduates and the requirements of high-tech enterprises. Modern studies indicate that 88% of young specialists entering the labor market for the first time experience a deficit in the necessary professional skills, which hinders their adaptation to production conditions [3]. According to statistical data, only 25.3% of graduates have sufficient training for work at complex technological facilities, while 34.5% experience significant difficulties in performing professional tasks related to the operation of high-tech equipment [3].

Taking into account the rapid development of nuclear technologies, the need for specialists possessing not only fundamental knowledge in the field of nuclear physics and engineering but also practical skills in working with innovative technological solutions is growing. In particular, competencies in the application of

digital twins, predictive analysis, and automated control systems that ensure increased safety and efficiency of nuclear facilities are gaining special importance. Solving this problem requires the modernization of educational programs, the introduction of practice-oriented teaching methods, as well as the development of interaction between universities and industrial enterprises, which will allow graduates to more successfully integrate into the professional environment of the nuclear industry.

Voronezh State University (VSU) plays a key role in training specialists for the nuclear industry, acting as one of the supporting universities of the Rosatom State Corporation. Within the framework of strategic partnership with the Rosatom Technical Academy, educational initiatives are being implemented aimed at integrating advanced scientific achievements and technological developments into the educational process. This cooperation provides students with access to modern laboratories, internships at leading enterprises in the nuclear industry, and practical training on real equipment. One of the significant results of joint work was the large-scale modernization of the master's program in the direction 14.04.02 "Nuclear Physics and Technologies," aimed at integrating relevant knowledge and advanced teaching methods that meet the modern requirements of the nuclear industry [4]. The updated educational process includes the study of non-destructive testing technologies, the application of digital twins, predictive analysis methods, and automated control systems. A comprehensive approach to training, combining fundamental preparation with practical modules, contributes to the formation of competencies necessary for work in the high-tech environment of nuclear energy.

The purpose of this work is to study the possibility of integrating training courses from APE programs tested and implemented in the real educational process of training Russian and foreign specialists, implemented at the Rosatom Technical Academy for industry specialists, into the educational programs of classical universities. Within the framework of the updated master's program, a comprehensive adaptation of training modules was carried out, aimed at deepening the practical training of specialists for the nuclear industry. Disciplines focused on the study of advanced engineering solutions have been integrated into the educational process: "Methods of Destructive and Non-Destructive Equipment Control," "Electrical Equipment of NPPs," "Thermohydraulic Equipment of NPPs," and "Automated Systems for Managing Technological Processes at NPPs." These disciplines were developed taking into account the advanced experience of APE programs implemented for practicing specialists in the nuclear industry, which contributes to the unification of requirements for the competencies of graduates and practicing engineers [5].

A key aspect of modernization should be the formation of a practice-oriented educational environment in which students master methods of diagnostics, maintenance, and design of complex engineering systems of nuclear power plants. Spe-

cial attention is planned to be paid to the application of digital technologies, including predictive analysis systems and digital twins, which ensure the modeling of operational processes and emergency scenarios in conditions close to real ones. Such a transformation of educational programs contributes to the harmonization of academic standards with the current professional requirements of the industry, forming in graduates the skills necessary for work in the conditions of dynamically developing nuclear energy.

Methods of Implementing Courses and Their Practical Orientation

The integration of specialized disciplines into educational programs for training personnel for the nuclear industry is an essential condition for forming competent specialists capable of effectively working in the conditions of dynamic development of nuclear technologies. Within the framework of cooperation between VSU and the Novovoronezh branch of the Rosatom Technical Academy (RTA), a base department "Nuclear Power Plants with Water-Water Power Reactors" was created at the address: Novovoronezh, Voronezh Region, Southern Industrial Zone, P.O. Box No. 5. The educational process is planned to be conducted with students traveling to the territory of the Novovoronezh branch of the Rosatom Technical Academy, using equipment employed by the RTA for training foreign specialists for NPPs in Turkey ("Akkuyu"), Egypt ("El-Dabaa"), Bangladesh ("Rooppur"), Iran ("Bushehr"), and several other countries. Classes are conducted by employees of the base department, who are also RTA employees at their main place of work. As part of the modernization of the RTA's material and technical base, about half a billion rubles have been invested over the last five years alone. Using well-established APE programs offered by the RTA for foreign specialists, the faculty leadership, together with the RTA leadership, selected four disciplines adapted to the requirements of the standards in the direction 14.04.02 "Nuclear Physics and Technologies." This involves including the following courses in the master's curriculum, such as "Methods of Destructive and Non-Destructive Control," "Thermohydraulic Equipment of NPPs," "Electrical Equipment of NPPs," and "Automated Systems for Managing Technological Processes at NPPs," aimed at in-depth study of the fundamental principles of functioning of nuclear power installations. Mastering these disciplines contributes to the formation of a systemic understanding of technological processes in students, as well as the development of practical skills necessary for ensuring the safe and efficient operation of nuclear energy facilities [6].

Internships at operating nuclear power plants, as well as cooperation with the Rosatom Technical Academy, provide students with the opportunity to work with real equipment, allowing them to apply the acquired knowledge in conditions as close as possible to industrial operation. Such a model of personnel training not only increases the level of professional competence of future engineers but also

contributes to the development of skills in teamwork, prompt decision-making, and interaction with various technical services within complex production processes.

One of the key directions in training specialists is the study of electrical systems of nuclear power plants. The discipline "Electrical Equipment of NPPs" was created based on the eponymous APE program developed and taught by the RTA for more than 15 years to foreign and domestic specialists. Special attention is paid to the analysis of processes of transmission and distribution of electricity, the principles of functioning of backup and emergency power sources, as well as issues of electromagnetic compatibility of equipment. Mastering this course allows future specialists to develop and implement solutions aimed at increasing the reliability of power supply to nuclear power plants, which plays a decisive role in ensuring the overall safety and sustainability of the nuclear energy infrastructure [7].

Within the study of this discipline, students become familiar with the main electrical equipment of NPPs, acquire knowledge in the field of maintenance of relay protection and automation devices, master skills in the operation and adjustment of complete switchgear (CSG) 10 kV, including their design, electrical protection, and operating modes. In addition, the course includes mastering skills in working with CSG 0.4 kV, uninterruptible power supply units, as well as direct current panels, which allows students to develop practical competencies in the operation and adjustment of these systems.

An important role in this process is played by the introduction of project-based learning, which contributes to the development of systemic thinking in students, skills in critical analysis, and the ability to develop optimal engineering solutions. The use of digital technologies and simulation modeling allows not only to study the theoretical aspects of the operation of nuclear installations but also to perform complex engineering calculations, model the behavior of equipment in various operating modes, and develop strategies for managing technological processes [8].

Special significance in educational programs is acquired by the discipline "Methods of Destructive and Non-Destructive Control," within which students study systems for assessing compliance in the field of nuclear energy use, including unified control methods. The course contributes to the improvement of competencies in destructive control through methods of mechanical testing for hardness characteristics (MT) and metallographic studies (MS). In addition, students develop skills in non-destructive control, mastering visual and measurement control (VMC), radiographic control (RC), and eddy current control (ECC). The inclusion of laboratory-project practicums in the educational process contributes to the adaptation of theoretical knowledge to real conditions of NPP operation, which increases the level of training of graduates and their competitiveness in the labor market [9].

The course “Thermohydraulic Equipment of NPPs” plays a key role in training specialists for the nuclear industry, providing fundamental knowledge about heat exchange processes and hydraulic systems that underlie the functioning of nuclear power plants. In the course of mastering this discipline, students acquire the ability to explain the basics of heat exchange, types, principles of operation, and purpose of heat exchange apparatus of NPPs, demonstrate theoretical knowledge of the basics of hydraulics, the design and principles of operation of pumping equipment. They also master the purpose and principle of operation of pipelines, fittings, filters, and vessels at NPPs, including the classification and main elements of their design. In addition, the course develops skills in organizing measures to ensure safety during work on thermohydraulic equipment (THE). Using fitting mock-ups, students explain the principle of operation of control, safety, check valves, and shut-off fittings, indicate their structural parts, determine readiness for commissioning. Similarly, with heat exchanger mock-ups, they analyze the principle of operation, structural elements, patency, and cleanliness of tubes, and with pump mock-ups — determine the type, principle of operation, possible malfunctions, their causes, and methods of elimination. Special attention is paid to digital analysis methods that allow developing and evaluating the efficiency of heat exchange systems using engineering calculation complexes and simulation modeling platforms.

Modern approaches to engineering education emphasize the importance of digitizing design solutions, which is reflected in the course structure. In particular, students study methods for calculating heat and mass transfer processes using computer technologies, master work with CAD systems, digital twins, and virtual reality tools, which allows modeling the operating modes of equipment in various NPP operating conditions [8]. Such an approach forms in students’ skills in systemic analysis and design, as well as contributes to the development of engineering thinking necessary for solving complex technical problems in nuclear energy.

The discipline “Automated Systems for Managing Technological Processes at NPPs” plays an important role in training specialists capable of effectively working with high-tech control and monitoring systems. In the learning process, students demonstrate knowledge of the functioning of ACS TP of the power unit, the organization of operational dispatch control of BPC and RPC, describe the composition, purpose, and principle of operation of technical means for measuring flow, level, pressure, and temperature. They also explain the principles of controlling electrically driven fittings, describe the composition, functions, and structure of KRUSA P, possess knowledge about the functioning of the low-level automation PTC and the complex of technical means of the upper block level system (UBLS). In addition, the course includes demonstrating knowledge about the functioning of the initiating part of emergency protections and the safety control system based on technological parameters (SCS-STP).

Effective training of specialists for the nuclear industry requires the integration of theoretical training with practical activities, which ensures the formation of competencies in students necessary for work in high-tech and dynamically developing conditions of operation of nuclear power installations. One of the key factors for successful mastery of professional disciplines is the combination of fundamental theoretical preparation with practical classes aimed at applying modern methods of diagnostics, monitoring, and management of technological processes in real operating conditions [10].

Conclusion

The possibility of integrating training courses from RTA APE programs into the curriculum of higher educational institutions has been demonstrated. The disciplines "Methods of Destructive and Non-Destructive Control," "Thermohydraulic Equipment of NPPs," "Automated Systems for Managing Technological Processes at NPPs," and "Electrical Equipment of NPPs" have strategic importance in the issues of training highly qualified personnel for nuclear energy. These disciplines provide students not only with theoretical foundations but also with practical competencies necessary for the safe and efficient operation of installations.

After completing training under RTA APE programs adapted for universities, students receive not only the necessary set of theoretical knowledge and skills but also extensive practical experience. This significantly strengthens their positions in the labor market, increases competitiveness, and ensures successful employment. Such training of specialists has strategic importance for ensuring the stable operation of nuclear energy, based on the importance of high-quality maintenance of nuclear power plants and their safety in the long term.

In modern conditions of training specialists for the nuclear industry, special attention is paid to the introduction of digital technologies. One of the promising directions is the use of immersion simulators based on complex modeling. Such systems allow not only to visualize processes but also to recreate real work scenarios, which contributes to improving the quality of specialist training. Computer simulators with elements of virtual reality play an important role in training operators, especially in preparing for emergency situations, as they allow modeling a wide range of scenarios without risk to equipment and personnel.

When integrating APE programs into university educational processes, it is important to take into account new teaching methods. The application of virtual reality and simulators in training specialists in the nuclear industry allows minimizing risks associated with the operation of complex equipment and increases the level of personnel training.

The implementation of such technologies requires the development of specialized training modules and methodological aids adapted to the features of digital simulators. The use of complex modeling in educational programs contributes to

increasing student engagement and allows practicing critically important skills in a safe environment.

Successful integration of APE programs requires not only technological equipment but also a comprehensive restructuring of teaching methodology, including the development of skills in critical thinking and decision-making under conditions of uncertainty [11].

Moreover, our plans for modernizing the master's program in the specialisation 14.04.02 "Nuclear Physics and Technologies" are far from ending with the proposed four disciplines. Since on October 23, 2024, an agreement was signed between the RTA Rector Yuri Seleznev and the International Atomic Energy Agency (IAEA), within the framework of which the Technical Academy not only extends cooperation with the IAEA in its traditional directions but also expands the scope of interaction with the Agency to the field of nuclear medicine and radiopharmaceuticals. And VSU has extensive experience in implementing the specialisation 03.03.02 Physics in the profile "Medical Physics," it is planned to additionally introduce the following disciplines "Dose Assessment in Radiation Therapy" and "Production of Radiopharmaceuticals," which will be included in the curriculum and will allow expanding the set of competencies of students in the specialisation 14.04.02 "Nuclear Physics and Technologies."

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低年级学生的环境素养教育新方向
ENVIRONMENTAL LITERACY OF YOUNGER SCHOOLCHILDREN AS A NEW DIRECTION OF EDUCATION

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注释：社会与自然互动问题是我们这个时代最重要的问题，其正确解决在很大程度上决定了地球的命运和人类的未来。实用素养

因此，解决环境问题总体上需要重塑人们的意识和思维，这种意识和思维从儿童生命的最初几年开始形成，并在学校环境中发展和巩固。

国内教育正处于改革之中。学校的一大进步是随着第三代全球环境基金（GEF）和新基础课程（尤其是其可变部分）等新文件的采用而发生的变革。这些变革将帮助学校克服年轻一代标准化、刻板化和单一化的教育。

关键词：实用素养；学生环境素养。

Annotation. *The problem of the interaction of society with nature is the most important problem of our time, the correct solution of which largely determines the fate of the planet, the future of mankind. functional literacy*

Consequently, the solution to environmental problems in general requires a restructuring of the consciousness and thinking of people, which is laid down from the first years of a child's life, develops and consolidates in the school environment.

Domestic education is now in the process of reform. A big step forward are the changes in the school that are taking place in connection with the adoption of such a qualitative new document as the third generation GEF and the new basic curriculum, and especially its variable part. It is she who will help the school to overcome the standard, stereotyped, single-variant education of the younger generation.

Keywords*: functional literacy environmental literacy of schoolchildren.*

The relevance of the problem of environmental literacy of schoolchildren lies in its connection with the solution of such important problems of pedagogy as the problem of the formation of personality, all its moral aspects, and including the attitude towards nature.

At present, a fundamental change in the priorities of educational goals is envisaged, where the developmental function of education is brought to the forefront, ensuring the formation of the personality of primary school students and the disclosure of their individual abilities and capabilities, the formation of functional literacy. And the composition of functional literacy includes literacy in natural sciences. However, in our opinion, environmental literacy is indispensable. Therefore, the development and implementation of criteria and indicators for the results of modern environmental education, as well as methods for their assessment, is underway, including: environmental literacy (knowledge of the main environmental patterns; the ability to identify environmental problems, consider options for their solution, make a choice based on scientific knowledge and environmental values; predict the conditions for a practical solution to the problem, including through personal feasible participation); environmental and cultural literacy (knowledge and value attitudes specific to environmental culture, including the features and historical stages of its development; environmental traditions of the peoples of Russia as the basis for the cultural self-identification of the individual).[1]

Schools in our region, throughout the Sverdlovsk region, and in Verkhnyaya Pyshma are already actively working to develop new curricula and programs that take into account local and regional specifics, varying the specific set of subjects within each educational area. Schools in Verkhnyaya Pyshma also have a real opportunity to choose alternatives in defining the content of the regional component of environmental education.

In the context of modernizing environmental education, focused on incorporating federal, regional, and national components of its content, the chosen topic of research into schoolchildren's environmental literacy is particularly valuable. Primary general education and grades 5-6 of basic general education are the stage for developing the foundations of environmental literacy, scientifically grounded and culturally appropriate models (principles) of environmentally safe behavior in the surrounding socio-natural environment. This is currently being realized through the interplay of environmental and patriotic education.[5]

According to the Concept of General Environmental Education, environmental education is a continuous process of training, education and personal development aimed at forming a system of scientific and practical knowledge, value orientations, behavior and activities that ensure a responsible attitude of a person to the surrounding social and natural environment [1].

School environmental education as an important link in the general education system is designed to ensure the achievement of educational goals aimed, in particular, at:

- the formation of environmentally literate people who understand biological patterns, the connections between living organisms, their evolution, and the reasons for their species diversity;
- establishing harmonious relationships with nature, society, oneself, and with all living things as the main value on Earth.

That is, environmental education must represent a holistic system encompassing a person's entire life. It also aims to develop a worldview based on the concept of unity with nature. [3]

One way to update the current primary education system, in our view, is to create regional and ecological-local history natural science courses. These should serve an integrative function – providing a foundational understanding of the natural environment of one's region and its functioning; promoting the overall development of children of this age; and addressing a range of educational needs.

The content of environmental education is systemically determined and is determined by many socio-economic and psychological-pedagogical factors and conditions, the most important of which are the following:

- the interest of society in preserving an ecologically clean environment;
- the need of society for environmentally conscious citizens;
- the state and achievements of environmental science;
- psychological patterns of mental activity of schoolchildren;
- psychological, age-related and cognitive characteristics of students;
- the general state and development trends of the comprehensive school and society as a whole [2].

The content of environmental education is a dynamic, constantly evolving phenomenon. The development and continuous improvement of educational content is a problem of enduring socio-pedagogical significance [4].

There are main trends in the development of the theory and practice of environmental education for schoolchildren:

- enhancing the role of environmental education in solving modern environmental problems, as well as in the holistic process of developing the personality of students in the third millennium;
- intensification of international cooperation in the field of environmental education of youth and education in the field of the natural environment;
- ensuring the organic unity of education, extracurricular educational work, and socially useful activities of students in the study and protection of the natural environment;

- shifting the "center of gravity" of environmental education work from extracurricular activities to the educational process;
- the use of elements of a systems approach, modeling methods and historicism in the process of environmental education;
- strengthening the value aspects of the content of environmental education;
- greening of the educational content of subjects in the humanities and natural sciences;
- introduction of special courses with environmental content into the curricula of general education schools;
- differentiation and individualization of environmental and educational influences on the individual;
- taking into account, in the process of developing a responsible attitude towards nature in schoolchildren, the psychological, age-related and individual characteristics of the individual, as well as the specifics of his or her real attitude towards nature;
- the introduction of new forms of environmental education for students into the practice of comprehensive schools (interdisciplinary lessons, role-playing and story-based games, simulation and game modeling techniques, student conferences, expeditions to explore and protect the nature of their native land, role-playing workshops). [6]

The progressive and long-term nature of the above trends, which are undoubtedly the emergence of certain patterns, must be taken into account when constructing a system of psychological and pedagogical ways, means and conditions for improving the environmental education of primary school students [3].

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纹理分析在腰椎椎体海绵物质成分评估中的应用
TEXTURAL ANALYSIS IN THE ASSESSMENT OF THE SPONGY SUBSTANCE ELEMENTS OF THE LUMBAR VERTEBRAL BODIES

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注释：本研究通过对未出现结构性椎体异常的患者进行MRI扫描纹理分析，建立了腰椎椎体内骨小梁信号强度的参考值。结果发现，在成年早期个体中，不同椎体的信号强度值无统计学显著差异，支持使用单一参考标准。相比之下，在成年后期个体中，LIII-LIV和LIV-LV椎体之间存在显著差异。这些发现强调了信号强度作为骨质疏松预测指标的潜力，并凸显了将定量分析方法应用于临床实践以早期发现骨密度变化的前景。

关键词：影像组学、信号强度、结构异质性系数、磁共振成像、定量成像生物标志物。

Annotation. *The study established reference values for the signal intensity of the trabecular bone within the lumbar vertebral bodies using texture analysis of MRI scans in patients exhibiting no structural vertebral abnormalities. It was observed that in individuals in the first period of adulthood, signal intensity values showed no statistically significant differences among vertebrae, supporting the use of a single reference standard. In contrast, among those in the second period of adulthood, significant differences emerged between the* L_{III}-L_{IV} *and* L_{IV}-L_{V} *vertebrae. These findings underscore the potential of signal intensity as a predictive marker for bone rarefaction and highlight the promise of incorporating*

quantitative analytical methods into clinical practice for the early detection of alterations in bone mineral density.

Keywords: *radiomics, signal intensity, coefficient of structural heterogeneity, magnetic resonance imaging, biomarkers of quantitative imaging.*

Introduction

Modern methods of studying medical images mostly involve their objective, numerical evaluation. One of these methods is texture analysis, a method based on determining the numerical characteristics of the area under study [1]. The term "texture" in this context reflects the morphological substrate of the area of interest, respectively, the characteristic of the image texture is identical to the characteristic of the morphological substrate. The method of texture analysis involves studying the properties of the area of interest according to the spatial dependencies of halftones: each pixel or voxel has a number of numerical characteristics, respectively, their analysis allows us to obtain objective quantitative data characterizing the image as a whole [4].

To date, and at the current level of progress in medical imaging methods, the most valuable method for diagnosing osteoporosis, which is a medical and social problem of our time, is an in-depth pixel and voxel analysis of the spongy substance of the lumbar vertebral bodies based on the study of their medical images [2]. Among the basic characteristics of the area of interest and, as a result, the morphological basis of the image, the signal intensity stands out [6]. This parameter is a specific biomarker used to assess the structure of the trabecular bone normally and during its modification. Previously, scientists investigated the possibility of using signal intensity characteristics to diagnose primary and secondary changes in bone structure, including for differential diagnosis between osteoblastic and osteolytic metastatic foci, as well as to assess the structure of bone tissue in general. The use of the described parameter seems promising to us due to the fact that a certain change in the morphological substrate (trabecular bone due to various pathological processes) entails predictable fluctuations in the intensity of the signal from the studied area. Statistical indicators of the signaling characteristics of the studied image are an excellent tool that should be included in the standard set of diagnostic tools, since it can be used both for the differential diagnosis of existing changes and for the timely detection of early, preclinical changes in bone mineral density [5].

It is natural to assume that with a decrease in the mineral density of the spongy substance of the bone, the intensity of the signal of this image will change somewhat [3]. Due to the fact that at this stage there are no standards for the norm of the parameter under discussion depending on gender and age group, it is not possible to introduce signal intensity characteristics into the daily practice of diagnostic

doctors. However, these limitations set the vector for a thorough statistical and mathematical study of numerical indicators that can become a quantitative criterion for the normal structure of the spongy substance of the lumbar vertebral bodies in individuals of different periods of adulthood.

The aim of the work

To establish the values of the signal intensity of the spongy substance of the lumbar vertebral bodies of individuals of the I and II periods of maturity in normal conditions.

Research methodology

The design of the study assumed three stages of work:

1. Highlighting the area of interest, namely, the spongy substance of the L_I–L_V vertebral bodies in the medical image. At the same time, magnetic resonance imaging of the lumbar spine of individuals of both sexes, the first and second periods of adulthood, performed in the mid-sagittal projection, was used. The sample included 35 CT scans, which showed no structural changes in the vertebrae. Segmentation was performed in an interactive environment using the RadiAnt DICOM Viewer.

2. Recording and collecting parameters such as: the average value of the signal intensity, its maximum and minimum values, the area of the studied area, the standard square deviation of the signal intensity. It is important to emphasize that due to the absence of a morphometric label on the studied tomograms, it was impossible to calculate the absolute value of the projection area of the spongy substance of the L_I-L_V vertebral bodies, however, given that the images have the same scale, we can talk about the reliability of differences in the projection area of the studied area of interest. For segmentation, the "Open poligone" selection tool was used, which allows you to outline the segmentation zone in more detail.

3. Statistical processing of the received data using the StatMed computer program. Both parametric and nonparametric criteria were used for statistical processing. Their choice was determined by the correspondence or inconsistency of the data obtained with the normal law of frequency distribution of quantities. The DAgostino-Pearson criterion was used to determine compliance with the normal frequency distribution law. If the significance level under the criterion turned out to be >0.05, the distribution was assessed as normal.

The results of the study and their discussion

At the first stage of the work, the presence of statistically significant differences between the values of the projection area of the spongy substance of the lumbar vertebral bodies was determined. There were no differences between the values of this variable in the bodies L_I and L_{II}, L_{II} and L_{III}, L_{IV} and L_V ($p^*>0.05$, where p^* is the significance level for the Wilcoxon coefficient). However, this indicator turned out to be statistically significantly higher in body L_{IV} than in body L_{III} ($p^*=0.036$).

In the total sample, the median values of the signal intensity of the area of interest in body L_I were 1730.28±12.32 absolute dimensionless units (AU hereafter), in body L_{II} – 1687.19±16.73 AU, in body L_{III} -1736.68±14.01 au. The average value of the studied. The variable in body L_{IV} is equivalent to 1722±8.89 AU, the median value of the studied variable in body L_V turned out to be 1689.93±17.12 AU.

The table shows other statistical criteria characterizing the intensity of the signal from the spongy substance of the lumbar vertebral bodies.

Table 1

Statistical characteristics of the signal intensity of the spongy substance of the lumbar vertebral bodies according to magnetic resonance imaging (n=35)

Variable	1st lumbar vertebra	2nd lumbar vertebra	3rd lumbar vertebra	4th lumbar vertebra	5th lumbar vertebra
M	-	-	-	1722	-
Me	1730,28	1687,19	1736,68	-	1689,93
m	-	-	-	9,624	-
m*	12,24	16,22	14,11		17,01
MSD	-	-	-	86,52	-
min	1542,77	1471,03	1530,21	1540,59	1467,68
max	1875,21	1943,98	1956,43	1875,13	1944,67
left CI (95%)	1680,54	1653,27	1692,69	1704	1662,34
right CI (95%)	1743,97	1732,89	1770,59	1729	1733,61

Note: M is the average value, Me is the median value, m is the error of the mean, m* is the error of the median, MSD is the mean square deviation, min is the minimum value, max is the maximum value, n is the number of examined tomograms of the lumbar vertebrae, CI is the confidence interval

Conducting paired statistical comparisons of the centers of two independent samples did not reveal statistically significant differences between the values of signal intensity from bodies L_I and L_{II}, as well as L_{II} and L_{III} ($p^*=0.372$, $p^*=0.061$, respectively). At the same time, the value of this criterion was statistically significantly higher in the spongy substance of bodies L_{III} than L_{IV} ($p=0.034$, where p is the significance level for the Student's coefficient). In the L_{IV} body, the value of the signal intensity was significantly higher than in the spongy substance of the L_V body ($p^*=0.023$). Based on these results, in the general sample, the value of the signal intensity from the bodies of the lumbar vertebrae, excluding the age group, remains stable from the first to the third lumbar vertebra, after which it decreases from the third to the fifth vertebra.

Correlations between the values of the studied variable and the age of all subjects are either absent or poorly expressed, linear in nature and positive in orientation (Spearman correlation coefficient $r < 0.04$, significance level at this coeffi-

cient p>0.05). The results obtained need to be clarified when analyzing individual groups differentiated by age.

Next, the values of descriptive statistics of the intensity of the signal from the spongy substance of the lumbar vertebral bodies in various age groups were calculated. Thus, in the group of subjects in the first period of adulthood, the median of the values of the studied variable in the spongy substance of bodies L_I was 2121±9.87 AU; the average value of the signal intensity from the spongy substance of bodies L_{II} was 1697±15.85 au, from bodies L_{III} – 1736±13.45 au.E., from bodies L_{IV} – 1771+13.73 AU, from the spongy substance of bodies L_V – 1704+16.61 AU.

After analyzing magnetic resonance imaging of individuals in the second period of adulthood, we were able to obtain the following data: the average signal intensity from the spongy substance of bodies L_I was 1729.75±15.64 AU, from bodies L_{II} – 1708±29.01 AU, in the area of interest of bodies L_{III}, the median signal intensity was 1728±10.15 AU, in the spongy substance of bodies L_{IV}, the average value of the studied variable corresponded to 1724+17.09 AU, the median signal intensity from bodies L_V was 1698+21.04 AU.

It was not possible to establish reliable differences between the numerical values of the signal intensity from the spongy substance in individuals of the first period of adulthood when conducting paired comparisons: in L_I and L_{II} (p=0.324), L_{II} and L_{III} (p=0.213), L_{III} and L_{IV} (p=0.057), L_{IV} and L_V (p=0572). From this we can conclude that in the first period of adulthood there is no statistical relationship between the number of the vertebra and the intensity of the signal.

It was possible to establish statistically significant differences in individuals of the second period of adulthood between the values of the studied variable in L_{III} and L_{IV} (p=0.043), L_{IV} and L_V (p=0.013), namely, a more pronounced signal intensity from the third lumbar vertebra than from the fourth, and from the fourth – than from the fifth. The data obtained may be related to a regular decrease in the mineral density of the spongy substance of the lumbar vertebral bodies occurring in this age period.

A comparison of the values of the studied variable in individuals of different age groups did not reveal statistically significant differences between the intensity of the signal in the first and second periods of adulthood in all vertebrae of the lumbar spine (p>0.05 and p*>0.05). The correlation between the values of the signal intensity and the age of the representatives of both groups was either absent or interpreted as linear, weak in strength, negative – and therefore not statistically significant (r<0.4, p≥0.05).

The values of the minimum and maximum values of the intensity of the signal from the spongy substance of the lumbar vertebral bodies are shown in the table.

Table 2

Values characterizing the intensity of the signal from the spongy substance of the lumbar vertebral bodies in individuals of the first and second periods of adulthood in normal

Variable	The first period of adulthood				
	I	**II**	**III**	**IV**	**V**
M	1721	1697	1736	1771	1704
min	1109	1110	1119	1132	1111
max	2315	2322	2335	2311	2332
Variable	The second period of adulthood				
	I	II	III	IV	V
M	1729,75	1708	1728	1724	1698
min	1112	1106	1126	1135	1110
max	2321	2320	2330	2314	2334

Note: M is the median or average value, min is the minimum value, max is the maximum value, I is the first lumbar vertebra, II is the second lumbar vertebra, III is the third lumbar vertebra, IV is the fourth lumbar vertebra, V is the fifth lumbar vertebra

Conclusion

Numerical values of one of the indicators of the textural analysis of magnetic resonance imaging of the lumbar spine were established - an indicator of the intensity of the signal from the spongy substance of the lumbar vertebral bodies in normal representatives of the first and second periods of adulthood, which can be used in the study and evaluation of the bone structure of the lumbar vertebral bodies.

During the study, it was found that the values of the signal intensity from the spongy substance of the lumbar vertebral bodies did not differ statistically significantly in all vertebrae in the representatives of the first period of adulthood, and in the subjects of the second period of adulthood – in the first-second, second-third vertebrae. Thus, for representatives of the first period of adulthood, the same reference value of signal intensity can be used without taking into account the vertebra number, and in the second period of adulthood, different reference values should be used to assess the structure of the spongy substance of the bodies of different lumbar vertebrae.

The signal intensity indicator can be used not only to diagnose pathological conditions of bone tissue, but also as a predictor of its modification. A promising direction for the development of this field of mathematical morphology is the determination of the values of other textural characteristics of bone tissue in normal conditions and their implementation into the practical activities of a diagnostic doctor.

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COVID-19背景下支气管肺集合管淋巴结结构改变的特点

FEATURES OF STRUCTURAL CHANGES IN THE LYMPH NODES OF THE BRONCHOPULMONARY COLLECTOR ON THE BACKGROUND OF COVID-19

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摘要。本研究旨在基于系统综述，回顾并比较COVID-19支气管肺部淋巴结形态学改变的证据基础。材料与方法：使用PRISMA方法，在PubMed、Cochrane图书馆和eLibrary数据库中检索文献，检索时间截至2025年9月。使用筛选条件筛选系统综述（Lee et al., 2012）并采用滚雪球法。分析纳入符合系统综述标准并描述COVID-19淋巴结形态学改变的论文。证据级别采用俄罗斯联邦卫生部标准（第103n号令）进行评估。结果。分析了五篇系统评价（Polak 等人，2020 年；Hammoud 等人，2022 年；Caramaschi 等人，2021 年；Torge 等人，2022 年；Parra-Medina 等人，2020 年）。COVID-19 中淋巴结损害最一致的体征是淋巴细胞耗竭、生发中心减少、窦组织细胞增生症和浆母细胞增生症。差异在于坏死、血管病变和 T 细胞亚群分布变化的检出率。结论：COVID-19 支气管肺组淋巴结的形态学改变反映了 SARS-CoV-2 免疫病理反应的全身性特征，并可能具有预后意义。

关键词：COVID-19、SARS-CoV-2、淋巴结、形态学、系统评价、PRISMA。

Abstract. *The aim of the study. To review and compare the evidence base for morphological changes in the lymph nodes of the bronchopulmonary group in COVID-19 based on systematic reviews. Materials and methods. The literature search was performed in the PubMed, Cochrane Library and eLibrary databases until September 2025 using the PRISMA methodology. Filters were used to identify systematic reviews (Lee et al., 2012) and the snowballing method. The*

analysis included papers that met the criteria of a systematic review and described morphological changes in the lymph nodes in COVID-19. The level of evidence was assessed using the scales of the Ministry of Health of the Russian Federation (Order No. 103n). Results. Five systematic reviews were analyzed (Polak et al., 2020; Hammoud et al., 2022; Caramaschi et al., 2021; Torge et al., 2022; Parra-Medina et al., 2020). The most consistent signs of lymph node damage in COVID-19 are lymphocytic depletion, reduction of germinal centers, sinus histiocytosis, and plasmablastosis. The differences concern the frequency of detection of necrosis, vasculopathy, and changes in the distribution of T-cell subpopulations. Conclusion. Morphological changes in the lymph nodes of the bronchopulmonary group in COVID-19 reflect the systemic nature of the immunopathological response to SARS-CoV-2 and may have prognostic significance.

Keywords: *COVID-19, SARS-CoV-2, lymph nodes, morphology, systematic review, PRISMA.*

Introduction

The COVID-19 pandemic caused by SARS-CoV-2 has necessitated an in-depth study of the pathogenesis and morphological changes in the organs of the immune system. The lymph nodes of the bronchopulmonary group play a key role in the formation of local and systemic immune responses to coronavirus infection. Their lesions reflect both the features of virus interaction with immunocompetent cells and the degree of systemic inflammation. Since the beginning of the pandemic, a significant number of autopsy and immunohistochemical studies have been published, but data heterogeneity complicates summarization. Systematic reviews and meta-analyses make it possible to identify the most consistent morphological features, confirm their reproducibility, and evaluate potential clinical significance.

Aim of the study

To review and compare data from systematic literature reviews on morphological changes in the lymph nodes of the bronchopulmonary group in COVID-19.

Materials and Methods

The study followed the PRISMA methodology. Literature searches were conducted in PubMed, Cochrane Library, and eLibrary databases up to September 2025. Keywords included: COVID-19, SARS-CoV-2, lymph nodes, systematic review, meta-analysis. Filters recommended by Lee et al. (2012) were applied to identify systematic reviews, supplemented by manual searching using the snowballing method. Inclusion criteria: publications in English or Russian meeting systematic review criteria (structured search, inclusion/exclusion criteria, quality assessment) and containing morphological data on lymph nodes. Exclusion criteria: absence of lymph node data, lack of morphological or IHC descriptions, data duplication. The level of evidence was evaluated according to the Ministry of Health of the Russian Federation (Order No. 103n, Appendix No. 2).

Results

The analysis includes five reviews:

Polak S.B. et al. (2020) — an early systematic review with PRISMA, summarizing autopsy data, described lymphocytic depletion, reduction of germinal centers, and sinus histiocytosis [1-5].

Hammoud H. et al. (2022) — a full-format SR with PRISMA, including a frequency analysis of findings: lymphocytic depletion [1-5] (up to 80% of cases), plasmoblastosis [2-4], sinus dilation with macrophages, apoptosis [2,4] of lymphocytes.

Caramaschi S. et al. (2021) — a structured review with clinical and morphological correlations: depletion of T and B zones, plasmoblastosis [2-4], vascular changes (microthrombosis [3]s), vasculopathy [3].

Torge D. et al. (2022) — SR with a focus on extra-respiratory tissues, with a separate section on lymphoid organs, pointed to the frequent predominance of $CD8^+$-lymphocytes [2,4], revealed by IHC.

Parra-Medina R. et al. (2020) — a review of the early period, confirmed the presence of depletion, histiocytosis and atrophy of germinal centers.

The PRISMA flowchart with the stages of selecting the evidence base during the systematic search is shown in Fig.1

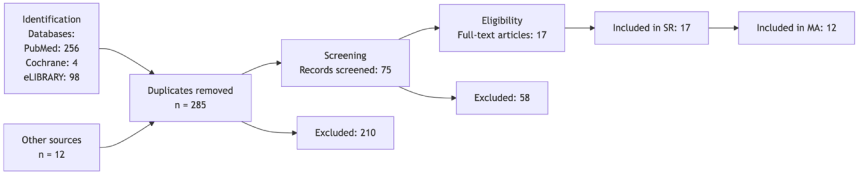

Figure 1. *Block diagram of the PRISM*

Coincident signs are marked lymphocytic depletion [1-5], reduction of germinal centers [1-5], sinus histiocytosis [1-5] with accumulation of macrophages, plasmoblastosis [2-4].

Differences: vascular changes (vasculopathy, microthrombosis [3]) were not mentioned in all reviews; apoptosis [2,4] and necrosis of lymphoid cells were more often detected in later studies; information on $CD4^+$/$CD8^+$ is presented only in reviews using IHC (Hammoud et al., Torge et al.).

Probably discrepancies They are related to the time frame of the included studies and the heterogeneity of methodological approaches.

Conclusion

The lymph nodes of the bronchopulmonary group in COVID-19 demonstrate a complex of morphological alterations, including lymphocytic depletion, follicular

structural disruption, and activation of macrophages. The most reliable features confirmed by systematic reviews include germinal center reduction, sinus histiocytosis, and plasmablastosis. These changes reflect the systemic nature of immune pathology in COVID-19 and may hold diagnostic and prognostic value.

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COVID-19 淋巴结中 IGG 和 IGM 表达：形态学和免疫组织化学特征
IGG AND IGM EXPRESSION IN LYMPH NODES IN COVID-19: MORPHOLOGICAL AND IMMUNOHISTOCHEMICAL FEATURES

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摘要：COVID-19 引起的淋巴结损伤伴有显著的形态功能改变，影响淋巴结的结构和细胞组成。在病毒感染的情况下，可观察到淋巴组织耗竭、生发中心消失、巨噬细胞因子激活以及淋巴窦和血管床结构破坏等现象。参与 B 细胞分化的关键调节蛋白表达的变化尤为重要。这一系列已发现的变化表明，SARS-CoV-2 感染过程中存在严重的免疫反应失调，并强调了免疫形态学研究在理解该疾病发病机制中的重要性。

关键词：COVID-19、淋巴结、IgG、IgM、免疫组织化学。

Abstract. *Lymph node damage in COVID-19 is accompanied by pronounced morphofunctional changes affecting both the structure and cellular composition. Under conditions of viral infection, the phenomena of lymphoid tissue depletion, disappearance of germinal centers, activation of macrophage elements, and disruption of the architecture of the sinuses and vascular bed are observed. Changes in the expression of key regulatory proteins involved in B-cell differentiation are of particular importance.. The set of identified changes indicates a profound dysregulation of the immune response characteristic of the course of SARS-CoV-2 infection and emphasizes the importance of immunomorphological studies in understanding the pathogenesis of the disease.*

Keywords: *COVID-19, lymph nodes, IgG, IgM, immunohistochemistry.*

The novel coronavirus disease (COVID-19) has posed a serious challenge for domestic and international healthcare systems due to the difficulties in patient care and the disease's high contagiousness [1]. Therefore, understanding the role of immune mechanisms and the body's humoral response during this infection is vital. However, there is a clear lack of research examining the pathological effects of COVID-19 on the immune system [2].

One of the most important components of the immune response to viral infection is the lymph nodes, key organs of the secondary immune response where B- and T-lymphocyte activation and differentiation, antibody production, and the formation of immune memory occur [3].

Studying morphological and immunohistochemical changes in the lymph nodes of patients who died from COVID-19 will provide a deeper understanding of the pathogenesis of the disease, its immunogenicity, and the persistence of antibodies produced against the coronavirus infection [1, 3].

The aim of the work. The aim of this work is a comprehensive morphological and immunohistochemical study using IgG and IgM markers of lymph nodes in patients who died from laboratory-confirmed COVID-19.

Materials and research methods of the study. This study analyzed bronchopulmonary lymph node tissue samples obtained by autopsy from 30 patients (22 women and 8 men) who died from laboratory-confirmed SARS-CoV-2 infection. The average age of the subjects was 66 ± 16 years (66 ± 18 years for women and 70 ± 31 years for men).

Autopsy specimens from patients whose deaths were not related to COVID-19 served as a control group. The average age in the control group was also 66 ± 16 years.

Lymph nodes were fixed in 10% neutral buffered formalin. Pathological examination was performed using standard hematoxylin and eosin staining.

Monoclonal antibodies to immunoglobulins G and M were used for immunohistochemical analysis. Immunohistochemical staining was performed on an automated ST5010 AXL Leica CV5030 Leica system.

Semiquantitative analysis of IgG and IgM expression was performed in 10 fields of view at ×400 magnification.

Results of the study and their discussion. Macroscopic and microscopic examination of lymph nodes from patients who died from severe COVID-19 revealed the following features.

Macroscopically, the lymph nodes were enlarged, edematous, gray-red, and encapsulated. The length of the lymph nodes was 9.72 ± 4.05 mm.

Microscopically, signs of disruption of the lymphoid tissue architecture were observed: absence of germinal centers, dilated sinuses, and isolated areas of necrosis. Characteristic findings included small vessel thrombosis, primarily local-

ized in the paracortical region. Furthermore, in most cases, a marked reduction in lymphoid tissue was observed, manifested by a significant decrease in the number of lymphocytes in both the cortical and paracortical zones.

The morphological picture was accompanied by the development of a pronounced macrophage response with numerous macrophages demonstrating active phagocytosis, including hemophagocytosis.

The lymph nodes in the comparison group were macroscopically oval, measuring 7.36 ± 3.82 mm in size, with clear contours. On section, the node tissue was gray-pink, homogeneous, without areas of necrosis or hemorrhage, and the cortical-medullar demarcation was clearly defined. The capsule was tense, approximately 0.5 mm thick, and gray-pink in color.

Histological examination revealed the intact structure of the lymph nodes, with a clear separation of the cortical and medullary zones. Numerous secondary lymphatic follicles with well-defined germinal centers were detected in the cortical zone. The paracortical zone was represented by diffuse lymphoid tissue with a predominance of small and medium-sized lymphocytes.

The sinuses were moderately dilated, filled with macrophages and a small number of plasma cells.

The production of specific antibodies by the body in response to SARS-CoV-2 antigens is a necessary component of pathogenesis. IgM can be detected already in the earliest stages of infection, providing the first line of defense against the immune system. High-affinity IgG responses are then initiated, playing a key role in long-term immune memory.

A qualitative comparison of IgG marker expression in the lymph nodes of patients who died from severe COVID-19 with a control group (without SARS-CoV-2) revealed significantly increased immunoglobulin expression in the former.

For a more accurate quantitative assessment, morphometric measurements were performed. The percentages of lymph node areas stained with markers were compared and analyzed in both groups.

In the COVID-19 group, the average percentage of stained area was 56.53% [51.44%-63.3%], while in the control group, similar figures were significantly different – 28.64% [20.35%-34.3%].

A comparative analysis using the Mann-Whitney test revealed statistically significant differences ($U = 0.00$; $p = 0.0002$), indicating a more pronounced presence of IgG+ clusters in the lymph nodes of patients with COVID-19.

A similar qualitative and quantitative assessment of IgM expression revealed a similar pattern.

In the COVID-19 group, the average percentage of stained area was 47.0% [37.48%-54.94%], while in the control group it was 33.33% [13.68%-40.23%].

Statistically significant differences were confirmed by comparative analysis using the Mann-Whitney test ($U = 4.00$; $p = 0.00019$).

Taken together, the data from the semi-quantitative analysis, based on determining the proportion of stained area as a percentage of the total section area, demonstrate that in severe COVID-19, characteristic morphological changes in the lymph nodes are observed, including partial depletion of B follicles with fragmentation of germinal centers and a significant increase in the lymph node's response to the infectious process.

The morphological changes identified in this study, affecting both the cellular composition and the organ's architecture, confirm the activation and redistribution of plasma cells during SARS-CoV-2 infection, which is consistent with previously published data on the development of a hyperergic response and activation of inflammatory mediators in patients with coronavirus infection. Statistically significant differences between the groups ($p < 0.01$) in both the proportion of IgG staining and IgM expression allow us to consider the identified changes as reliable and characteristic of lymph nodes in SARS-CoV-2 infection.

Conclusion. Certain patterns in morphological and immunohistochemical changes in bifurcation lymph nodes in COVID-19 demonstrate the importance of immune system organs as diagnostic targets in this disease. Studies have shown that lymph node activation, accompanied by changes in their architecture, occurs in response to SARS-CoV-2 infection.

Patients with COVID-19 exhibit signs of hyperplasia, infiltration, and follicular destruction, which may indicate a disruption in the normal functioning of the immune system. At the same time, lymph node damage may be associated with the development of systemic inflammatory processes, which also impacts the course of the disease.

Severe forms of COVID-19, caused by uncontrolled viral replication, stimulate the body's immune system to produce specific IgM and IgG antibodies. Several studies provide evidence that IgG and IgM can be detected early in the disease; however, while IgM titers significantly decrease during treatment, IgG levels remain unchanged for a long period of time.

Therefore, time-dependent changes in immunoglobulin levels should be addressed for further immune research, as well as for a more in-depth understanding of the pathophysiological processes occurring in the lymphatic system during coronavirus infection.

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引入纹身颜料后皮肤的形态功能变化
MORPHOFUNCTIONAL CHANGES IN THE SKIN AFTER THE INTRODUCTION OF TATTOO PIGMENTS

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摘要：纹身过程中，外源性色素进入皮肤会导致一系列持续性的形态功能性组织改变。现代科学数据分析表明，该过程的特征是急性炎症反应的发生，随后转入慢性期，伴随淋巴组织细胞浸润、巨噬细胞吞噬颗粒以及肉芽肿的形成。特别值得关注的是表皮的假上皮瘤样增生，这是一种组织学上类似于鳞状细胞癌的良性病变。红色色素的使用与特定并发症（包括恶性肿瘤）的发生之间存在相关性。色素在体内和激光去除过程中的降解过程可能导致毒性和潜在致癌代谢物的形成。研究结果证实，有必要进一步研究纹身色素对人体的长期影响。

关键词：纹身、皮肤、真皮、淋巴结、色素、纹身后并发症、感染性并发症、过敏反应、肉芽肿。

Abstract. *The introduction of exogenous pigments into the skin during tattooing causes a complex of persistent morphofunctional tissue changes. The analysis of modern scientific data demonstrates that this process is characterized by the development of an acute inflammatory reaction followed by a transition to a chronic phase with lymphohistiocytic infiltration, phagocytosis of particles by macrophages and the formation of granulomas. Special attention is paid to pseudoepitheliomatous hyperplasia of the epidermis, a benign change histologically similar to squamous cell carcinoma. A correlation has been established between the use of red pigment and the development of specific*

complications, including malignant neoplasms. The processes of degradation of pigments in vivo and during laser removal can lead to the formation of toxic and potentially carcinogenic metabolites. The results obtained confirm the need for further research on the long-term effects of tattoo pigments on the human body.

Keywords: *tattooing, skin, dermis, lymph nodes, pigment, post-tattoo complications, infectious complications, allergic reaction, granuloma.*

Introduction

Tattoos, which are permanent injections of exogenous pigments into the skin, are one of the oldest forms of body modification dating back thousands of years. However, in recent decades, there has been an unprecedented increase in their popularity, which has transformed tattooing from a marginal phenomenon into an element of popular culture.

Despite their widespread use, the fundamental aspects of the long-term interaction of synthetic pigments with human tissues remain poorly understood [1, 7]. Modern tattoo pigments are complex chemical compounds containing metal salts (iron, mercury, chromium, cobalt, nickel), organic azopigments, polycyclic aromatic hydrocarbons, and other components whose behavior in the biological environment is difficult to predict.

The introduction of foreign particles triggers a cascade of pathophysiological reactions, ranging from nonspecific tissue damage by a needle to a complex, multicomponent immune response. This process leads to the formation of persistent anatomical and morphological changes in the skin structure, which can persist throughout an individual's life [2, 3, 6]. Histologically, these changes range from a relatively "normal" response in the form of pigment persistence in dermal macrophages to pathological conditions: chronic granulomatous inflammation, pseudoepitheliomatous hyperplasia, lichenoid reactions and, which causes the greatest oncological alertness, the development of malignant neoplasms such as squamous cell and basal cell carcinoma [1, 2].

The problem is particularly relevant due to the fact that the processes of degradation of pigments in vivo, as well as attempts to remove them using laser technologies, can lead to the formation of unexplored metabolites with potentially mutagenic and carcinogenic properties [5, 8]. Thus, tattooed skin represents a unique and not fully understood biological model of chronic inflammation, persistence of foreign particles, and potential carcinogenesis.

Materials and Methods

The work uses the PRISMA systematic methodology. The electronic search was conducted in Russian and English databases in PubMed, Cochrane Library, Scopus, eLibrary and CyberLeninka databases until August 2025. Filters were applied to identify systematic reviews (Lee et al., 2012), and additional manual search was performed using the snowballing methodology.

The analysis includes works that meet the inclusion criteria: publications in Russian and English in the period up to August 2025; systematic reviews, meta-analyses, randomized (RCTs) and non-randomized controlled trials (RCTs); studies on histopathological, immunohistochemical or clinico-morphological changes in human skin associated with application or removal tattoos.

Exclusion criteria: case reports, case series without control groups, editorial materials, research protocols, conference abstracts; studies focused exclusively on tattoo removal, studies devoted exclusively to technical aspects of tattooing, sociological or cultural aspects; publications with inaccessible full text; systematic reviews of low methodological quality (assessment by AMSTAR 2 < 5 points).

Scales approved by the Ministry of Health of the Russian Federation (Order No. 103n) were used to assess the level of evidence.

Keywords to search for: tattooing, skin, dermis, lymph nodes, pigment, post-tattoo complications, infectious complications, allergic reactions, granuloma.

Results and Discussion

The PRISMA flowchart with the stages of selecting the evidence base during the systematic search is shown in Figure 1.

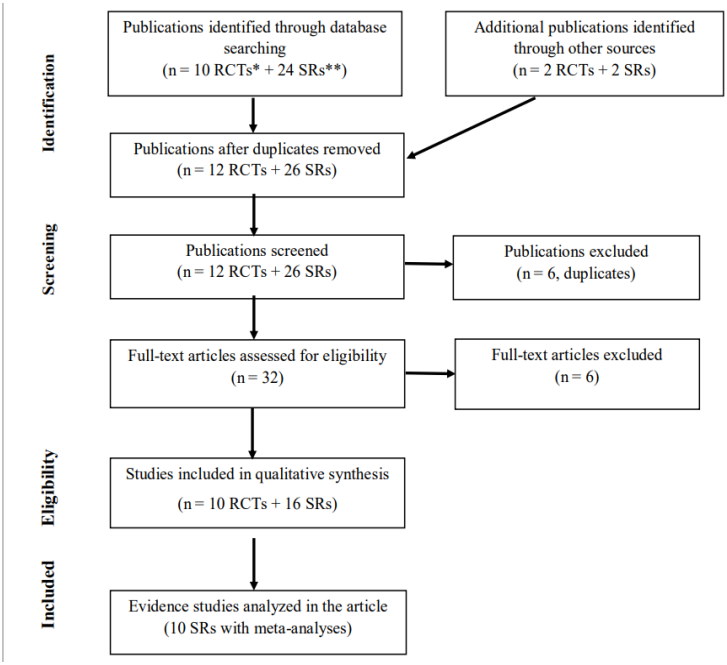

Figure 1. *PRISMA block diagram. Symbols: *RCTs – randomized controlled trials, ** SRs–systematic review and meta-analysis.*

The analysis includes 10 systematic reviews and meta-analyses.

Baumler W. et al. (2015) is a fundamental systematic review on the kinetics of tattoo pigments in the body. The author summarizes the data from 18 papers, proving that the pigments are not inert, but persist in dermal macrophages and fibroblasts for decades, and also undergo translocation to regional lymph nodes. The work highlights key gaps in knowledge about the metabolism and long-term safety of pigments, laying the foundation for future research [1].

Agarwal P. et al. (2021) is a systematic review based on the analysis of 127 biopsies from a single tertiary center, which ensures uniformity of histological assessment. The study revealed that the most common patterns were perivascular lymphocytic infiltration (78% of cases) and granulomatous reaction (22%). The work provides valuable data on the actual prevalence of various types of reactions and emphasizes the importance of histological confirmation of the diagnosis in clinically atypical manifestations [2].

Torre-Castro J. et al. (2022) is a comprehensive systematic review offering a detailed classification of dermatopathological complications of tattoos based on an analysis of more than 500 cases from the literature. The authors systematize the spectrum of histological changes, highlighting the most common findings: lymphohistiocytic infiltrate (68% of cases), granulomatous reactions (22%) and pseudoepitheliomatous hyperplasia (7%). The work serves as an exhaustive guide for dermatopathologists, providing clear criteria for the differential diagnosis of various types of reactions to pigment [3].

Munoz-Ortiz J. et al. (2021) is a large–scale systematic review analyzing more than 200 cases of inflammatory, infectious and tumor reactions associated with tattoos, including rare ophthalmological complications with periorbital placement. The authors emphasize the polymorphism of clinical and histological manifestations and the role of immune mechanisms in their development. The study is a valuable resource for clinicians of various specialties who are faced with complications of tattoos [4].

Rahbarinejad Y. et al. (2023) is a systematic review combining the presentation of a series of clinical cases with literature analysis and focusing on the correlation between the use of red pigment and the development of proliferative reactions. The authors describe in detail the pathogenesis, histological diagnostic criteria and management tactics of patients with squamous cell carcinoma and pseudoepitheliomatous hyperplasia that have arisen in the area of red tattoos. The study highlights the diagnostic difficulties associated with the histological similarity of benign pseudoepitheliomatous hyperplasia and the malignant process, and calls for oncological alertness [5].

Jacobs J. et al. (2024) is a systematic review focused on a retrospective analysis of published cases of skin malignancies that have arisen within tattoos. The

authors identified and analyzed 63 cases, among which squamous cell carcinoma (41 cases), basal cell carcinoma (16 cases) and melanoma (6 cases) were the most common. The study emphasizes that, despite the absence of a direct causal relationship, chronic inflammation induced by pigment and the potential carcinogenic properties of its degradation products are considered as significant provoking factors [6].

Reiter O. et al. (2016) is a systematic review with meta-analysis, one of the first to comprehensively evaluate the efficacy and safety profile of picosecond lasers based on an analysis of 16 clinical trials (10 RCTs and 6 RCTs). Meta-analysis confirmed the high effectiveness of the method (complete removal of pigment in 89.3% of cases), but also revealed the risk of side effects such as hypopigmentation (15.7%) and scarring (4.2%). This work provided an evidence base for the widespread introduction of picosecond technologies into clinical practice [7].

Fraser T.R. et al. (2022) is a systematic review focused on the analysis of 28 experimental studies investigating pigment degradation products under the influence of UV radiation, laser and metabolic processes. The authors conclude that the tattoo removal process can lead to the formation of potentially toxic and carcinogenic compounds (aromatic amines, azo compounds), whose effect on the body requires further study. This study is critically important for assessing the risks associated with laser tattoo removal [8].

Gurnani P. et al. (2022) is a systematic review with meta-analysis, including 42 studies (25 RCTs and 17 RCTs) to compare the effectiveness and safety of tattoo removal lasers. Meta-analysis demonstrated a statistically significant advantage of picosecond lasers over nanosecond lasers in the efficiency of complete pigment removal (OR: 2.45; 95% CI: 1.78-3.24). The study provides top-level evidence, guided by which clinicians can choose the optimal treatment method [9].

Tjipta A. et al. (2023) is a systematic review analyzing 17 studies (7 RCTs, 10 sockeye salmon) on the immune response induced by laser tattoo removal. The authors conclude that laser destruction of pigment causes a complex cascade of immune reactions similar to the primary response to pigment injection, which carries the risk of exacerbation of latent complications and systemic spread of decay products. The work highlights the need for careful monitoring of patients after laser removal procedures. [10].

An analysis of the included studies demonstrates that the introduction of exogenous pigment is a traumatic process that triggers a cascade of persistent anatomical and morphological rearrangements of the skin.

The acute phase (the first days and weeks) is characterized by a diffuse distribution of pigment particles in the dermis, limited tissue necrosis along the needle insertion channel, infiltration by polymorphonuclear leukocytes, and pronounced edema in the papillary layer of the dermis.

Within a few weeks, acute inflammation is replaced by a chronic phase (persistent condition), which can last for decades. The main morphological changes include:

• Cellular infiltration. Macrophage phagocytosis dominates. Macrophages, whose cytoplasm is filled with pigment granules ("tattoo macrophages"), form the basis of tattoo persistence. [5, 6, 7, 8]. Dense lymphohistiocytic infiltration (mainly T cells) is observed along the perivasculars and around the pigment granules as a manifestation of a chronic immune response [1, 2, 3, 4, 5, 6].

• Specific types of inflammatory reactions. The most characteristic is the granulomatous reaction – organized clusters of epithelioid histiocytes and giant multinucleated cells of foreign bodies surrounding large pigment particles. This reaction is most often associated with red, green, and blue pigments [1, 5, 6]. pseudolymphomatous reaction, a dense atypical lymphocytic infiltrate requiring differential diagnosis with lymphoma, is less common [1, 5].

• Changes in the epidermis. A key finding is pseudoepitheliomatous hyperplasia, a significant reactive thickening of the epidermis with elongation and expansion of epidermal processes that penetrate deeply into the dermis. This benign change can be histologically misinterpreted as a well-differentiated squamous cell carcinoma and is most characteristic of reactions to red pigment [2, 5]. Vacuolization of the basal layer of the epidermis may also occur, resembling the pattern of lichen planus [5].

• The distribution and fate of the pigment. The pigment is localized intracellularly (in macrophages, fibroblasts) and extracellularly in the dermis. Some macrophages migrate through the lymphatic vessels, leading to the permanent presence of pigment in the regional lymph nodes [8, 9]. Over time, under the action of enzymes, UV radiation, and laser, the particles fragment to form potentially toxic and carcinogenic decomposition products (for example, aromatic amines) [10].

According to a number of authors, the exogenous pigment in the skin is distributed in various cellular and tissue structures. In the epidermis, particles were detected in keratinocytes, basal and dendritic cells, which is confirmed by modern imaging methods. At the dermis level, the main pigment-carrying cells were macrophages, fibroblasts, and mast cells, in which granules were located intracellularly and surrounded by membrane structures. Long-term preservation of the pattern is associated with a cycle of "capture and recapture" of pigment by macrophages, which ensures the durability of tattoos for many years. Fibroblasts also play a significant role by forming a stable pigment reservoir in the connective tissue matrix [1, 2].

The phenomenon of pigment migration outside the skin deserves special attention. A number of clinical observations and pathoanatomic studies have shown that the particles move to the regional lymph nodes, where they accumulate in the

macrophages of the sinuses. This can lead to false positive results when searching for melanoma metastases [1, 3].

Conclusion

The analysis of the evidence base allows us to conclude that the introduction of exogenous tattoo pigments leads to significant and persistent morphofunctional changes in the skin. The key features are chronic inflammation (lymphohistiocytic infiltration), active phagocytosis (macrophages, giant cells), and reactive epithelial proliferation (pseudoepitheliomatous hyperplasia). These changes create a unique morphological environment, which, on the one hand, ensures tattoo permanence, and on the other hand, it is the ground for the development of complications, from benign granulomas to malignant neoplasms. The findings highlight the need for risk awareness, as well as the development of standardized protocols for histopathological diagnosis and long-term monitoring of tattoo patients.

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BCL-6 和 CD138 标记在评估 COVID-19 淋巴结形态学变化中的作用

THE ROLE OF BCL-6 AND CD138 MARKERS IN ASSESSING MORPHOLOGICAL CHANGES IN LYMPH NODES IN COVID-19

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摘要。本文介绍了重症COVID-19患者淋巴结的形态学和免疫组化改变，重点关注BCL-6和CD138。

将30例COVID-19患者的尸检材料与SARS-CoV-2阴性对照进行了比较。COVID-19患者的淋巴结肿大；组织学检查显示淋巴细胞耗竭、生发中心缺失/发育不全（约90%）、窦性组织细胞增生症和微血栓形成。免疫组化(IHC)显示大BCL-6$^+$区域减少，小BCL-6$^+$灶增加（p≤0.008），大CD138$^+$簇的总面积增加，小CD138$^+$结构的比例增加（p≤0.004）。 COVID-19淋巴结表现出生发中心反应的破坏和明显的浆细胞浸润，表明体液反应向滤泡外反应转变，具有潜在的预后意义。

关键词：COVID-19、淋巴结、BCL-6、CD138、免疫组织化学。

Abstract. *The article presents morphological and immunohistochemical changes in lymph nodes in severe COVID-19, focusing on BCL-6 and CD138. Autopsy material from 30 COVID-19 patients were compared with SARS-CoV-2–negative controls. COVID-19 LNs were enlarged; histology showed lymphoid depletion, loss/hypoplasia of germinal centers (~90%), sinus histiocytosis, and microthromboses. IHC revealed reduced large BCL-6$^+$ areas with increased small BCL-6$^+$ foci ($p \leq 0.008$) and higher total area of large CD138$^+$ clusters with an increased fraction of small CD138$^+$ structures ($p \leq 0.004$). COVID-19 LNs*

exhibit breakdown of the germinal center reaction and prominent plasmacytic infiltration, indicating a shift toward an extrafollicular humoral response with potential prognostic relevance.

Keywords: *COVID-19, lymph nodes, BCL-6, CD138, immunohistochemistry.*

The outbreak of the new coronavirus infection caused by the SARS-CoV-2 virus has led to a global pandemic, and a significant reconsidering of the pathogenesis of respiratory diseases [1]. COVID-19, which extends far beyond lung damage, is characterized by a systemic inflammatory response, coagulopathies, immune dysregulation, and multiorgan damage [2, 3]. Lymph nodes are a key component of the immune response to viral infection. These are key organs of the secondary immune response, where B- and T-lymphocyte activation and differentiation, antibody production, and the formation of immune memory occur [2].

Studying morphological and immunohistochemical changes in the lymph nodes of patients who died from COVID-19 allows a deeper understanding of the pathogenesis of the disease, including impairments in humoral and cellular immunity [1, 4]. Of particular interest is the study of the expression of BCL-6, a transcription factor key to the formation of germinal centers and the differentiation of follicular T-helper cells [1], as well as CD138, a plasma cell marker involved in antibody production [2].

Now days, numerous publications have described changes in the lungs, kidneys, heart, and liver associated with COVID-19 [3]. However, morphological changes in lymph nodes, particularly those with immunohistochemical analysis, are limited. Studies show that SARS-CoV-2 infection is characterized by hypoplasia or complete disappearance of germinal centers, thinning of the cortex, a decrease in the number of follicular dendritic cells, and a sharp decline in antibody production [1, 3].

The aim of the work. The purpose of this study is to conduct a comprehensive morphological and immunohistochemical study using BCL-6 and CD138 markers on lymph nodes of the patients who died from laboratory-confirmed COVID-19.

Materials and research methods of the study. During the study there was the analyzation of the tissue samples obtained during autopsy from 30 patients (22 women and 8 men) who died from laboratory-confirmed severe forms of the new coronavirus infection (COVID-19). The average age of the subjects was 66 ± 16 years (66 ± 18 years for women and 70 ± 31 years for men).

Autopsy specimens from the bronchopulmonary lymph nodes of patients whose deaths were not related to SARS-CoV-2 infection were used as a comparison group. The average age in the control group was also 66 ± 16 years.

Lymph nodes were fixed in 10% neutral buffered formalin.

Pathological examination was performed using standard hematoxylin and eosin staining. Monoclonal antibodies to BCL-6 (Abcam, UK) and CD138 (Abcam,

UK) were used for immunohistochemical analysis. Immunohistochemical staining was performed on an ST5010 AXL Leica CV5030 automated immunohistochemical system.

Semiquantitative analysis of BCL-6 and CD138 expression was performed in 10 fields of view at ×400 magnification.

Results of the study and their discussion. Macroscopically, the lymph nodes were enlarged, edematous, gray-red, and encapsulated. The length of the lymph nodes was 9.72 ± 4.05 mm. Histological examination revealed a marked reduction in lymphoid tissue in most cases, manifested by a significant decrease in the number of lymphocytes in both the cortical and paracortical zones. In 90% of cases the absence of germinal centers was noted due to severe hypoplasia or complete loss of follicular structure. The morphological picture was accompanied by the development of a pronounced macrophage response with the presence of numerous macrophages demonstrating active phagocytosis, including hemophagocytosis. In addition, signs of disruption of the lymphoid tissue architecture were observed, with blurred follicular contours, dilated sinuses, and the formation of individual areas of necrosis. Characteristic findings included thrombosis of small vessels, predominantly localized in the paracortical region. The lymph nodes in the comparison group were macroscopically oval, measuring 7.36 ± 3.82 mm in size, with clear contours. The capsule was tense, approximately 0.5 mm thick, and grayish-pink in color. On section, the node tissue was grayish-pink, homogeneous, without areas of necrosis or hemorrhage, and the cortical-medullary demarcation was clearly defined.

Microscopically, the lymph node structure was characterized by preserved architecture with a clear separation of the cortical and medullary zones. Numerous secondary lymphatic follicles with well-defined germinal centers were detected in the cortical zone. The paracortical zone was represented by diffuse lymphoid tissue with a predominance of small and medium-sized lymphocytes. The sinuses were moderately dilated, filled with macrophages and a small number of plasma cells. When analyzing BCL-6 expression in the control group, distinct BCL-6 expression was observed in the nuclei of germinal center cells. In the lymph nodes of COVID-19 patients, BCL-6 expression was significantly reduced or absent. In the remaining lymph nodes, weak focal expression was observed, predominantly in single follicles.

To quantify germinal center activity, morphometric measurements of the percentage of area stained with the BCL-6 marker were performed in two groups: patients who died from COVID-19 and a control group (without SARS-CoV-2).

In the COVID-19 group, the average percentage of stained area corresponding to large germinal centers was 93.55% [91.80–95.29%]. The percentage of small positive structures averaged 6.12% [4.56–7.67%]. In the control group, the average

percentage of staining of large areas was higher—96.96% [95.98–97.94%], while the proportion of small objects was significantly lower—2.00% [1.04–2.96%].

Comparative analysis using the Mann-Whitney test revealed statistically significant differences in the proportion of small positive structures ($U = 3.0$; $p = 0.002$), indicating a more pronounced presence of small BCL-6+ clusters in the lymph nodes of patients with COVID-19. Differences in the proportion of large germinal centers also reached statistical significance ($U = 5.0$; $p = 0.008$), reflecting a partial reduction in the area of preserved follicular structures in coronavirus infection.

A significant increase in the number of $CD138^+$ plasma cells was observed in the lymph nodes of patients with COVID-19, especially in the parafollicular and subcapsular zones.

An increase in $CD138^+$ cells without a preceding active germinal response indicates extrafollicular B-cell differentiation, a process that leads to the production of low-affinity, nonfunctional antibodies, which can potentially worsen the disease.

Immunohistochemistry using anti-CD138 antibodies allowed us to quantify the severity of plasma cell infiltration in lymph nodes from patients who died from COVID-19 and in controls without SARS-CoV-2.

In the COVID-19 group, the mean percentage of the staining area corresponding to large CD138-positive aggregates was 97.0% [96.1–97.9%]. The mean proportion of small CD138-positive structures was 7.8% [5.9–9.7%]. In the control group, similar indicators were significantly different: the average area of large CD138-positive structures was 92.2% [90.3–94.1%], and the proportion of small structures was 3.0% [2.1–3.9%].

A comparative analysis performed using the Mann–Whitney test revealed statistically significant differences in the proportion of small CD138-positive structures between the groups ($U = 8.0$; $p = 0.002$), as well as in the proportion of large clusters ($U = 9.0$; $p = 0.004$).

Thus, patients with COVID-19 had a significantly higher proportion of small CD138+ elements and a relative decrease in large plasma cell clusters. To assess the expression of BCL-6 and CD138 markers in lymph nodes, a semi-quantitative analysis was performed based on determining the proportion of stained area as a percentage of the total section area.

Immunohistochemical testing for BCL-6 in patients who died from COVID-19 revealed a partial reduction in germinal centers in most cases. Analysis of CD138 expression revealed a significant increase in the area of plasma cells in the COVID-19 group. The average proportion of CD138-positive cells, in the form of large compact clusters, was 4.8% higher. Moreover, the proportion of small CD138-positive structures in the study group was 2.6 times higher than in the control group ($p=0.003$), reflecting plasma cell activation and migration.

These morphological changes confirm the activation and redistribution of plasma cells during SARS-CoV-2 infection, consistent with known pathogenetic mechanisms of humoral immune hyperactivation.

The results of the study demonstrated that, in severe COVID-19, complex morphofunctional changes develop in the bronchopulmonary lymph nodes, affecting both the cellular composition and the organ's architecture. The observed macroscopic signs of lymph node enlargement and swelling are consistent with previously published data on the development of a hyperergic response and activation of inflammatory mediators in patients with coronavirus infection.

Histological examination revealed marked depletion of lymphoid tissue, the disappearance or reduction of germinal centers, and disruption of the follicular architecture. These changes are thought to be a consequence of hyperproduction of proinflammatory cytokines, disruption of interactions between B cells and follicular T helper cells, and the direct damaging effects of the virus. A significant decrease in BCL-6 expression, demonstrated by both semiquantitative analysis and morphometric analysis, indicates weakened centroblast activity and disruption of germinal center formation. These data support the hypothesis that SARS-CoV-2 infection interferes with the complete maturation of B cells in lymphoid tissue and reduces the effectiveness of the humoral response.

At the same time, a significant increase in CD138 expression and the number of plasma cells, predominantly localized outside the follicles, was noted. This phenomenon reflects the activation of the extrafollicular B cell differentiation pathway, accompanied by the production of predominantly low-affinity antibodies, which may contribute to insufficient virus clearance and increased inflammatory tissue damage.

Statistically significant differences between the groups ($p < 0.01$) in both the proportion of BCL-6 staining and CD138 expression allow us to consider the identified changes as reliable and characteristic of lymph nodes in SARS-CoV-2 infection.

Conclusion. COVID-19 causes severe lymph node damage, characterized by lymphocyte depletion, destruction of follicular architecture, and disruption of immune cell interactions. These data are important for understanding the mechanisms of immune dysfunction in COVID-19 and may serve as a morphological basis for the development of new immunomodulatory treatment strategies.

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非金属烤瓷结构修复效果对口腔状况的临床研究
CLINICAL STUDY OF THE ORAL CAVITY CONDITION BASED ON THE RESULTS OF PROSTHETICS WITH METAL-FREE CERAMIC STRUCTURES

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注释。根据世界卫生组织 (WHO) 的数据，世界各国牙齿和牙列缺损的患病率平均为 78% 至 80%。在某些地区，这一比例高达 89%。据一些作者称，牙齿和牙列缺损的患病率范围很广，平均为 44% 至 100%。由此可以得出结论，这种病理在所有牙科疾病中占主导地位。这项工作致力于临床研究无金属结构修复体的适应和补偿机制，以及这些结构对口腔矿物质和酸碱平衡变化的影响。研究表明，随着牙列缺损的增加，口腔微生物群落发生变化，为致病性和条件致病菌株的生长和繁殖创造了条件。临床放射学研究表明，牙齿缺失会导致牙颌系统发生代偿适应性改变，表现为剩余牙齿位置和牙弓的改变以及咬合关系的破坏，即牙列变形，而牙列缺损的增加也会影响颞下颌关节的正常功能。鉴于数字化技术在口腔正畸领域的蓬勃发展，在修复非金属陶瓷固定结构假体时，应进一步研究组织和口腔液体状况，以控制修复前后的代偿适应机制。

关键词：非金属矫形结构，代偿适应机制。

Annotation. *The prevalence of dental and dental row defects in various countries worldwide, according to the World Health Organization (WHO) data, averages from 78% to 80%. In some regions, it reaches 89%. According to some authors, the range of prevalence of dental and dental row defects is quite wide, averaging from 44% to 100% of lesions. From this, it can be concluded*

that this pathology is leading among dental diseases in general. This work is devoted to the clinical study of adaptation and compensatory mechanisms in prosthetics with metal-free constructions, the influence of these constructions on changes in the mineral and acid-base balance of the oral cavity. Studies have shown that with increasing dental row defects, the oral cavity microbiocenosis changes, creating conditions for the growth and reproduction of pathogenic and conditionally pathogenic strains. Clinical-radiological studies have shown that compensatory-adaptive changes of the dental-jaw system in response to tooth loss manifest in changes in the position of remaining teeth, dental arches and disruption of occlusal relationships, i.e., development of dental row deformations, and with increasing dental row defects also affect the normal function of the temporomandibular joint. Considering the most active development of digital technologies in orthopedic dentistry, additional studies of tissue and oral fluid conditions should be conducted when prosthetics with metal-free ceramic fixed constructions for control and development of compensatory-adaptive mechanism schemes before and after prosthetics.

Keywords: *metal-free orthopedic constructions, compensatory-adaptive mechanisms.*

Introduction. Undoubtedly, leading positions in restoring dental row defects today belong to metal-free ceramic constructions as the most aesthetic and durable orthopedic materials [7,9,11]. An increasing number of young orthopedic dentists give preference to these constructions, and the internet is “replete” with advertisements and promises of durability, strength and aesthetics of metal-free orthopedic constructions [1,3,6]. Therefore, today the study of the influence of such types of materials and constructions on the oral cavity condition, on physiological parameters of the oral cavity, saliva composition, periodontal tissues, is particularly interesting and relevant [2,5,8]. Also, studying mechanisms of adaptation to metal-free ceramic constructions, studying compensatory mechanisms, considering this pathology in the aspect of construction durability, causes special interest [4,13]. The practical significance of the conducted study lies in studying the influence of metal-free ceramic constructions on the oral cavity mineral homeostasis condition, acid-base balance, and improving the effectiveness and safety of using the studied constructions, as well as the influence on compensatory-adaptive adaptation mechanisms [10,12]. Conducting such studies can lead to improving the quality of dental care and patient satisfaction. Over 10 years, a series of studies were conducted on studying the results of treating partial tooth absence with metal-free ceramic constructions, but today, in our view, studies of compensatory-adaptive mechanisms and studies describing dynamic and comparative changes in oral cavity acid-base balance when prosthetics with this type of orthopedic constructions is relevant and in demand.

Methodology. The study object consisted of 30 patients (15 women and 15 men) with partial tooth absence aged 21 to 35 years, without chronic diseases, before and after prosthetics with metal-free ceramic constructions. The study subject included dental rows, periodontal tissues, oral fluid, chewing muscles. To solve the set tasks, clinical methods (complaint collection, oral cavity examination), radiographic, microbiological and statistical methods were used. All patients underwent prosthetics with metal-free ceramic constructions in the shortest possible time after extraction: from 1 to two months. Patients were divided into several groups depending on the dental row defect prevalence: absence of one, two and three adjacent teeth. Before conducting the study, we paid great attention to normalizing oral hygiene and conducted explanatory conversations with patients about the specifics of caring for metal-free ceramic constructions. All patients underwent the same oral cavity examination scheme using objective and subjective examination methods, with additional radiograph analysis and microbiological study.

The practical significance of the conducted study lies in studying the influence of metal-free ceramic constructions on the oral cavity mineral homeostasis condition, acid-base balance, and improving the effectiveness and safety of using the studied constructions, as well as the influence on compensatory-adaptive adaptation mechanisms. Conducting such studies can lead to improving the quality of dental care and patient satisfaction.

Results and discussion. In patients with single dental row defects, complaints were identified about discomfort when chewing, trauma to the gum mucosa when chewing hard food, and aesthetic defect.

During external examination, facial symptoms were absent, the height of the lower third of the face was preserved. Examination and palpation of TMJ and chewing muscles showed no pathological changes. The red border of the lips showed no pathological changes. The mucosa of lips and cheeks was pale pink, did not differ from normal.

When examining dental rows of patients with medium and large defects, changes in tooth position were more often observed: bodily displacement, rotation around the tooth axis limiting the dental row defect, as well as teeth deprived of antagonists. In the absence of first and second molars, vertical displacement of teeth occurred according to dento-alveolar or dental types.

Radiological examination of periodontal tissues and TMJ was conducted. Based on the conducted radiological study, it was revealed that with small dental row defects, bone elements of the temporomandibular joint changed insignificantly.

With the loss of two or three teeth, small changes in the temporomandibular joint were observed, manifested in minor structural changes of the bone-ligament

apparatus. These changes can be regarded as one of the stages of developing compensatory-adaptive reactions that arise in all components of the temporomandibular joint due to biological necessity, i.e., for the best performance of its working functional load.

All patients in the studied groups underwent collection and examination of oral fluid for the amount of mineral components. Studies were conducted at the stage of preparation for orthopedic treatment and after it. Patients had oral fluid samples taken for analysis of its mineral composition and acid-base balance. Data were collected and analyzed using statistical methods. Results were compared between groups of patients with and without prostheses, and also compared with normative values. Analysis of the obtained results is being conducted.

Practically all obtained results on shifts in oral cavity biocenosis with small defects were also identified with large defects, but the above-mentioned changes were of a deeper nature in the predominant majority of cases.

Thus, it can be said that with increasing dental row defects, oral cavity microbiocenosis changes, creating conditions for the growth and reproduction of pathogenic and conditionally pathogenic strains.

Clinical-radiological studies showed that compensatory-adaptive changes of the dental-jaw system in response to tooth loss manifest in changes in the position of remaining teeth, dental arches and disruption of occlusal relationships, i.e., development of dental row deformations, and with increasing dental row defects also affect the normal TMJ function.

Currently, studies continue, additional functional (electromyographic and flowmetric) methods of studying the influence will be used. Considering the most active development of digital technologies in orthopedic dentistry, additional studies of tissue and oral fluid conditions should be conducted when prosthetics with metal-free ceramic fixed constructions for control and development of compensatory-adaptive mechanism schemes before and after prosthetics.

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输液治疗对7岁以上儿童急性脑衰竭血流动力学及呼吸参数的影响

THE EFFECT OF INFUSION THERAPY ON HEMODYNAMIC AND RESPIRATORY PARAMETERS IN ACUTE CEREBRAL FAILURE IN CHILDREN OVER 7 YEARS OF AGE

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注释：重症肺炎合并急性脑衰竭患儿在机械通气期间，每日输液总量增加一倍以上，静脉输液次数是静脉输液次数的8倍，口服液体量比第1组高50%。对于7岁以上合并格拉斯哥脑供血不足评分（6.5±1）的重症肺炎患儿，在ICU综合重症监护的前7天内，机械通气联合适当的药物支持治疗具有积极作用，其压力限制作用更为明显。

关键词：输液治疗、血流动力学、呼吸、急性脑衰竭、儿童。

Annotation. *During mechanical ventilation in children with severe pneumonia complicated by acute cerebral failure, the total daily volume of fluid administered was more than doubled, the number of intravenous solutions administered was 8 times greater than intravenous fluids, and oral fluids were 50% higher than in Group 1. A positive effect of mechanical ventilation with appropriate drug support was observed, with a more pronounced stress-limiting effect during the first 7 days of comprehensive intensive care in the ICU for severe pneumonia complicated by a Glasgow cerebral insufficiency score of 6.5 ± 1 in children over 7 years of age.*

Keywords: *infusion therapy, hemodynamics, respiration, acute cerebral failure, children.*

Relevance. One of the many challenges of comprehensive intensive care for severe infections in children is infusion therapy. Severe acute pneumonia often

combines severe dehydration with impaired vascular permeability, intracellular edema with hypovolemic syndrome, and attempts to effectively restore blood volume, the need to correct blood rheology abnormalities, and correct blood component deficiencies with parenteral fluids lead to an even greater increase in vascular pressure in the pulmonary circulation and pulmonary artery, further increasing vascular resistance, stressing the heart, and worsening already impaired myocardial contractility due to myocarditis. Therefore, routine infusion therapy required for drug administration, correction of colloid-osmotic abnormalities, systemic and cellular dehydration, and detoxification can have a negative impact, aggravating infection-induced acute cerebrovascular insufficiency, acute respiratory failure, and acute heart failure. One of the contentious issues is the volume of parenteral infusion therapy. Some authors prefer the oral route of administration [1-3]. We attempted to analyze the effects of changes in water balance on hemodynamics during infection complicated by acute cerebral insufficiency in children over 7 years of age.

Purpose of the work. To study and evaluate the effect of infusion therapy on hemodynamic and respiratory parameters in acute cerebral insufficiency in children over 7 years of age.

Material and methods of research. The results of continuous prolonged monitoring of body temperature, hemodynamic parameters, respiration, fluid balance (daily, intravenous, enteral volume of administration), urinary activity were studied in children admitted to the ICU of the RSCEM in critical condition due to infection complicated by respiratory, acute cerebral failure at the age of 7.1-18 years. Intensive care was carried out according to the recommendations in the relevant clinical protocols. In group 1, the study data of 8 children (the average age was 13 ± 3 years) were studied. Upon admission to the clinic and throughout intensive care, there were no indications for mechanical respiratory support (MRS). All patients of group 2 (8 children) aged 12.6 ± 2.6 years from the moment of admission to the clinic, according to indications, were transferred to mechanical ventilation. Of the 8 children in group 1, 7 were males and 1 girl, of the 8 children in group 2, 1 girl, that is, patients Males accounted for 88% in each group. Factors aggravating the general condition of patients in group 1 were severe pneumonia, observed in 88% (7), AHF grade 1-2A in 50% (4), ARF grade 1-2 in 75% (6) of children. While in group 2, the severity of the condition and the need for external respiration prosthetics in children was associated with the severity of pneumonia in 100% (8), secondary encephalopathy in 100% (8), ARF grade 2-3 in 87% (7), AHF grade 2 AB in 75% (6), convulsive syndrome 37% (3). In general, the most severe pathological conditions that were a complication of the underlying disease were observed in group 2. These were complicated pneumonias, which accounted for 50% of the total number of patients studied, secondary encephalopathy complicated by grade 1-2 coma (50%), convulsive syndrome (36%), acute respira-

tory failure (42%), and acute heart failure (AHF) – 36%. Cerebral dysfunction upon admission to the clinic was assessed using the Glasgow scale and amounted to 9.1±0.4 points in group 1 and 6.5±1.0 points in group 2, corresponding to a significantly increased brain function of 29% in group 2, which determined the duration of MCI and the duration of intensive care in the ICU. After awakening and restoration of adequate breathing, reflexes, and consciousness within one to two days, the children were transferred to a specialized department.The study data were processed using the variation statistics method in Excel, calculating arithmetic means (M) and standard errors of the mean (m). The parametric Student's t-test (t) was used to assess the significance of differences between two variables. The relationship between the dynamics of the studied parameters was determined using pairwise correlations. The critical significance level was set at 0.05.

Results and their discussion. From the first day of intensive care, in the complex intensive care, which included infusion therapy, preference was given to the enteral route of resuscitation, correction of water-electrolyte imbalance, and nutritional support via the enteral route of administration in both groups of children. Clinical and functional examination data reflected features due to the severity of the underlying disease and its complications, as follows. In Group 2, more severe pneumonia and acute cerebral insufficiency, as well as the severity and tendency to persistence of respiratory distress syndrome, were detected due to mechanical ventilation. During the first 7 days, the daily volume, intravenous administration, and the volume of renal excretory activity were significantly higher by 58%, 268%, and 50%, respectively, in children of Group 2 (Table 1). Infusion therapy against the background of mechanical ventilation prolonged to 35 days also differed significantly from intensive care during spontaneous breathing. Thus, the total daily volume of administered fluid was increased by more than 2 times, the number of intravenous solutions administered was 8 times higher than the intravenous administration in group 1, and oral administration was 50% more than in group 1 (Fig. 2).

Table 1.

Volume of infusion therapy in the intensive care unit in ml/day.

Parameters	**1 group 7 days**	**Group 1 19 days**	**Group 2, 7 days**	**Group 2 35 days**
Daily fluid volume	2027±468	2214±316	3219±466*	4983±1309‴
parenterally	392±86	261±100	1442±221*	2032±700 ‴
into the tube/inside	1635±483	1958±374	1786±308	2925±723 ‴
diuresis	1381±341	1536±318	2059±217*	3713±322 ‴

*- the difference is reliable relative to the indicator in group 1 in the first 7 days.

‴ - the difference is reliable relative to the indicator in group 1 for 19 days.

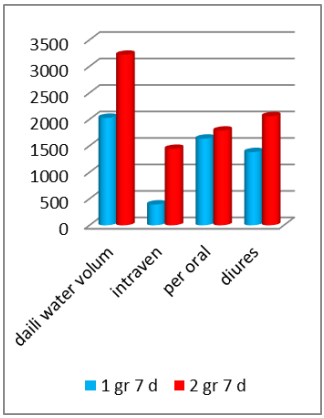

Figure 1. *Infusion therapy in the first 7 days, ml/day.*

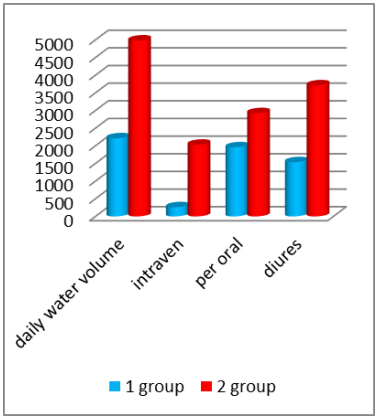

Figure 2. *Infusion therapy in the intensive care unit, ml/day.*

A strong direct correlation between the daily volume and the enteral route of administration was observed in Group 1 for 7 days (0.99) and 19 days (0.96). In Group 2, a strong direct correlation between the total daily volume and enteral fluid intake was observed for the first 7 days (0.9) and 19 days of intensive care (0.91). The findings confirm a direct relationship between the total daily fluid load and the enteral route of administration.

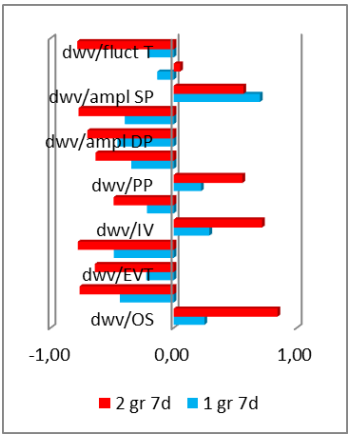

Figure 3. *Correlation relationships of daily fluid volume and hemodynamics (7 days).*

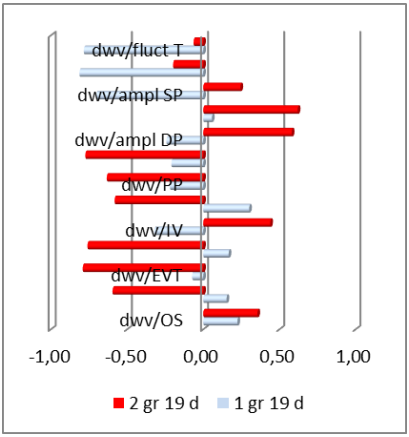

Figure 4. *Correlation relationships of daily fluid volume and hemodynamics (7 days).*

In group 1, no significant correlations were found between the daily fluid volume and hemodynamic parameters. A strong direct correlation was found between the daily fluid volume of 3219±466 ml and the oxygen saturation index, indicating a positive effect of administration in the acute period (7 days) on blood oxygenation in the lung parenchyma in group 2 (Fig. 3). The positive effect of this amount was expressed in a decrease in heart rate (-0.76), with this trend maintaining over the next 19 days in the intensive care unit (-0.60) against the background of mechanical ventilation. A tendency toward a decrease in the sympatholytic effect (-0.64) was also found in the first week of treatment, which became significantly significant in the following days, amounting to (-0.79) with a daily volume of administered fluid of 3926±846 ml/day (Fig. 4). A more pronounced beneficial effect of infusion therapy in the first 7 days in group 2 was expressed in a reliably significant increase in SV (0.72), a decrease in body temperature (-0.63), daily temperature fluctuations (-0.78), stabilization of DBP (-0.70) with a decrease in both the amplitude and daily fluctuations of DBP (-0.77) (Fig. 3). The correlations between the daily fluid volume and HR (-0.6), with SV (0.44), and the daily range of body T (-0.06) observed in the first 7 days in group 2 slightly decreased. The beneficial effect on MVP (-0.76), OVT (-0.79), and body temperature (-0.77) continued for 19 days in group 2 (Table 4).

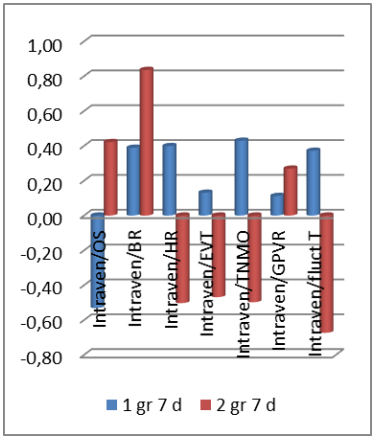

Figure 5. *Cor SVV first 7 days of treatment.*

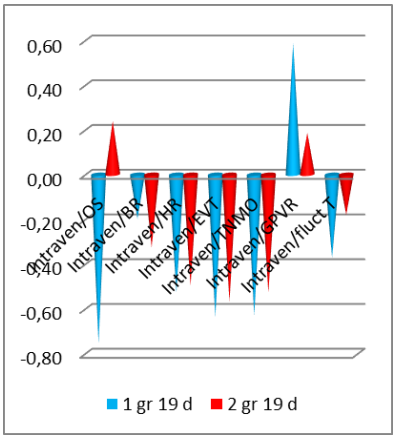

Figure 6. *Cor SV parenteral administration (19 days).*

Increase in parenteral infusion therapy within 392±86 for 7day in group 1 was accompanied by a tendency to decrease in oxygen saturation (-0.53), a tendency to increase in PMV (0.43) (Fig. 5). Infusion therapy for 19 days in the volume of 261±100 cl/day in group 1 led to a negative effect on oxygen saturation (-0.76), a

tendency to decrease in OVT (-0.64), PMV (-0.63), a tendency to increase in TPR (0.59) (Fig. 6). While a more volumetric increase of 268% in intravenous infusion with MCI in the first 7 days, which amounted to1442±221 ml/day, led to a tendency to decrease in MVP (-0.5), OVT (-0.47), an increase in oxygen saturation (0.42), a decrease in daily temperature fluctuations (-0.67). Mechanical ventilation for 19 days was accompanied by intravenous infusion therapy of 1550±372 ml/day (490% more than in Group 1). A tendency to decrease in HR (-0.5), OVT (-0.57), MVP (-0.53) was found (Fig. 6). The identified feature was assessed as a positive effect of mechanical ventilation with appropriate drug support, which had a stress-limiting effect in severe pneumonia complicated by OCSI according to the Glasgow scale of 6.5±1 points.

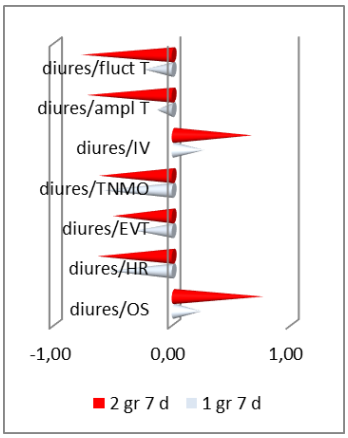

Figure 7. *Corresponds to the volume of urine excreted*

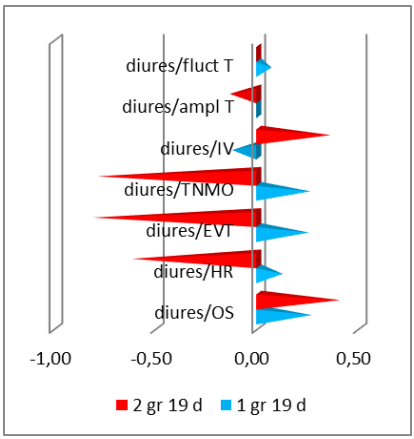

Figure 8. *Corresponds to the volume of urine excreted over 19 days*

A direct correlation was found between changes in renal function and oxygen saturation indicators (0.76) in the first 7 days in children of group 2 with a urine output of 2059±417 ml/day. While in group 1 with diuresis of 1381±341 ml/day in group 1 for 7 days, only a tendency towards a decrease in PMC (-0.6) was found (Fig. 7). Over the course of 19 days in group 1 with urinary activity of 1536±318 ml/day, no effect on hemodynamics was observed. In group 2 over the course of 19 days with diuresis 2673±755 ml/a decrease in the OVT (-0.82), PMC (-0.8), and a decrease in the heart rate (-0.63) were detected (Fig. 8).

Conclusion. In complex intensive care, including mechanical ventilation, in children over 7.1 years of age with severe complicated acute respiratory failure (ARF), the total daily volume of administered fluid was more than doubled, the amount of intravenous solutions was 8 times greater than in Group 1, and oral

administration was 50% greater than in Group 1. A positive effect of mechanical ventilation with appropriate drug support was revealed, exerting a stress-limiting effect on hemodynamic parameters, autonomic regulation, myocardial oxygen demand, and thermoregulation in severe pneumonia complicated by ARF (Glasgow Oxygen Score 6.5±1).

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光动力疗法治疗皮肤鳞状细胞癌的致病机理
PATHOGENETIC JUSTIFICATION OF PHOTODYNAMIC THERAPY IN PATIENTS WITH SKIN SQUAMOUS CELL CANCER

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摘要。本研究探讨了光动力疗法对鳞状细胞皮肤癌患者止血功能和金属蛋白酶指标的影响。结果发现，鳞状细胞皮肤癌的手术治疗并不能纠正已发现的改变。同时，在鳞状细胞皮肤癌患者中，如果在手术治疗前接受光动力疗法和激光疗法，其TIMP-1的含量显著增加，这自然导致MMPs-2、MMPs-7和MMPs-9的含量与健康对照组相比有所下降。这些指标的正常化可防止胶原蛋白的破坏和血管内壁的内皮功能障碍。这反过来又不会导致内皮素释放到血液中，从而阻止血管扩张的延长。最终，这导致了导致止血功能改变的机制的缺失。

关键词：鳞状细胞皮肤癌，止血指标，光动力疗法。

Abstract. *A study was conducted on the effect of photodynamic therapy on hemostasis and metalloproteinase indicators in patients with squamous cell skin cancer. It was found that surgical treatment of squamous cell skin cancer does not lead to correction of the identified changes. At the same time, in the group of patients with this pathology, who underwent photodynamic therapy and laser therapy before the start of surgical treatment, there was a statistically significant increase in the amount of TIMP-1, which naturally led to a decrease in the amount of MMPs-2, MMPs-7, and MMPs-9 compared to the data obtained in the comparison group of relatively healthy individuals. The normalization of these indicators prevented the destruction of collagen and endothelial dysfunction of the vascular lining. This, in turn, did not lead to the release of endothelin into the bloodstream, which prevented prolonged vasodilation. Ultimately, this contributed to the absence of mechanisms that led to changes in hemostasis.*

Keywords: *squamous cell skin cancer, hemostasis indicators, photodynamic therapy.*

The relevance of this study stems from the fact that over the past ten years, there has been a significant increase in malignant skin tumors worldwide. Moreover, some countries have become leaders in the incidence of this pathological condition.

The aim of the study was to establish patterns of changes in the parameters of matrix metalloproteinases and hemostasis systems and their interrelations in patients with squamous cell skin cancer under the influence of photodynamic therapy to provide a pathogenetic justification for its effectiveness.

To achieve the set objective, the disease course was analyzed in 185 patients with squamous cell carcinoma of the skin. Of the total number of patients, 129 (69.7%) were male, and 56 (31.2%) were female. All patients who agreed to participate in the study were divided into three groups. The first group (group 1) consisted of 74 patients (40%) who were treated with a combined method, which consisted of the following stages: photodynamic therapy, laser irradiation, and wide excision of the tumor under intravenous anesthesia. The second group (group 2) was formed from 111 (60%) patients whose treatment consisted of excision of squamous cell carcinoma of the skin under intravenous anesthesia. To control and compare the obtained laboratory parameters, a third group was created, which consisted of relatively healthy volunteers without established oncological pathology (group 3). This group included 17 people who gave voluntary consent to the study.

The study included patients with early-stage squamous cell skin cancer (stage T1-2N0M0) who were referred for treatment immediately after diagnosis. Patients with disseminated cancer, known lymph node and hematogenous metastases, and those who had undergone radiation and/or chemotherapy were excluded. Patients with comorbidities that could indirectly impact the study parameters, as well as those with individual drug intolerance or who refused to consent to the study, were excluded.

Treatment of early-stage squamous cell skin cancer using photodynamic therapy was performed in several stages. During the first stage, photodynamic therapy was administered before surgery, using Photolon as a photosensitizer at a dose of 1.0–2.0 mg/kg, administered intravenously. According to the instructions, after calculating the required dosage, the drug was added to 200 ml of saline solution. The resulting solution was administered via intravenous drip over approximately 30 minutes. Laser irradiation of the blood was performed simultaneously with the infusion therapy. A krypton laser was used for this purpose. The characteristics of this laser included the following parameters: wavelength from 647 nm to 675 nm,

power from 120 mW/cm2 to 300 mW/cm2. The total dose received by the patient from laser irradiation was at least 100 J/cm2. After completion of infusion therapy, the second stage of treatment was performed: 3-4 hours later, a session of local tumor irradiation was performed using the Latus laser (λ-662 nm), E = 100-200-300-600 J/cm2, in three sessions. Sessions were performed daily. The third stage involved surgical treatment. Surgery for patients in this group was performed 5 days after completion of photodynamic therapy. This delay was necessary because the photosensitizer accumulated in the tumor tissue during this time.

During the study, the levels of inhibitor of metalloproteinase-1 (TIMP-1) and matrix metalloproteinases-2, -7, -9 (MMPs-2, -7, -9) in the blood serum were determined. These parameters were chosen based on their significant role in the development and progression of malignant tumors. The hemostatic system was studied using laboratory methods. The parameters characterizing the following hemostatic components were studied: vascular-platelet, coagulation, and thrombinase formation, occurring along both the intrinsic and extrinsic pathways. The final stage was assessed by fibrin formation. Blood coagulation capacity was assessed by studying the clotting time of unstabilized blood, silicone clotting time, plasma recalcification time, and thrombin time. Endothelin-1 levels were determined to determine the most potent vasoconstrictor. Von Willebrand factor (vWF) was selected to determine the factor that ensures platelet adhesion to the collagen of the vessel wall, thereby participating in vascular-platelet hemostasis. The fibrinolytic complex of tissue plasminogen activator - plasminogen inhibitor (tPA-PAI-1), which is a fibrinolytic enzyme, was also used. Thrombophilia markers were determined using factor VIIIa activity and factor Va resistance to active protein C. Markers of disseminated intravascular coagulation (DIC) were detected by determining the amount of D-dimer and soluble fibrin-monomer complex. Blood viscosity properties were studied using an AKR-2 rotational viscometer. In patients with squamous cell skin cancer, blood was sampled before surgery and on days 1, 3, 5, 7, and 10 after surgery. In addition, laboratory studies were conducted in the late postoperative period, which lasted at least 18 months after surgery. The study found that early-stage squamous cell carcinoma leads to disturbances in blood rheological properties, with increases observed at all shear rates. In the group of patients with squamous cell carcinoma who underwent photodynamic therapy and laser therapy before surgery, the studied parameters did not differ from those obtained in the healthy donor group. In the late postoperative period, in the group of patients with squamous cell carcinoma who did not receive combination therapy, the studied parameters remained unchanged and corresponded to those obtained before surgery. This suggests that surgery for squamous cell carcinoma does not lead to correction of blood viscosity. Meanwhile, in the group of patients who received combination therapy, the studied parameters did not differ from those obtained in the healthy donor group.

Furthermore, the study found that in patients with early-stage squamous cell skin cancer, before surgery, endothelin levels were elevated compared to healthy donors. This also led to the development of vasoconstriction and increased procoagulant activity. In this group of patients with squamous cell skin cancer, a prolonged increase in procoagulant activity was observed, along with a simultaneous suppression of anticoagulant and fibrinolytic activity, as evidenced by increased activity of anthrombin III and vWF and a simultaneous decrease in the tPA-PAI-1 complex. All of this indicates that the vascular endothelium produces low levels of antithrombin III and tissue plasminogen activator (tPA), which is present in the blood in 90% of patients with squamous cell skin cancer as the tPA-PAI-1 complex. Patients with squamous cell carcinoma of the skin show signs of thrombophilia, as evidenced by high D-dimer levels and thrombodynamic potential. To confirm this, we studied thrombophilic markers—factor VIIIa activity and factor Va resistance to active protein C—in patients with squamous cell carcinoma of the skin. This suggests that early-stage squamous cell carcinoma, before surgery, causes prolonged endothelial activation, leading to prolonged vasodilation and increased coagulation factor synthesis. In a group of patients with squamous cell carcinoma receiving combination therapy, prolonged vasodilation was observed due to activation of the vascular endothelium. However, no changes in the coagulation factor synthesis system occurred, which did not lead to significant microcirculation disorders. When studying the fibrin-monomer complex dynamics after surgical treatment, the following was revealed: in the group of patients with squamous cell skin cancer using combination therapy, no dynamics of this indicator was noted on the first postoperative day, it was identical to the indicator obtained before the start of surgical treatment. Subsequently, on the third postoperative day, normalization of this indicator occurred, which corresponded to normal values. The same indicators were obtained in the late postoperative period. When studying the fibrin-monomer complex in patients with squamous cell skin cancer without the use of combination therapy, it was found that before the start of surgical treatment it was increased compared to the data of group 3. At the same time, in the group of patients with squamous cell skin cancer using combination therapy, before the start of surgical treatment there was an insignificant increase in this indicator. In the group of patients with squamous cell skin cancer without the use of combination therapy, changes in the fibrin-monomer complex in both the immediate, no changes were noted in either the long-term or late postoperative periods. A study of another important indicator that contributes to the development and spread of malignant tumors—TIMP-1 and the levels of MMPs-2, MMPs-7, and MMPs-9 in the blood serum—revealed the following results. Squamous cell skin cancer leads to a decrease in TIMP-1 levels, which naturally increases the levels of MMPs-2, MMPs-7, and MMPs-9. By the first day after surgery, patients

with squamous cell skin cancer in group 1 showed a decrease in TIMP-1 in the blood, which led to an increase in MMPs. However, in patients operated on for squamous cell skin cancer, who constituted group 2, no changes in the studied indicators were observed; all indicators corresponded to the data obtained before surgery. By the third day after surgery, laboratory tests showed that patients with squamous cell carcinoma in Group 2 showed no statistically significant changes in their results, with all parameters consistent with those obtained on the previous day. Meanwhile, patients with squamous cell carcinoma in Group 1 showed a further increase in TIMP-1 levels. This increase was statistically significant and reached the level observed in healthy donors, which naturally led to a decrease in MMPs-2, MMPs-7, and MMPs-9. By the fifth day after surgery, patients with squamous cell carcinoma in Group 2 showed no statistically significant changes in laboratory parameters. At the same time, in patients with squamous cell carcinoma of the skin, who made up Group 1, the fact was noted that the MMPs-2, MMPs-7 and MMPs-9 indicators statistically significantly decreased and did not differ from the data obtained in the group of patients who made up the healthy donor group. The results of laboratory studies show that by the tenth day after surgery, statistically significant changes were not obtained in patients who made up Group 1, while in the group of patients with squamous cell carcinoma of the skin, included in Group 2, an increase in the TIMP-1 indicator was noted, as a result of a decrease in MMPs-2, MMPs-7, MMPs-9. However, they remained statistically significantly elevated compared to the data obtained both in patients of Group 1 and in patients of the healthy donor group. The obtained data began to correspond to the results established before the start of surgical treatment. In the late postoperative period, no changes in the analyzed indicators were noted in patients of both groups. Thus, the study found that the use of combination therapy for squamous cell skin cancer contributed to a decrease in TIMP-1 and an increase in MMPs-2, MMPs-7, and MMPs-9. At the same time, Tumor removal without combination therapy does not restore the studied parameters, which remained statistically significantly elevated in both the immediate and late postoperative periods. However, the use of combination therapy, including photodynamic therapy and surgery, allowed for a statistically significant increase in TIMP-1 levels even before surgery, which naturally led to a decrease in MMPs-2, MMPs-7, and MMPs-9. A dynamic study of this parameter revealed complete restoration of TIMP-1, which, in turn, contributes to an increase in MMPs-2, MMPs-7, and MMPs-9 levels and the restoration of hemostatic parameters.

Changes in the hemostatic system in patients with squamous cell carcinoma can be described as follows: the cancerous tumor produces substances that reduce the amount of TIMP-1, which leads to an increase in the amount of MMPs-2, MMPs-7, and MMPs-9 in the blood. Tissue collagenases (MMPs-2) are known to

hydrolyze type IV collagen, the basis of the basal lamina at the dermoepidermal junction, facilitating intraepithelial and deep invasion. MMPs-2 and MMPs-9 degrade type IV collagen, which contributes to deep damage of epithelial cells from membranes and vascular invasion. MMPs-2 and MMPs-9 also release a number of angiogenic factors, including MMPs-9 and VEGF, which is considered the main polyclonal inducer of angiogenesis. Destruction of vascular collagen leads to vascular wall damage, leading to endothelial dysfunction, as evidenced by increased endothelin. This, in turn, leads to the development of severe vasoconstriction and increased procoagulant activity. In this group of patients with squamous cell carcinoma, a prolonged increase in procoagulant activity was observed, along with a simultaneous suppression of anticoagulant and fibrinolytic activity. Furthermore, the following changes in the hemostatic system were observed in the squamous cell carcinoma group: increased blood rheology and increased platelet aggregation. It should be noted that surgical treatment of squamous cell carcinoma does not correct these changes. Moreover, in the group of patients with squamous cell skin cancer who underwent photodynamic therapy and laser therapy before surgery, a statistically significant increase in TIMP-1 levels was observed, which predictably led to a decrease in MMPs-2, MMPs-7, and MMPs-9 levels compared to data obtained in the comparison group of relatively healthy individuals. Normalization of these parameters prevented collagen destruction and vascular endothelial dysfunction. This, in turn, prevented the release of endothelin into the bloodstream, preventing prolonged vasodilation. Ultimately, this prevented the triggering of mechanisms that lead to changes in hemostasis parameters. In conclusion, it should be noted that the use of combination therapy for the treatment of squamous cell skin cancer contributes to improved treatment outcomes.

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用于确定急性炎症过程中胆囊壁病理变化类型的创新标记物

INNOVATIVE MARKERS FOR DETERMINING THE TYPE OF PATHOLOGICAL CHANGES IN THE WALLS OF THE GALLBLADDER DURING THE ACUTE INFLAMMATORY PROCESS

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摘要。急诊外科仍然存在一个重大问题——选择急性胆囊炎症的最佳治疗策略。这个问题仍然没有得到解决，对外科医生构成了严峻的挑战。本研究旨在创建一种技术，可以预测胆囊急性炎症患者组织病理过程的强度。方法。对105例确诊为急性胆囊炎并接受腹腔镜胆囊切除术的患者进行了单阶段研究，这些患者的年龄、性别和伴随病理具有可比性。入院时，用动力学比色法测定肌酸磷酸激酶（CK）、乳酸脱氢酶（LDH）、γ-谷氨酰转肽酶（GGTP）和碱性磷酸酶（ALP）的活性。结果。急性破坏性胆囊炎患者CK平均值为302.2±32.5 U/l，LDH平均值为318.3±29.4 U/l，高于急性非破坏性胆囊炎患者的CK平均值（168.7±18.3 U/l，LDH平均值为282.6±18.3 U/l）。此外，CK、LDH浓度升高与胆囊壁破坏程度呈正相关。同时，非破坏性胆囊炎患者的平均GGTP值为340±116.9 U/l，碱性磷酸酶值为160.3±34.2 U/l，高于急性破坏性胆囊炎患者的平均GGTP值（70.5±18.5 U/l，碱性磷酸酶值93.5±16.5 U/l）。随着胆囊壁破坏过程的进展，GGTP和碱性磷酸酶的

浓度降低。结论：基于所获得的数据，我们提出了一种预测破坏性胆囊炎发展的方法。将我们提出的方法与已知的诊断方法相结合，可以及时预测胆囊壁变化的严重程度，并据此针对每种具体情况选择最合理的治疗策略。

关键词：预后；急性胆囊炎；破坏性胆囊炎；胆石症；肌酸磷酸激酶、乳酸脱氢酶、γ-谷氨酰转肽酶、碱性磷酸酶。

Abstract. *There is still a significant problem in emergency surgery - choosing the optimal treatment strategy for acute gallbladder inflammation. This issue remains unresolved and poses a serious challenge for surgeons.* ***The study aims*** *to create a technique that allows predicting the intensity of pathological processes in the tissues of the gallbladder in patients with acute inflammatory disease of this organ. Methods. A single-stage study was performed in 105 patients with an established diagnosis of acute cholecystitis who underwent laparoscopic cholecystectomy, comparable in age, gender, and concomitant pathology. Upon admission to the hospital, the activity of creatine phosphokinase (CK), lactate dehydrogenase (LDH), gamma-glutamyltranspeptidase (GGTP) and alkaline phosphatase (ALP) was determined by kinetic colorimetric method. Results. In patients with acute destructive cholecystitis, the average values of CK were 302.2 ±32.5 U/l and LDH was 318.3 ±29.4 U/l, which is higher than the values obtained in the group with acute non-destructive cholecystitis, CK was 168.7±18.3 U/l and LDH - 282.6±18.3 U/l. Along with this, a direct correlation was found between an increase in the concentration of CK, LDH and the degree of destructive process in the gallbladder wall. At the same time, in patients with non-destructive cholecystitis, the average values of GGTP were 340 ±116.9 U/l and alkaline phosphatase was 160.3 ±34.2 U/l, which exceeded these values in the group of patients with acute destructive cholecystitis, GGTP was 70.5 ± 18.5 U/l, and alkaline phosphatase – 93.5 ±16.5 U/l. As the destructive processes in the gallbladder wall progress, the concentration of GGTP and alkaline phosphatase decreases. Conclusion. Based on the data obtained, we have proposed a method for predicting the development of destructive cholecystitis. The use of our proposed method in combination with known diagnostic methods opens up the possibility of timely predicting the severity of changes in the gallbladder wall and, accordingly, choosing the most rational tactics in each specific case.*

Keywords: *prognosis; acute cholecystitis; destructive cholecystitis; cholelithiasis; creatine phosphokinase, lactate dehydrogenase, gamma-glutamyltranspeptidase, alkaline phosphatase.*

Introduction. The problem of acute cholecystitis in emergency surgery remains important due to the constant increase in the number of patients with cholelithiasis. According to Russian experts, 25% of all general surgical patients suffer from acute calculous cholecystitis [1,2,3]. Acute cholecystitis is one of the

leading causes of mortality from acute surgical pathology, ahead of acute appendicitis, pinched hernias and perforated ulcers of the gastroduodenal zone. In Russia, the mortality range for acute cholecystitis ranges from 2 to 12% [1,4,5,6,7] Recent years have been characterized by an increase in operational activity, but this has not led to a decrease in mortality in certain diseases. According to various studies, the main cause of mortality from acute cholecystitis is the destruction of the gallbladder, accounting for 42-48% [7,8,9,10]. By predicting the course of the disease, it is possible to predict the outcome of the pathological process, reduce the number of complications and, ultimately, reduce mortality [11,12]. In emergency surgery, predicting the development of destructive cholecystitis is extremely important, which is recognized by most specialists. However, despite the increased attention to predictive methods in recent years, reliable methods of such assessment have not yet been developed. Modern diagnostic techniques can only record the current state of the gallbladder, but they cannot predict the likelihood of the progression of destructive changes or predict their dynamics [12,13].

The study aims to create a technique that allows predicting the intensity of pathological processes in the tissues of the gallbladder in patients with acute inflammatory disease of this organ.

Research methodology. As part of our simultaneous analysis, we studied 135 patients with various forms of acute calculous cholecystitis. The patients were divided into three equal groups of 45 people: with catarrhal, phlegmonous and gangrenous forms of the disease. All study participants had similar demographic characteristics and concomitant diseases, as shown in Table 1. The age range of the subjects ranged from 30 to 70 years. The criterion for inclusion in the study was surgical intervention for acute calculous cholecystitis using either laparoscopic or traditional open cholecystectomy. Persons under 30 and over 70 years of age with cholelithiasis complicated by obstructive jaundice were excluded from the study. For a comparative analysis,45 patients with chronic calculous cholecystitis in the age range of 30-70 years were involved. An important condition for inclusion in the comparison group was the absence of pathological changes in the stomach and duodenum, as well as standard laparoscopic cholecystectomy. The comparison group did not include patients with acute or chronic calculous cholecystitis, those aged less than 30 or more than 70 years, as well as those diagnosed with diseases of the stomach or duodenum.

Table 1.

Demographic characteristics of patients by age group and gender

Subgroups of patients	Number, people, %					
	Up to 30 years old		From 30 to 50 years old		Over 50	
	M	F	M	F	M	F
Acute catarrhal cholecystitis (n=45)	4 (8,9%)	6 (13,3%)	5 (11,1%)	20 (44,4%)	2 (4,5%)	8 (17,8%)
Acute phlegmonous cholecystitis (n=45)	2 (4,5%)	9 (20%)	6 (13,3%)	18 (40%)	4 (8,9%)	6 (13,3%)
Acute gangrenous cholecystitis (n=45)	6 (13,3%)	4 (8,9%)	9 (20%)	15 (33,3%)	2 (4,5%)	9 (20%)
Chronic calculous cholecystitis (clinical comparison group) (n=45)	4 (8,9%)	6 (13,3%)	6 (13,3%)	19 (42,3%)	4 (8,9%)	6 (13,3%)
Total (n=180)	16 (8,9%)	25 (13,9%)	26 (14,4%)	72 (40,0%)	12 (6,7%)	29 (16,1)

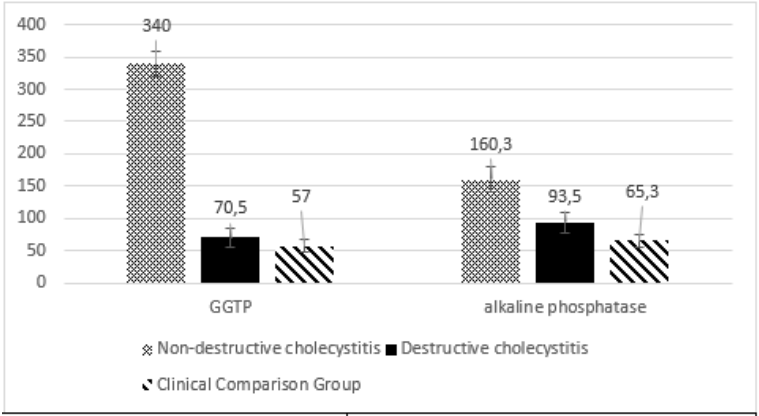
If acute cholecystitis was suspected in patients admitted to the hospital, the activity of a number of enzymes in the blood serum was analyzed during the first two hours. Kits of VITAL brand reagents were used for standard kinetic colorimetric studies of such parameters as gamma-glutamyltranspeptidase (GGTP), alkaline phosphatase (ALP), lactate dehydrogenase (LDH) and creatine phosphokinase (CKK). The determination of these enzymatic parameters was carried out using specialized reagents from the VITAL company, designed for each of these enzymes.

The study was approved at a meeting of the local ethics committee at the Chita State Medical Academy (extract from Protocol №. 112 dated 04/23/2021).

Statistical processing of the obtained results was carried out using the SPSS Statistics 19.0 program in compliance with the principles of statistical analysis adopted for research in biology and medicine. The results are given in the average value with the average square error (M ± m). To study the relationships between the studied parameters, a paired Pearson correlation analysis was performed. The distribution of degrees of freedom was evaluated using the chi-square criterion to evaluate qualitative data in three or more independent groups. When comparing the average values of a quantitative trait in three or more independent groups, with a normal distribution of data in all groups, a one-factor analysis of variance (ANOVA) was performed. The Friedman criterion was used to compare three or more

related samples whose data did not follow the law of normal distribution. The Mann–Whitney test was used for a pairwise comparison of independent samples.

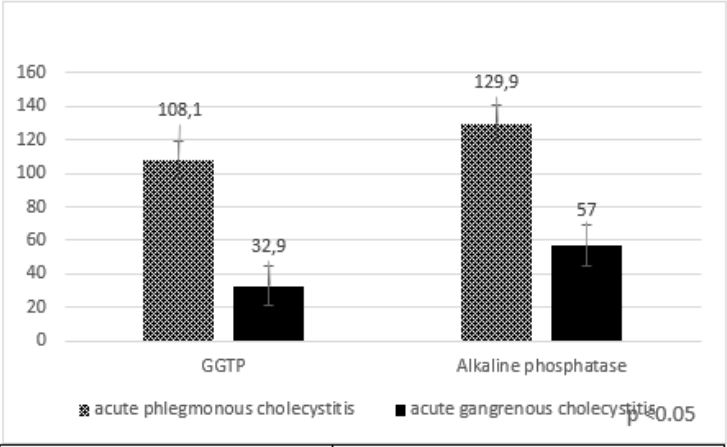
The results of the study. By examining the activity of enzymes in destructive cholecystitis, we have identified an interesting pattern: as destructive processes in the gallbladder wall intensify, the concentration of some enzymes increases, while others decrease. In catarrhal (acute non-destructive) cholecystitis, there is a significant increase in the level of alkaline phosphatase to 160.3 ±34.2 U/l and GGTP to 340 ±116.9 U/l. At the same time, in the group of patients with acute destructive cholecystitis, the index of these enzymes is significantly lower than GGTP -70.5 ± 18.5 U/l ($p < 0.001$), and alkaline phosphatase – 93.5 ±16.5 U/l ($p < 0.001$) (Fig. 1.). In the clinical comparison group, the following values were established: GGTP - 57±27.5 U/l ($p < 0.001$, $p < 0.001$) and alkaline phosphatase - 65.3±15.2 U/l ($p < 0.001$, $p < 0.001$).



Gammaglutamyltransferase	*p <0,001 in non-destructive cholecystitis and destructive cholecystitis; 2*p <0,001 in non-destructive cholecystitis and the clinical comparison group; 3*p <0,001 in group destructive cholecystitis and the clinical comparison group
Alkaline phosphatase	*p <0,001 in non-destructive cholecystitis and destructive cholecystitis; 2*p <0,001 in non-destructive cholecystitis and the clinical comparison group; 3*p <0,001 in group destructive cholecystitis and the clinical comparison group

Figure 1. *Distribution of GGTP and alkaline phosphatase concentrations in destructive and non-destructive acute cholecystitis*

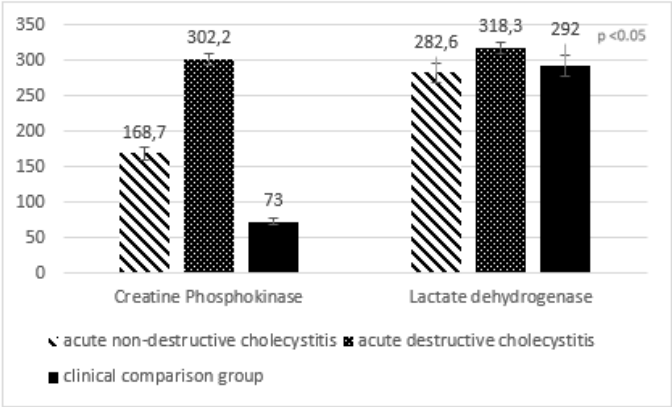
As destructive processes intensify, there is a decrease in certain biochemical markers. The analysis showed that the concentration of alkaline phosphatase in patients with gangrenous cholecystitis is significantly lower (57±18.5 U/l) than in patients with acute phlegmonous cholecystitis (129.9±14.6 U/l, p =0.002), as shown in Figure 2. A similar trend can be observed for GGTP: in the gangrenous form of the disease, the values drop to 32.9±7.5 U/l, while in the phlegmonous form they reach 108.1±29.5 U/l (p =0.001).



Gammaglutamyltransferase	*p=0,001 in subgroup phlegmonous and subgroup gangrenous;
Alkaline phosphatase	*p=0,002 in subgroup phlegmonous and subgroup gangrenous;

Figure 2. *Distribution of GGTP and alkaline phosphatase values in patients with various clinical variants of acute destructive cholecystitis*

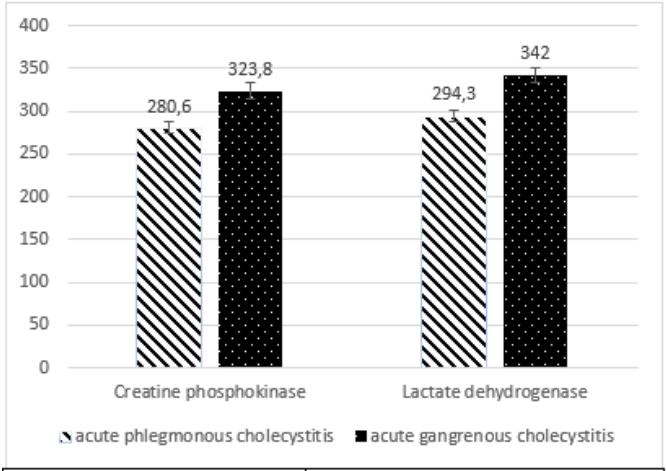
The study revealed significant differences in enzyme concentrations in different forms of cholecystitis. When comparing the groups, it was found that the level of CFRP reached maximum values in patients with a destructive form of the disease - 302.2 ±32.5 U/l, which significantly exceeds the indicators of other groups. A similar trend was observed for LDH, which was 318.3 ±29.4 U/l in destructive cholecystitis. The control group of the clinical comparison showed minimal CPK values - only 73±29.7U/l (p<0.001), while LDH levels were 292±29.7 U/l (p <0.001), as shown in Fig. 3. In patients with non-destructive cholecystitis, intermediate values were recorded: CPK - 168.7±18.3 U/l (p <0.001) and LDH - 282.6±18.3 U/l (p <0.001).



Creatine phosphokinase	*p <0,001 in non-destructive cholecystitis and destructive cholecystitis; 2*p <0,001 in non-destructive cholecystitis and the clinical comparison group; 3*p <0,001 in group destructive cholecystitis and the clinical comparison group
Lactate dehydrogenase	*p <0,001 in non-destructive cholecystitis and destructive cholecystitis; 2*p <0,001 in non-destructive cholecystitis and the clinical comparison group; 3*p <0,001 in group destructive cholecystitis and the clinical comparison group

Figure 3. *Distribution of CK and LDH concentrations in destructive and non-destructive acute cholecystitis*

The study showed the relationship between the intensity of destructive processes and biochemical markers. In gangrenous cholecystitis, higher enzyme indices were observed compared with the phlegmonous form of the disease (Fig. 4). Thus, in patients with gangrenous cholecystitis, the level of Creatine phosphokinase reached 323.8±39.5 U/l, and the concentration of Lactate dehydrogenase was 342.1±32.9 U/l. In cases of acute phlegmonous cholecystitis, these indicators were lower: Creatine phosphokinase - 280.6±25.8 U/l ($p < 0.001$), Lactate dehydrogenase - 294.3±25.8 U/l ($p < 0.001$). The progression of pathological changes was accompanied by a significant increase in these biochemical parameters.



Creatine phosphokinase	*p<0,001 in subgroup phlegmonous and subgroup gangrenous;
Lactate dehydrogenase	*p<0,001 in subgroup phlegmonous and subgroup gangrenous;

Figure 4. *Distribution of CPK and LDH values in patients with different clinical variants of acute destructive cholecystitis*

Conclusion. Involvement of the muscular layer of the gallbladder wall is presumably the reason for the increase in CPK and LDH levels in patients with destructive cholecystitis. In non-destructive cholecystitis, there is an increase in alkaline phosphatase and GGTP, which is probably due to alkaline pH values and pathological changes in the mucous membrane. Mucosal desquamation and a decrease in pH may explain the observed significant decrease in the concentration of alkaline phosphatase and GGTP in cases of destructive cholecystitis.

Based on a comprehensive assessment of the results obtained, we have created a method for predicting destructive cholecystitis. The methodology assumes a point-based ranking system for certain biochemical markers (shown in Table 2). Upon admission to a medical facility, a laboratory blood test is immediately performed to measure key enzymatic parameters: creatine phosphokinase, lactate dehydrogenase, gamma-glutamyl transpeptidase and alkaline phosphatase.

Table 2.

Ranking table by points

Scores						
		ABOVE THE NORM			**BELOW THE NORM**	
		-2	**-1**		**1**	**2**
	NORM	**>50%**	**25-50%**	**0**	**25-50%**	**50-100%**
GGTP U/l	64	>96	80-96	48-80	32-48	0-32
alkaline phosphatase U/l	117	>175,5	146,25-175,5	87,75-146,25	58,5- 87,75	0-58,5
	Scores					
		BELOW THE NORM			ABOVE THE NORM	
		-2	-1	0	1	2
	NORM	50-100%	25-50%		25-50%	50-100%
Lactate dehydrogenase U/l	300	0-150	150-225	225-375	375-450	>450
Creatine phosphokinase U/l	190	0-95	95-142,5	142,5-247	247-285	>285

Based on the information gathered, we have developed a method for predicting the occurrence of destructive cholecystitis. If the index of prognostic dynamics (SDI) is negative, the probability of destructive processes is minimal, whereas a positive value of SDI indicates a significant risk of destructive complications.

Our method of predicting destructive cholecystitis, used in conjunction with traditional diagnostic approaches, allows us to assess the degree of pathological changes in the gallbladder in advance. This gives doctors the opportunity to customize the treatment strategy for each patient, choosing the optimal algorithm of actions depending on the specific clinical situation [14].

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主动脉瓣置换术中间隔肌切除对术后远期逆转心肌重塑的影响
THE IMPACT OF SEPTAL MYECTOMY DURING AORTIC VALVE REPLACEMENT ON REVERSE MYOCARDIAL REMODELING IN THE LONG-TERM POSTOPERATIVE PERIOD

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摘要。引言。主动脉瓣置换术中间隔肌切除术是改善左心室流出道和主动脉瓣人工瓣膜血流动力学参数的方法之一，可更有效地逆转心肌重塑。然而，关于实施该手术的建议往往存在争议。这一事实决定了分析该主题长期结果的相关性。

目的。分析重度主动脉瓣狭窄和左心室心肌肥厚患者主动脉瓣置换术中间隔肌切除术后逆转心肌重塑的长期结果。

方法。回顾性分析220例重度主动脉瓣狭窄和室间隔肥厚≥1.5 cm的患者。患者年龄为65（62；68.5）岁。该研究包括 128 名（58.2%）男性和 92 名（41.8%）女性。62.7% 的患者被归类为 NYHA 功能 III 级心力衰竭，29.1% 为 II 级。患者被分成两组；两组在术前临床和超声心动图特征方面没有差异。在 AVR+SME 组中，主动脉瓣置换术期间进行了室间隔心肌切除术，而在 AVR 组中则未进行。

结果。进行室间隔心肌切除术改善了主动脉瓣置换术的长期结果，促进了术后更有效的逆转心肌重塑。术后五年随访显示，AVR+SME 组中 74% 的患者在一年、85% 和 93% 时观察到心肌质量退化超过 25%；在AVR组中，一年后72%的患者出现这种情况，三年后77%的患者出现这种情况，五年后88%的患者出现这种情况。

结论： 主动脉瓣置换术中行室间隔肌切除术可改善主动脉瓣狭窄的外科治疗效果，研究组术后远期心肌质量消退更为明显，证实了这一点。

关键词： 主动脉瓣狭窄，主动脉瓣置换术，左心室逆向重塑，室间隔肌切除术。

Abstract. Introduction. S*eptal myectomy during aortic valve replacement is one of the methods aimed at improving hemodynamic parameters in the left ventricular outflow tract and across the aortic valve prosthesis, which promotes more effective reverse myocardial remodeling. However, recommendations regarding the performance of this procedure are often controversial. This fact determines the relevance of analyzing long-term results on this topic.*

Objective. *To analyze the long-term results of reverse myocardial remodeling after septal myectomy during aortic valve replacement in patients with severe aortic stenosis and left ventricular myocardial hypertrophy.*

Methods. *A retrospective analysis of 220 patients with severe aortic stenosis and interventricular septum hypertrophy ≥ 1.5 cm was conducted. The patients' age was 65 (62; 68.5) years. The study included 128 (58.2%) men and 92 (41.8%) women. 62.7% patients were classified as NYHA functional class III heart failure, and 29.1% as class II. Patients were divided into two equal groups; the groups did not differ in preoperative clinical and echocardiographic characteristics. In the AVR+SME group, septal myectomy was performed during aortic valve replacement, while in the AVR group, it was not.*

Results. *Performing septal myectomy improved the long-term outcomes of aortic valve replacement, promoting more effective reverse myocardial remodeling after surgery. Over five years of follow-up after surgery, myocardial mass regression of more than 25% in the AVR+SME group was observed in 74% of patients at one year, 85% at three years, and 93% at five years; in the AVR group, it was observed in 72% of patients at one year, 77% at three years, and 88% at five years.*

Conclusions. *Performing septal myectomy during aortic valve replacement improves the results of surgical treatment for aortic stenosis, as confirmed by a more pronounced regression of myocardial mass in the long-term postoperative period in the study group.*

Keywords: *aortic stenosis, aortic valve replacement, left ventricular reverse remodeling, septal myectomy.*

Introduction

Aortic valve stenosis is the most common valvular heart disease. Progressive aortic valve stenosis primarily negatively affects the left ventricle, which adapts to the increased load. In aortic stenosis, the prognosis is predicted not only by the initial degree of left ventricular hypertrophy or its regression after surgery but also by diffuse fibrosis. Histological studies show that disease progression significantly impacts the myocardium. Macroscopic changes manifest as thickening of the left ventricular walls and dimensions, while microscopic changes are characterized by cardiomyocyte hypertrophy, expansion of the extracellular matrix, and diffuse replacement fibrosis. According to world literature, after aortic valve replacement, left ventricular hypertrophy decreases by 20-30% by 1 year [1]. Performing concomitant septal myectomy (SME) favorably influences the regression of left ventricular hypertrophy due to the elimination of the blood flow obstruction in the left ventricular outflow tract. The aim of our study was to demonstrate whether performing septal myectomy during aortic valve replacement has a favorable effect on reverse remodeling of the left ventricular myocardium in the long term.

Materials and Methods

Study design: a comparative prospective interventional study, which included 220 patients. Patients were divided into two groups: the first group - the study

group, septal myectomy and aortic valve replacement (AVR+SME); the second group - the control group, aortic valve replacement (AVR).

The inclusion criteria for this study were: patients of both sexes aged 18 years and older; isolated aortic valve stenosis, combined aortic valve disease with predominant stenosis and insufficiency ≤ grade 2; interventricular septum thickness ≥ 15 mm; implantation of a mechanical aortic valve prosthesis.

The exclusion criteria for this study were: combined aortic valve disease with predominant insufficiency; history of prior cardiac surgery; need for combined surgeries for surgical treatment of other heart defects, cardiac arrhythmias, aneurysms of the ascending aorta, coronary artery disease; diagnosis of hypertrophic cardiomyopathy; presence of severe heart failure with LVEF < 30%; implantation of a biological aortic valve prosthesis.

Echocardiographic parameters were assessed before surgery and over five years after surgery. Based on initial clinical, anthropometric characteristics, and echocardiography data, the patients in the two groups were comparable. The primary endpoint of the study was the analysis of reverse myocardial remodeling in the long-term period.

Statistical analysis was performed using STATISTICA 10.0 (developer - StatSoft.Inc Dell) and SPSS 26.0 (SPSS Inc., Chicago, IL, USA) software. Distribution was assessed according to the Shapiro-Wilk test. For normal distribution, data are presented as mean (M) ± standard deviation (SD); for non-normal distribution, as median and 25th and 75th percentiles. The Kaplan-Meier method and life tables were used to assess freedom from reverse myocardial remodeling. Spearman's correlation coefficient was calculated to identify correlations.

Results

During the analysis of long-term results over five years after surgery in the two groups, it was found that reverse myocardial remodeling was more frequently recorded in the AVR+SM group in the first year of observation (Table 1).

Table 1.

Echocardiographic data during the first year of observation.

Indicator	AVR+SM	AVR	P
LVM (g)	178 (110; 229)	236 ± 72	0.01
LVMI (g/m²)	90.7 (75.9; 106.9)	118.4 (78.13; 171.56)	0.01
IVSd (cm)	1.2 (1.0; 1.4)	1.4 (1.2; 1.75)	0.01
LVPWd (cm)	1.0 (0.8; 1.2)	1.3 ± 0.18	0.01

LVM: Left Ventricular Mass; LVMI: Left Ventricular Mass Index; IVSd: Diastolic Interventricular Septum thickness; LVPWd: Diastolic Left Ventricular Posterior Wall thickness.

The next stage of the work was a correlation analysis, which established a correlation between performing SM during AVR and reverse myocardial remodeling (ΔLVMI), assessed using Spearman's rank correlation coefficient. Thus, a statistically significant (p=0.002) correlation of moderate strength (r=0.35) according to the Chaddock scale was revealed; a weak statistically significant correlation (r=0.22, p=0.009) was also found between the proportion of patients with reverse myocardial mass regression of more than 25% and the performed surgical intervention (AVR+SME).

We constructed a Kaplan-Meier plot to assess long-term myocardial regression of more than 25% over the years depending on the performance of SM during AVR (Figure 1, Table 2).

The mean time to achieve myocardial regression of more than 25% in the long term depending on the performance of SM during AVR was 0.84 ± 0.19 years (95% CI: 0.48-1.21 years), and in the AVR group, it was 1.10 ± 0.22 years (95% CI: 0.66-1.54 years). These time differences in the onset of reverse myocardial remodeling between the two groups are statistically significant (p = 0.04).

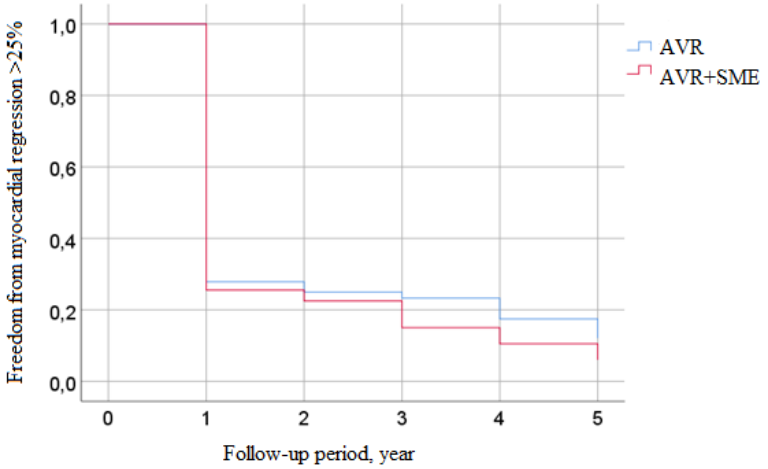

Figure 1. *Assessment of long-term myocardial regression of >25% over years depending on SME performance during AVR.*

Table 2.

Assessment of long-term results of reverse remodeling by year.

Follow-up Period	Groups	Baseline	1 Year	2 Years	3 Years	4 Years	5 Years
N patients reaching interval, n	AVR	110	20	16	13	8	5
Freedom from myocardial regression >25%, %		100%	28%	25%	23%	17%	12%
N patients reaching interval, n	AVR+SM	110	17	15	10	7	4
Freedom from myocardial regression >25%, %		100%	26%	23%	15%	11%	7%

Over five years of follow-up after surgery, myocardial regression of more than 25% in the AVR+SM group was observed in 74% of patients at one year, 85% at three years, and 93% at five years; in the AVR group, it was observed in 72% of patients at one year, 77% at three years, and 88% at five years. Based on the obtained results, it is clearly visible that myocardial regression was recorded more frequently in the AVR+SM group than in patients undergoing isolated AVR.

Discussion

Asymmetric hypertrophy of the basal septum is found in approximately 20% of patients with hemodynamically significant aortic stenosis [2,3]. This, in turn, can contribute to residual left ventricular outflow tract obstruction after isolated aortic valve replacement [4]. The question of whether performing concomitant septal myectomy provides better postoperative outcomes in patients with severe aortic stenosis and pronounced myocardial hypertrophy remains open due to the small number of publications on this topic [5]. All publications represent retrospective analyses investigating different endpoints. Furthermore, not every study reports important factors contributing to left ventricular remodeling, such as the mismatch between the patient's anthropometric data and the size and type of the implanted prosthesis. This makes it impossible to establish a cause-and-effect relationship for performing septal myectomy during aortic valve replacement.

In reverse remodeling, cellular and matrix regression contribute to the reduction of left ventricular hypertrophy over five years, with the greatest regression occurring in the first year after surgery. In our study, in the SM+AVR group, the process of reverse myocardial remodeling was more significant in the first

and subsequent years after surgery. Our analysis demonstrates that performing septal myectomy during aortic valve replacement promotes reverse myocardial remodeling to a greater extent than performing isolated aortic valve replacement. This is confirmed by a more significant recorded percentage of myocardial mass regression, reduction in left ventricular posterior wall thickness, and left ventricular end-diastolic dimension in the long-term period in the study group compared to the control group.

Thus, the results of the conducted meta-analysis confirm that performing AVR+SM in the presence of asymmetric interventricular septum hypertrophy, suspected or directly visualized on echocardiography, appears to be an effective procedure.

Conclusions

Concomitant septal myectomy during aortic valve replacement in patients with severe aortic stenosis and hypertrophy of the interventricular septum is a safe and effective procedure. Compared to isolated aortic valve replacement, it improves reverse left ventricular remodeling. However, larger prospective studies are needed to confirm the procedure's effect on long-term survival and functional status.

The authors declare no conflict of interest.

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改变多发性硬化症病程的药物对患者外周血淋巴细胞亚群组成的影响
EFFECT OF DRUGS THAT ALTER THE COURSE OF MULTIPLE SCLEROSIS ON THE SUBPOPULATION COMPOSITION OF PERIPHERAL BLOOD LYMPHOCYTES IN PATIENTS

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摘要：采用六色流式细胞术研究了多发性硬化症 (MS) 不同组别患者外周血淋巴细胞亚群组成和功能活性的特征：一组为未接受过治疗的初治患者，另一组为接受疾病修饰疗法 (DMT) 治疗的患者，即干扰素-β、那他珠单抗和奥瑞珠单抗。

MS 患者接受第一疗程抗 B 细胞治疗后，循环 B 淋巴细胞池的共刺激和活化能力显著降低，而接受干扰素-β 或那他珠单抗治疗的患者则未观察到这种现象。这一发现可能表明奥瑞珠单抗具有更高的疗效。

关键词：多发性硬化症、那他珠单抗、干扰素-β、奥瑞珠单抗、细胞免疫、流式细胞术。

Abstract. *The features of the subpopulation composition and functional activity of peripheral blood lymphocytes were studied using six-colour flow cytometry in various groups of patients with multiple sclerosis (MS): treatment-naïve patients who had not received therapy, and groups of patients receiving disease-modifying therapies (DMTs) — Interferon-β, Natalizumab, and Ocrelizumab.*

Administration of a first course of anti-B-cell therapy in MS patients demonstrated a pronounced reduction in the co-stimulatory and activation capacity of the circulating B-lymphocyte pool, which was not observed in patients treated with Interferon-β or Natalizumab. This finding may indicate the higher therapeutic efficacy of Ocrelizumab.

Keywords: *multiple sclerosis, Natalizumab, Interferon-β, Ocrelizumab, cellular immunity, flow cytometry.*

Introduction

Multiple sclerosis (MS) is an autoimmune neurodegenerative disease of the central nervous system (CNS) characterised by demyelinating processes and a progressive course with alternating periods of exacerbation and remission [1, 2].

Over recent decades, numerous disease-modifying therapies (DMTs) have been developed, yet complete control of the disease remains elusive. The main DMTs include Interferon-β (IFN-β), Natalizumab, and Ocrelizumab.

Interferons (IFNs) are a family of cytokines with antiviral, antiproliferative, and immunomodulatory properties. The mechanism of action of IFN-β is mediated via activation of the JAK/STAT pathway upon binding to the IFNAR-2 receptor, which leads to the expression of a wide range of genes [3, 4].

Natalizumab (Tysabri) is a humanised recombinant monoclonal IgG4 antibody directed against the α4-subunit of integrin VLA-4 (CD49d), a component of α4β1 and α4β7 integrins. The action of Natalizumab effectively prevents the migration of autoreactive immune cells into the CNS, while prolonged administration may also influence their function. Natalizumab is administered intravenously once every four weeks and is generally well tolerated by patients [5, 6].

Ocrelizumab (Ocrevus) is a glycosylated humanised monoclonal IgG1 antibody targeting the CD20 antigen, specifically binding to the large extracellular loop of the molecule at amino acid residues 165–180 [7]. This protein is expressed on pre-B cells, mature B cells, and memory B cells, but not on plasma cells. Anti-CD20 monoclonal antibodies reduce the number and function of B cells through antibody-dependent mechanisms such as phagocytosis, cell-mediated cytotoxicity, and apoptosis, thereby decreasing immune-pathological inflammation in MS. Ocrelizumab is administered intravenously once every six months.

Recent findings suggest that not only CD4+ T-cell subpopulations but also B cells play a central role in MS pathogenesis. B cells present antigens to T lymphocytes, secrete pro-inflammatory cytokines, and produce specific autoantibodies against myelin. Ultimately, most DMT protocols for patients with relapsing MS culminate in switching to Ocrelizumab — a monoclonal antibody (mAb) against CD20 that has been approved for MS therapy [3].

Given this, the investigation of systemic effects of major DMT groups on adaptive T- and B-cell immunity parameters in MS patients is of particular importance.

The aim of our study was to evaluate the influence of various DMTs on the subpopulation composition and functional activity of peripheral blood lymphocytes in patients with active MS.

Materials and Methods

A total of 52 patients with multiple sclerosis (MS) were examined. Among them were 8 treatment-naïve patients with rapidly progressive MS (RPMS) who had never received DMTs, and 44 patients with relapsing–remitting MS (RRMS) (15 men and 29 women) undergoing disease-modifying therapy.

The RRMS group included:

- 12 patients receiving Interferon-β preparations;
- 20 patients with highly active MS (HAMS) receiving Natalizumab (80% of them had recent clinical exacerbations);
- 12 patients who had completed one course of Ocrelizumab therapy.

Immunological analyses for the Ocrelizumab group were performed 6 ± 1 months after the first infusion, immediately before the second administration.

A **control group** consisted of 12 healthy individuals matched for sex and age.

Flow Cytometric Immunophenotyping

Evaluation of cellular immunity parameters was carried out using **six-colour flow cytometry** (Becton Dickinson, USA). Monoclonal antibodies against differentiation antigens of peripheral blood lymphocytes were used.

The following were analysed:

- Total lymphocyte populations and subpopulations:

CD3+, CD3+CD4+, CD3+CD8+, CD3+CD16+CD56+, CD3–CD16+CD56+, CD3+HLA-DR+, CD19+, CD20+ (within the CD45+ lymphocyte gate);

- B-cell subpopulations:

Memory B cells, B-1 lymphocytes, and expression of activation and co-stimulatory molecules (CD40, CD25, CD38) on CD19+ B cells.

Statistical processing was performed using SPSS Statistics (IBM, USA) and GraphPad Prism 10 (GraphPad Software, USA). Quantitative data were presented as median and interquartile range (Me [Q0.25; Q0.75]) or mean ± SD. Normality of distribution was assessed using the non-parametric Mann–Whitney U-test, and $p < 0.05$ was considered statistically significant.

Results

The parameters of the lymphocyte subpopulation composition in MS patients are presented in **Table 1.**

Table 1.

Parameters of Cellular Immunity in Multiple Sclerosis Patients Depending on DMT Used (% of cells within the CD45+ lymphocyte gate)

Parameter	Group 1 – Healthy Controls (n=12)	Group 2 – Naïve RPMS (n=8)	Group 3 – Interferon-β (n=12)	Group 4 – Natalizumab (n=20)	Group 5 – Ocrelizumab (n=12)	P*
Total lymphocytes, 10^9/L	2,100 [1,800; 2,800]	1,450 [1,300; 1,900]	1,520 [1,450; 1,985]	1,900 [1,635; 2,080]	1,711 [1,300; 1,905]	1-2 0,017; 1-3 0,048; 1-5 0,02
T lymphocytes (CD3+), %	68,5 [63,7; 74,3]	76,5 [70,1; 78,7]	75,1 [70,5; 77,4]	75,6 [71,6; 78]	86,9 [82,9; 90]	1-2 0,045; 1-3 0,03; 1-4 0,019; 1-5 0,0001; 2-5 0,0004
T helpers (CD3+CD4+), %	39,5 [37,2; 42,9]	46,2 [38,9; 48,8]	46,7 [40,1; 54,2]	49,7 [46,3; 55,1]	54,5 [50,4; 58,8]	1-2 0,03 1-3 0,018 1-4 0,0006 1-5 0,0001 2-5 0,001
Cytotoxic T cells (CD3+CD8+), %	30,1 [23,3; 32,6]	26,7 [22,7; 36,6]	24,2 [22,2; 27,1]	23,7 [20,6; 30,3]	31,1 [24,2; 41]	1-3 0,019
NK lymphocytes (CD3-CD16+56+), %	11,5 [8,9; 17,0]	12,7 [9; 15,9]	9,9 [6,3; 14,3]	10,8 [7,7; 14,8]	13,9 [8,5; 16,6]	
NKT lymphocytes (CD3+CD16+56+), %	7,7 [76,1; 10,8]	9 [4; 10,4]	5,5 [2,6; 9,9]	1,2 [0,7; 3,2]	8,3 [5,2; 11,4]	1-4 0,019 2-4 0,02
B lymphocytes (CD19+), %	10,8 [8,7; 12,4]	8,9 [8,5; 13,7]	14,1 [10,9; 18,1]	13,5 [11,6; 26]	1,5 [0,4; 3,9]	1-3 0,042; 1-4 0,02; 1-5 0,0001; 2-5 0,0001
B lymphocytes (CD20+), %	10,4 [8,2; 12,7]	9,6 [7,4; 14,7]	11,6 [10,5; 17,3]	12 [9,8; 22,9]	0,5 [0,05; 1,2]	1-5 0,0001; 2-5 0,0001
Activated T lymphocytes (CD3+HLA-DR+), %	11,2 [9; 21,9]	11,4 [4; 11,6]	5,1 [4; 7,3]	8,2 [5,8; 10,7]	7,8 [6,2; 8,7]	1-3 0,012; 1-5 0,012

Note: Only statistically significant differences are shown.

Description of Results

A significant reduction in total peripheral lymphocyte counts compared with controls was observed in all groups except those treated with Natalizumab.

In *treatment-naïve* RPMS patients who had not received DMTs, pronounced T-cell immune disturbances were detected — including an increase in the total T-lymphocyte population (CD3+) due to an expansion of the helper T-cell subpopulation (CD3+CD4+) amid marked absolute lymphopenia. These abnormalities likely have immunopathogenetic relevance in this MS subtype.

A statistically significant rise in total T lymphocytes (CD3+), particularly in T-helper cells (CD3+CD4+), was observed across all patient groups relative to healthy controls.

Interferon-β therapy led to an increase in the proportion of total T lymphocytes (CD3+) through T-helper expansion (CD3+CD4+) combined with pronounced lymphopenia, along with a decrease in cytotoxic T cells (CD8+) and activated CD3+HLA-DR+ cells in circulation. These findings suggest that IFN-β selectively affects cell migration processes into the CNS — inhibiting neither activated nor cytotoxic effector T-cell migration.

Natalizumab treatment caused a significant reduction in NKT lymphocytes and an increase in CD19+ B cells, likely reflecting enhanced migration of effector NKT cells into the CNS and a correlation with increased relapse risk. The decline in activated HLA-DR+ T lymphocytes in circulation may reflect redistribution of these cells to the CNS.

In Natalizumab-treated patients, expansion of both total T lymphocytes and T-helper subsets (CD4+), as well as increased peripheral B lymphocytes, is consistent with the drug's mechanism: by binding to α4-integrin, Natalizumab prevents lymphocyte penetration into the CNS, resulting in peripheral accumulation [8, 9]. Other studies similarly report elevated CD4+ T cells in peripheral blood and reduced levels in cerebrospinal fluid [10, 11]. Discontinuation or switching from Natalizumab often results in disease relapse — seen in roughly one-third of cases.

Notably, after IFN-β and Natalizumab therapy, the proportion of CD20+ B lymphocytes remained unchanged, indicating that targets for Ocrelizumab therapy were preserved in these groups.

In patients receiving Ocrelizumab, a marked increase in total T lymphocytes (CD3+) due to T-helper expansion (CD3+CD4+) was observed compared to both controls and naïve patients. This reflects a compensatory rise in T cells following B-cell depletion.

The decreased relative levels of CD19+ and CD20+ lymphocytes are explained by Ocrelizumab's mechanism, as roughly 90% of all B cells are mature CD20+ cells — the drug's direct target. Six months after the first Ocrelizumab course, 85% of patients had not regained normal B-cell counts before the next infusion.

The characteristics of the B-cell compartment and their activation markers are shown in **Table 2.**

Table 2.

Parameters of B-cell Immunity in MS Patients Depending on the DMT Used (% of CD19+ lymphocytes)

Parameter	**Group 1 – Healthy Controls (n=12)**	**Group 2 – Naïve RPMS (n=8)**	**Group 3 – Interferon-β (n=12)**	**Group 4 – Natalizumab (n=20)**	**Group 5 – Ocrelizumab (n=12)**	**P***
Co-stimulatory molecule CD40+	49,20 +-4,45	67,35+-10,48	69,40 +-6,02	51,65+-8,09	18,1+-7,3	1-5 0,0007 1-2 0,04 1-3 0,007 2-5 0,0004 3-5 0,0000 4-5 0, 0008
B-1 lymphocytes CD5+	17,29+-3,96	16,57+-8,64	17,46+-1,61	11,35+-2,76	20,6+-6,3	
Memory B cells CD27+	28,30+-2,74	29,50+-6,90	32,53+-5,27	32,08+-4,6	24,9+-5,7	
Activated B lymphocytes CD38+	16,10+-2,63	31,40+-7,22	29,34+-4,23	43,00+-5,28	16,1+-2,6	1-2 0,005 1-3 0,004 2-5 0,03 3-5 0,006 4-5 0,000
Activated B lymphocytes CD25+	13,79+-2,52	17,70+-5,19	12,49+-1,77	23,13+-3,60*	13,9+-3,8	1-4 0,029 4-5 0,034

Note: Only statistically significant differences are shown.

A pronounced increase in B lymphocytes expressing the co-stimulatory molecule CD40 was observed in treatment-naïve patients before receiving DMTs, as well as after therapy with Interferon-β and Natalizumab. Following administration of the first course of Ocrelizumab, this parameter decreased significantly compared to all other patient groups.

The most prominent rise in the expression of CD25 and CD38 on B lymphocytes was recorded in patients treated with Natalizumab, while only CD38 expression was elevated in patients treated with Interferon-β and in treatment-naïve MS patients. After one course of Ocrelizumab, there was a significant decline in B lymphocytes expressing CD25 and CD38, compared with the Natalizumab group.

No significant differences were found in the proportions of memory B cells (CD27+) and B1-lymphocytes among all MS patient groups compared with healthy controls.

Conclusion

1. In patients with rapidly progressive MS (RPMS) who had not received DMTs, significant disturbances were identified in both the T- and B-cell components of immunity — manifested by an increase in total T lymphocytes (CD3+) due to T-helper expansion (CD3+CD4+) amid pronounced lymphopenia, and by a higher proportion of activated (CD38+) and co-stimulatory (CD40+) B lymphocytes. These alterations have immunopathogenetic significance in this MS form.
2. Distinct effects of various DMTs on the subpopulation structure and functional activity of peripheral blood lymphocytes were revealed, which allow assessing the baseline immune parameters in MS patients when switching to Ocrelizumab therapy.
3. Administration of a single course of anti-B-cell therapy in MS patients demonstrated a marked reduction in the co-stimulatory and activation capacity of the circulating B-lymphocyte pool, which was not observed in patients treated with Interferon-β or Natalizumab, suggesting the higher therapeutic efficacy of Ocrelizumab.

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非传染性疾病，特别是被动吸烟，对巴库学童饮食行为和人体测量指标的影响，以及采取药物措施对抗这种疾病对儿童健康和身体发育的有害影响

THE IMPACT OF NON-COMMUNICABLE DISEASES, IN PARTICULAR PASSIVE SMOKING, ON EATING BEHAVIOR AND ANTHROPOMETRIC INDICATORS OF SCHOOLCHILDREN IN BAKU AND THE ADOPTION OF PHARMACOLOGICAL MEASURES TO COMBAT THE DETRIMENTAL EFFECTS OF THIS DISEASE ON THE HEALTH AND PHYSICAL DEVELOPMENT OF CHILDREN

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摘要：据了解，约有 90% 的成年吸烟者尝试自行戒烟。不幸的是，约有 70% 的戒烟者会在三个月内复吸。然而，随着每次尝试，永久戒烟的可能性都会增加。尽管如此，那些无法自行戒烟的人仍然可以从非药物和药物治疗中获益。

关键词：饮食行为、烟草烟雾、人体测量指标、肥胖、体重、人工智能。

Abstract. *It is known that approximately 90% of adult smokers attempt to quit on their own. Unfortunately, approximately 70% of those who quit relapse, typically within three months. However, with each subsequent attempt, the likelihood of permanent cessation increases. Nevertheless, those who are unable to quit on their own can always benefit from non-pharmacological and pharmacological treatments for this addiction.*

Keywords: *eating behavior, tobacco smoke, anthropometric indicators, obesity, body weight, artificial intelligence.*

Nicotine is a tertiary amine consisting of a pyridine and pyrrolidine ring $C_{10}H_{14}N_2$ [1-3]. Nicotine contained in tobacco binds to nicotinic cholinergic receptors, or nicotinic acetylcholine receptors, which are activated by acetylcholine, as well as nicotine. In the human brain, there is an α4β2 receptor. It is believed that this receptor subtype is primarily responsible for the development of nicotine addiction [4,5,6-9]. Eating disorders have been studied for a long time and several of its types are known: 1-a person's tendency to try this or that food that stimulates appetite. 2-an emotional factor, as a result of which a person consumes an unregulated amount of food to eliminate problems with a particular depressive state; 3-eating in limited quantities due to excess body weight. The actual nutrition and eating behavior patterns of schoolchildren exposed to passive smoking influence the formation of excess body weight, which is a risk factor for the development of obesity [10]. There are a number of methods for combating tobacco-nicotine psychodependence. One of these is pharmacotherapy—treatment with medication. Doctors often prescribe antidepressants [11,12,13-15]. Many people experience depression and irritability upon starting treatment, but these temporary mental disorders must be overcome. Prompt consultation with a drug addiction specialist or psychotherapist can help overcome this harmful habit. It is known that approximately 90% of adult smokers attempt to quit on their own. Unfortunately, approximately 70% of those who quit smoking relapse, typically within 3 months [16]. However, with each subsequent attempt, the likelihood of permanently quitting increases. Nevertheless, those who are unable to quit on their own can always benefit from non-pharmacological and pharmacological treatments for this addiction [17,18-21]. Non-pharmacological treatments include numerous smoking cessation programs based on behavioral therapy. A free app with an artificial intelligence-powered chatbot is designed to help users quit smoking. The app, known as QuitBot, uses evidence-based strategies developed by experts at the Fred Hutch Center in Seattle [39,22,23-26]. Smokers who develop anxiety and depression are prescribed anti-anxiety medications and antidepressants. Antidepressants increase smoking cessation rates. Bupropion, a drug from the atypical antidepressant class that inhibits the uptake of norepinephrine and dopamine by neurons, is believed to be effective in the treatment of nicotine addiction, with a 2.73-fold increase in smoking cessation rates. Another drug, fluoxetine, an antidepressant from the group of selective serotonin reuptake inhibitors, is also effective for smoking cessation. Excessive carbohydrate intake leads to metabolic disturbances and increased insulin production by the pancreas [27,28-31]. Cellular sensitivity to the crucial hormone insulin, responsible for glucose breakdown, is reduced. When exposed to excess insulin, glucose is easily converted into fat. The distribution of adipose tissue in subcutaneous depots is associated with psychophysiological and metabolic characteristics underlying the development of primary obesity in men [40,32,33]. Furthermore, obesity reduces

tissue sensitivity to insulin itself. This leads to the development of type 2 diabetes. Since weight gain is one of the problems faced by those who quit smoking, fluoxetine, an appetite suppressant, can help address this issue. A gentle diet and vigorous exercise are also recommended. Smoking and a tendency toward depression are often linked, owing to both genetic predisposition and the neurochemical effects of nicotine. Therefore, antidepressants promote smoking cessation. Clinical trial data have demonstrated the effectiveness of the acetylcholine receptor agonist α4β2 varenicline and nortriptyline for smoking cessation [34]. Smoking cessation, in addition to withdrawal symptoms, is usually accompanied by weight gain. With age, weight gain occurs in both smokers and non-smokers, but is more pronounced among moderate smokers. Presumably, this is due to the acceleration of metabolic processes under the influence of nicotine [35,36]. Against the background of the appearance of excess body weight, smokers again resume the process of smoking, influenced by their appearance as a factor of psycho-emotional stress, which again, taking into account the memory of the hypothalamus, leads to its modification and dysfunction, manifested by a feeling of hunger (i.e., dependence on tobacco smoke) due to the activation of the sensitivity of nicotinic acetylcholine receptors [37-39]. For many smokers, especially women, fear of weight gain is the main motivating factor for continuing smoking [40].

Purpose of the work. A study of the impact of harmful components of tobacco smoke, based on a generalized review of literary sources and data obtained as a result of a social survey of the population, as well as according to indicators of the level of morbidity in different age groups of schoolchildren by analyzing their outpatient cards.

Materials and methods. Basic physical parameters of the body: height, weight, and chest circumference. These parameters are measured to identify the physical characteristics of children exposed and unexposed to passive smoking. We decided to determine height, weight, and chest circumference measurements by dividing schoolchildren into two groups: those exposed and those not exposed to passive smoking. This study was conducted as part of a study examining the impact of family passive smoking on children's health and academic performance. We developed a questionnaire containing seven sets of questions on various social and hygienic aspects of passive smoking. The questionnaires were divided into two parts: one for students and the other for their parents. The study was conducted in five city secondary schools (Yasamal, Narimanov, and Sabunchi districts). To eliminate bias, we proceeded as follows. Only fully completed questionnaires were included in the study. A total of 6,000 questionnaires were distributed to schoolchildren. Of these, 2,363 fully completed questionnaires contained responses from 3,895 parents—1,885 fathers and 2,010 mothers. The survey covered 2,363 families. Depending on the intensity of smoking, all families were divided

into two groups: 818 families (tobacco-dependent) and 1,545 families (tobacco-independent, i.e., the control group). Based on the intensity of passive smoking, the tobacco-dependent group of families was divided into: Group 1—204 families, mild tobacco dependence, less than 5 cigarettes per day; Group 2—252 families, moderate tobacco dependence—5-15 cigarettes per day; and Group 3—362 families, addicted smoking of parents, severe tobacco dependence, more than 15 cigarettes per day. Measurements were taken separately for boys and girls. Observations were conducted in the most anthropometrically significant age groups of schoolchildren. Each anthropometric indicator—weight, height, and chest circumference—was analyzed separately and, where necessary, compared with others.

Results and discussion. Analyzing Tab.1, schoolchildren in Group 1 were even heavier in some age groups than those in Group 2 – by 1.4-1.6 kg for boys and 0.5-1.2 kg for girls. We believe this explains this situation as follows. Schoolchildren exposed to passive smoking are not physically active and lead a sedentary lifestyle, which results in weight gain. Given their slower growth, weight gain, although not significant, is entirely acceptable. In general, boys in Group 1, weigh 2.4-4.7 kg less, and girls 2.6-5.3 kg less, than schoolchildren in Group 2. To determine the extent to which passive smoking affects schoolchildren's physical activity, we conducted the following study. We analyzed school attendance registers; the information of interest was obtained from 1483 of the 2363 surveyed schoolchildren, 566 of whom were exposed to passive smoking in the family, and 917 were not. According to the analysis of class registers and consolidated proposals of physical education teachers, we divided the physical activity of schoolchildren, or the nature of their attendance at physical education lessons, into the following categories: group 1 - exempt from classes for medical reasons, not always for objective reasons; group 2 - not exempt from classes, but do not attend them despite the taken educational and punitive measures; group 3 - attend classes, but are inactive during them, partially fulfill the prescribed volume of lessons; group 4 - attend classes, are quite active and fulfill all prescribed tasks; group 5 - attend and are quite active during classes, additionally do health-improving gymnastics in the morning or go jogging for 15-30 minutes; Group 6 – attend and are active in classes, and also participate in various sports. The data presented in the first figure indicate that in all the selected categories, the physical activity of schoolchildren exposed to passive smoking (group 1) is lower than that of schoolchildren not exposed to passive smoking (group 2). Thus, 16.8±1.6% of schoolchildren in the 1st group and 8.3±0.9% of schoolchildren in the 2nd group were exempt from physical education classes for medical reasons ($t=4.62$; $p<0.001$). 11.7±1.4% and 6.1±0.8% of schoolchildren, respectively, were not exempt, but did not attend classes despite the measures taken ($t=3.48$; $p<0.001$). 34.8±2.0% and 23.3±1.4% of schoolchildren attended classes but were inactive ($t=4.71$; $p<0.001$). As can

be seen, there are more schoolchildren in the 1st group who are exempt, do not attend, or are inactive in physical education classes than in the 2nd group. At the same time, there are much fewer schoolchildren who are more active in classes in the 1st group than in the 2nd group. For example, the proportion of schoolchildren attending and fairly active in classes in these groups was 23.1±1.8 and 36.3±1.6% (t=5.48; p<0.001). The proportion of schoolchildren attending classes and additionally doing health-improving gymnastics or jogging was 9.4±1.2 and 16.2±1.2% (t=4.00; p<0.001), and schoolchildren still involved in sports were 4.2±0.8 and 9.8±1.0% (t=4.38; p<0.001). The results obtained are shown in Fig.1

Conclusion. Unfortunately, even the presence of medical conditions does not lead many patients to quit their addiction. Therefore, in their daily practice, clinicians often face the challenge of prescribing medications to smokers. The situation is complicated by the fact that the use of certain medications may be limited or contraindicated due to various comorbidities. The use of modern, highly selective medications, the selection of effective doses, and careful monitoring of side effects and the progression of comorbidities will allow smokers to receive the most effective treatment. However, creating motivation to quit remains a mandatory aspect of treating smokers.

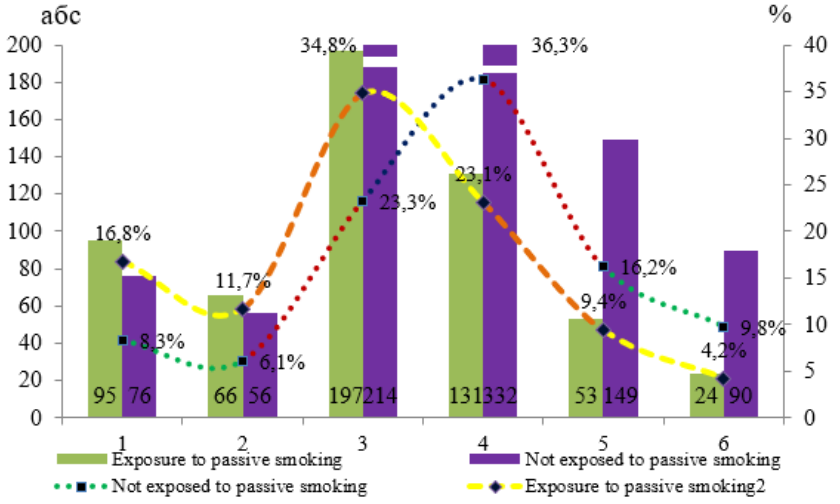

Figure 1. *Activity of schoolchildren during physical education classes exposed (n=566) and not exposed (n=917) to passive smoking*

Table 1

Calculation of average body weights of schoolchildren exposed and not exposed to passive smoking

Weight indicators of schoolchildren's development											
Boys						Girls					
Exposure to passive smoking		Not exposed to passive smoking		Reliability of differences		Exposure to passive smoking		Not exposed to passive smoking		Reliability of differences	
n	M ±m	n	M ±m	t	p	n	M ±m	n	M ±m	t	p
Age, years											
6,0 – 6,9											
22	26,9±0,5	24	25,3±0,4	2,19	<0,05	20	22,5±0,5	18	25,7±0,6	4,10	<0,001
7,0 – 7,9											
23	24,6±0,5	20	27,7±0,5	4,37	<0,001	28	25,1±0,4	21	28,4±0,5	5,16	<0,001
8,0 – 8,9											
17	28,1±0,5	16	31,6±0,6	4,49	<0,001	18	31,3±0,5	22	30,8±0,4	0,78	<0,05
9,0 – 9,9											
19	31,6±0,5	17	34,8±0,6	4,10	<0,001	21	32,3±0,5	17	35,5±0,4	5,00	<0,001
10,0 – 10,9											
26	35,3±0,4	25	37,7±0,4	4,21	<0,001	26	36,8±0,4	25	39,4±0,4	4,56	<0,001
11,0 – 11,9											
21	36,5±0,5	21	39,6±0,5	4,37	<0,001	19	41,3±0,5	20	40,8±0,5	0,70	>0,05
12,0 – 12,9											
18	38,6±0,5	19	41,7±0,5	4,37	<0,001	26	43,6±0,4	24	42,4±0,4	2,11	<0,05
13,0 – 13,9											
18	47,8±0,6	18	46,4±0,6	1,65	>0,05	25	44,6±0,4	19	49,7±0,6	7,08	<0,001
14,0 – 14,9											
25	48,3±0,4	23	51,6±0,4	5,79	<0,001	20	49,1±0,5	21	52,4±0,5	4,65	<0,001
15,0 – 15,9											
27	53,1±0,4	23	57,8±0,5	7,34	<0,001	24	52,7±0,5	23	56,6±0,5	5,49	<0,001
16,0 – 16,9											
17	58,3±0,6	19	62,6±0,6	7,54	<0,001	23	57,0±0,4	23	60,8±0,5	5,94	<0,001

Note: n is the number of schoolchildren; M ±m is the average value of the indicato

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中间普雷沃菌作为晚期炎症性牙周病诊断指标的作用
THE ROLE OF PREVOTELLA INTERMEDIA AS A DIAGNOSTIC INDICATOR IN ADVANCED FORMS OF INFLAMMATORY PERIODONTAL DISEASES

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摘要：全球统计数据表明，全球几乎所有成年人口（98%）都患有影响牙齿周围组织的炎症性疾病。此类牙周疾病的主要病原体之一是一种名为中间普雷沃菌的细菌。这种微生物属于厌氧革兰氏阴性菌，其特征是黑色素沉着；它是与牙周疾病相关的所谓橙色复合体的一部分。本研究旨在分析中间普雷沃菌在重度牙周炎患者牙周袋中的定植过程。材料与方法：实验包括39名无牙周疾病的健康参与者（对照组）以及126名诊断为慢性全身性牙周炎的患者（主要研究组）。研究结果：分析结果表明，在比较研究组时，中间普雷沃菌微生物的出现频率存在显著差异。结论。牙周组织的破坏性变化与中间普雷沃菌微生物的存在直接相关。

关键词：牙科，橙色牙周复合体，中间普雷沃菌，牙周炎，牙周病原体。

Abstract. Global statistics indicate that almost the entire adult population of the world (98%) suffers from inflammatory diseases affecting the tissues around the teeth. One of the key causative agents of such periodontal diseases is a bacterium called Prevotella intermedia. This microorganism belongs to anaerobic gram-negative bacteria and is characterized by the presence of black pigmentation; it is part of the so-called orange complex associated with periodontal diseases. ***The purpose of this study*** is to analyze the process of colonization by Prevotella intermedia bacteria of periodontal pockets in cases of severe periodontitis. ***Materials and methods.*** The experiment included 39 healthy participants without periodontal diseases, who made up the control group, as well as 126 patients diagnosed with chronic generalized periodontitis, who made up the main study group.. ***The results of the study.*** The results of the analysis demonstrated significant differences in the frequency of occurrence of the Prevotella intermedia microorganism when com-

paring the studied groups. ***Conclusion.*** Destructive changes in periodontal tissues are directly related to the presence of the Prevotella intermedia microorganism.

Keywords: dentistry, orange periodontal complex, Prevotella intermedia, periodontitis, periodontopathogen.

The problem of periodontal tissue health occupies one of the leading places in modern dental practice. Chronic inflammatory processes in periodontal structures demonstrate a steady upward trend among various age groups of the world's population. According to current international epidemiological studies, pathological changes in the tissues surrounding the tooth are diagnosed in almost every person – the indicator reaches a critical 98%. The dynamics of the spread of chronic forms of periodontitis is of particular concern to the medical community. Experts note that the frequency of detection of this disease among patients of dental clinics continues to increase steadily from year to year, almost approaching one hundred percent coverage of the population. This epidemiological situation requires close attention and the development of effective prevention programs. The nature of the development of chronic periodontitis is multifactorial, which significantly complicates both diagnosis and therapeutic approaches. Among the many causal factors contributing to the onset and progression of the inflammatory process, researchers assign a key role to the infectious component. It is the pathogenic microflora of the oral cavity that is recognized by most specialists as the primary and most significant etiological agent in the mechanism of development of periodontal pathology. Bacterial agents trigger a cascade of inflammatory reactions leading to destructive changes in the tooth-supporting tissues. [1,2].

Studies have shown that microbes constantly release various proteins and components into their environment during their lifetime. These proteins play a key role in the infection process, as they allow pathogens to gain a foothold in the host's body or activate its immune system. [1,2,5].

In modern periodontology, several key microorganisms responsible for the development of inflammatory diseases of periodontal tissues are identified. Prevotella intermedia is of particular clinical importance among the numerous pathogenic bacteria that colonize periodontal pockets. This microorganism is classified as an obligate anaerobe with a gram-negative cell wall, which determines its resistance to certain antibacterial drugs. A characteristic morphological feature of P. intermedia is the ability to produce a dark pigment that gives bacterial colonies a characteristic black color when cultivated on nutrient media. According to the modern microbiological classification of periodontal microflora developed by Socransky, this pathogen belongs to the so-called orange complex of periodontal pathogens. Bacteria of this group play an intermediate role in the formation of a mature biofilm and create favorable conditions for subsequent colonization by more aggres-

sive representatives of the red complex. Thus, P. intermedia occupies an important place in the pathogenesis of periodontal infections, acting as one of the key links in microbial succession in the subgingival region. Bacteria use various mechanisms to evade the body's immune defenses, including producing cysteine proteases and lipopolysaccharides (LPS), which not only promote inflammation, but also help them avoid detection by the immune system. [3,4].

The study of microorganisms in medical microbiology often leads to interesting discoveries that change our understanding of the classification and functions of various bacteria. So, initially, the bacterium P. intermedia was considered as one of the subspecies of Bacteroides melaninogenicus. This species included three subspecies: B. melaninogenicus subsp. melaninogenicus, B. melaninogenicus subsp. asaccharolyticus and B. melaninogenicus subsp. intermedius, all of them were known for their black pigmentation and anaerobic gram-negative structure. However, with the passage of time and the deepening of research, it became obvious that this classification requires revision. In particular, in 1992, studies were conducted that led to the division into two separate genera: Porphyromonas and Prevotella, and P. intermedia was assigned to the latter genus. This discovery was a significant step in understanding the diversity of microorganisms that affect human health. Moreover, during the same studies, a new species Prevotella nigrescens was identified. This type is also capable of causing periodontitis, which underlines its clinical significance. The discovery of Prevotella nigrescens has not only expanded our understanding of the oral microflora, but also highlighted the importance of accurate scientific classification for the development of effective methods for the diagnosis and treatment of periodontal diseases. [3,4].

It is important to emphasize that the scientific community pays considerable attention to the study of bacteria that contribute to the development of periodontitis. A special place on this list is occupied by Porphyromonas gingivalis, known for its role in the destruction of periodontal tissues. At the same time, P. intermedia is no less interesting for researchers, which is characterized by similar biochemical characteristics to P. gingivalis and contributes to its strengthening in the microbial film. The study of P. intermedia, unlike P. gingivalis, is not so deep yet, although this microorganism also plays a significant role in the pathogenesis of periodontal diseases. In the initial stage of colonization, P. intermedia activates the production of important mediators such as interleukin-6, prostaglandin E2, and matrix metalloproteinases. These substances, acting through signaling pathways in the fibroblasts of the periodontal ligament, contribute to the activation and maturation of osteoclasts, which eventually leads to the destruction of the ligamentous apparatus of the tooth. Thus, further studies of the mechanisms of interaction between P. gingivalis and P. intermedia can contribute to the development of new approaches to the treatment and prevention of periodontitis. Perhaps an in-depth understanding

of the biochemical processes behind the colonization of these bacteria will allow us to create more effective methods of combating this group of periodontal pathogens, which will have a significant impact on the preservation of teeth and oral health in general. [1,3,4].

The purpose of this study is to analyze the process of colonization by Prevotella intermedia bacteria of periodontal pockets in cases of severe periodontitis.

Materials and methods. To achieve the goals of scientific work, a comprehensive clinical experiment was organized with the involvement of volunteers. The participants were divided into two categories depending on their oral health status. The control cohort consisted of 39 people who had no diseases of the tissues surrounding the teeth and demonstrated an absolutely healthy periodontal condition. The study group included 126 patients with chronic generalized periodontitis. The group of patients was divided into 3 categories depending on the severity of the disease, which were comparable in age and gender. The first group included 39 patients with mild chronic generalized periodontitis, the second group included 42 patients with moderate severity, and group 3 included 45 patients with severe severity. The methodological approach to the study involved different procedures for collecting biological material, depending on the group's membership. Biomaterial for laboratory analysis in healthy subjects was extracted directly from the gingival furrows, which are natural depressions between the tooth and gum. On the contrary, in patients with periodontal pathology, samples were taken from deep periodontal pockets formed due to the destruction of connective tissues. The diagnostic procedure was performed using a specialized commercial kit called Periodontoscreen, designed to detect periodontal pathogens. The molecular genetic study of the obtained samples was carried out using polymerase chain reaction technology with real-time detection of the results. A thermal cycler model DT-96, manufactured by the Russian company NPO DNA Technology, was used to perform high-precision analysis, which ensured the reliability and reproducibility of the data obtained. The analysis of collected data utilized SPSS Statistics version 19.0, adhering to conventional statistical methodologies established for biological and medical investigations. A paired Pearson correlation analysis was conducted to examine interconnections among measured variables. Data presentation follows the format of mean values accompanied by standard error of the mean ($M \pm m$). For assessing categorical variables across three or more independent cohorts, the chi-square test was employed to determine the distribution of freedom degrees.

For pairwise assessment of unrelated samples, the Mann–Whitney test was applied. In cases where data across three or more dependent samples deviated from normal distribution patterns, the Friedman criterion served as the analytical method. Meanwhile, one-factor ANOVA was employed when examining mean quantitative characteristic values across three or more separate groups, provided all groups exhibited normally distributed data.

The results of the study. The results of the study showed that the highest detection rate of Prevotella intermedia is typical for patients with severe CGP and amounts to 66.6%. Compared with this indicator, in patients with moderate severity of the disease, this microorganism was detected less than 1.1 times (59.5%), with mild severity – 2.1 times less often, and in the control group the incidence was 2.9 times lower (Table 1).

Table 1

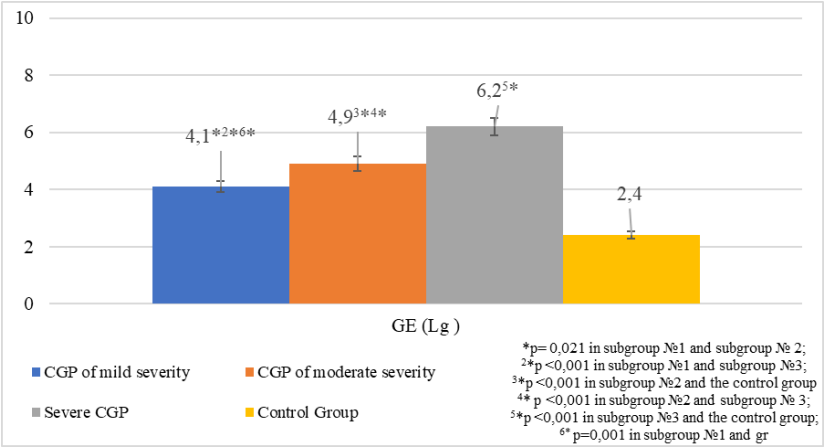
Frequency of Prevotella intermedia

	Control Groupn=39	Study group (number of people, %)		
		Subgroup №1 (Mild CGP) n=39	Subgroup №2 (CGP of moderate severity) n=42	Subgroup №3 (Severe CGP) n=45
Positive	9 (23%)	12*[2]* (31 %)	25[3]* (59,5%)	30[4]* (66,6%)
Negative ones	30 (67%)	27 (69%)	17 (40,5%)	15 (33,4%)

* p<0,001 in subgroup №1 and subgroup №2;
[2]* p< 0,001 in subgroup №1 and subgroup №3;
[3]* p< 0,001 in subgroup №2 and the control group;
[4]* p< 0,001 in subgroup №3 and the control group.
[1] The correlation coefficient is 0.972. The relationship between the studied features is direct, the closeness (strength) of the connection is strong, and the dependence of the features is statistically significant (p=0,028).

The results of the study showed a clear correlation between the level of Prevotella intermedia bacteria and the severity of chronic periodontal inflammation. In the control group, these microorganisms were 1.7 times lower than in patients with mild CGP, where the DNA concentration reached 4.1 Lg. During the transition to the moderate severity of the disease, a significant increase in the indicator is observed - up to 4.9 Lg, which demonstrates a twofold excess of the control values (p <0.001). The maximum values were recorded in severe CGP - the average microbial equivalent content was 6.2 Lg, exceeding the norm by 2.6 times (p <0.001), which confirms the direct relationship between the presence of Prevotella intermedia and the progression of periodontal pathology.

In subgroup № 3, where severe CGP was diagnosed, the maximum Prevotella intermedia index was recorded at 6.2 Lg. This value exceeded the results of subgroup №2 with moderate CGP by 1.3 times (p<0.001), and the indicators of subgroup № 1, characterized by mild CGP, were 1.5 times lower (p<0.001) (Figure 1).



Conclusion. Modern microbiological studies make it possible to identify the key pathogens of periodontal diseases and determine their role in pathogenesis. The results of the analysis convincingly demonstrate that the Prevotella intermedia microorganism plays a significant role in pathological changes in periodontal tissues. Identifying the presence of this bacterium in biological material is of significant clinical importance for dental practitioners. This pathogen is actively involved in the mechanisms of destruction of structures surrounding the tooth, including gingival tissue, periodontal ligament and alveolar bone. The laboratory identification of Prevotella intermedia has a high diagnostic value in determining the etiology of inflammatory processes in the periodontal area. Thus, the timely detection of this microorganism contributes to the selection of the optimal therapeutic strategy and allows predicting the course of the disease, which is especially important to prevent the progression of destructive changes.

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评估漱口水中药物成分白桦脂醇质量的方法开发

DEVELOPMENT OF METHODS FOR ASSESSING THE QUALITY OF THE PHARMACEUTICAL SUBSTANCE BETULIN IN A DENTAL MOUTHWASH

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牙龈炎和牙周炎等炎症性牙周疾病是最常见的口腔疾病，也是导致牙齿脱落的主要原因。因此，及时有效地治疗和预防这些疾病至关重要。

用于预防和治疗牙周疾病的最常见牙科产品之一是漱口水，其形式包括溶液和凝胶。

近几十年来，含有天然物质（尤其是植物性物质）的牙科漱口水产品越来越受到医生和患者的欢迎。

三萜化合物白桦脂醇（bitulin）具有显著的抗菌、抗炎、促进伤口愈合等药理活性，是一种极具前景的植物物质。

本研究的成果是基于高效液相色谱法开发了一种用于评估牙科漱口水中药物成分白桦脂醇质量的方法。

该方法使我们能够确定用于漱口的 Betadent 牙科产品中白桦脂醇的真实性和定量含量。

关键词：白桦脂醇，真实性，定量测定，高效液相色谱法。

Resume: *Inflammatory periodontal diseases such as gingivitis and periodontitis are among the most common oral conditions and are the leading causes of tooth loss. Therefore, treatment and timely, effective prevention of these conditions are highly important.*

Among the most common dental products used for the prevention and treatment of periodontal disease are mouthwashes, which can be presented in the form of both solutions and gels.

In recent decades, dental products containing natural substances, particularly plant-based ones, in their mouthwash have become increasingly popular among both doctors and patients.

The triterpene compound bitulin, which has pronounced antimicrobial, anti-inflammatory, wound-healing and other types of pharmacological activity, should be considered as a promising plant substance.

The result of the completed research was the development of a method for assessing the quality of the pharmaceutical substance betulin in the composition of a dental mouthwash, based on the use of high-performance liquid chromatography.

This method allows us to determine the authenticity and quantitative content of betulin in the Betadent dental product, intended for rinsing the oral cavity.

Keywords: *betulin, authenticity, quantitative determination, high-performance liquid chromatography.*

As noted previously, inflammatory periodontal diseases such as gingivitis and periodontitis represent a serious medical and social problem. Their high prevalence indicates the importance of not only treating this pathology but also its timely and effective prevention, as inflammatory periodontal diseases are one of the main causes of tooth loss and rank second among chronic diseases in frequency [2].

Mouthwashes, including those in the form of dental gels, occupy a significant place in the range of products used for the prevention and treatment of periodontal disease. The addition of various hydrophilic gelling agents, such as cellulose derivatives, polyethylene oxides, and polyethylene glycols, to dental gels enhances adhesion and focuses the action of the active ingredients, prolonging the pharmacological effect. As a result, dental gels exhibit good thixotropic properties, fluidity, and high permeability. [4]

A current trend is the development and production of dental gels for use in the oral cavity based on substances of natural origin, in particular plant-based.[3].

One naturally occurring substance with pronounced anti-inflammatory activity is betulin, a terpenoid compound known as a triterpenoid. Triterpenoids are natural plant compounds with a variety of biological activities, including anti-inflammatory, antimicrobial, and immunomodulatory properties, as is characteristic of betulin and its derivatives [1]. In the context of the oral microbiome, triterpenoids can significantly influence normal, indigenous, and pathogenic microflora. These compounds exhibit pronounced antimicrobial activity, which can target both pathogenic and opportunistic microorganisms. Triterpenoids such as betulin and ursolic acid inhibit the growth of Streptococcus mutans and Porphyromonas gingivalis by disrupting their cell membranes and metabolism. They are effective against Candida albicans, inhibiting biofilm formation and reducing fungal virulence. It should be noted that triterpene compounds can selectively target patho-

genic microorganisms without affecting normal microflora. This is due to their ability to interact with specific targets in pathogen cells, such as enzymes and membrane proteins [1,5]. Triterpenoids modulate the immune response by reducing the production of proinflammatory cytokines (e.g., IL-6 and TNF-α) and suppressing NF-κB activation. This helps control inflammatory processes caused by pathogens []. For example, betulin reduces inflammation in periodontitis by suppressing the activity of Porphyromonas gingivalis. Triterpenoids help strengthen the oral mucosa, preventing pathogens from penetrating deeper into the tissue. They can destroy biofilms formed by pathogenic microorganisms, which makes them more vulnerable to the action of antimicrobial agents [6].

Betulin, being a substance of plant origin, exhibits various types of biological activity: anti-inflammatory, capillary strengthening, antioxidant, antiviral, hepatoprotective, antitumor, immunomodulatory, hypolipidemic, antimutagenic, etc. Betulin's antiseptic properties are well known. [6,7] This served as the basis for the development of a dental product based on it in the form of a mouthwash.

In addition to betulin, other components with antimicrobial activity were added to the mouthwash, including chlorhexidine bigluconate solution and plant essential oils. Hydromethylcellulose and polyethylene glycol derivatives were used to impart a gel-like consistency.

When developing the technical specifications for a dental product called Betadent and its quality specifications, it was necessary to propose a method for assessing the authenticity of betulin, as the main active ingredient, as well as its quantitative determination in the composition of Betadent.

High performance liquid chromatography was used to assess the quality of the betulin substance.

Equipment: HPLC-MS system consisting of a Vanquish liquid chromatograph with a diode array detector (Thermo Fisher Scientific, USA) and an Orbitrap Fusion Lumos orbital ion trap mass spectrometer (Thermo Fisher Scientific, USA) equipped with an electrospray ionization (ESI) source.

Conditions for chromatographic separation:

Chromatographic separation was performed on a Shim-pack GIST-HP C18-Aq column (150 × 3 mm, 3 μm, Shimadzu, Japan) with a Security Guard pre-column (C18 cartridge, 4 × 3 mm, Phenomenex, USA). Mobile phase: 0.1% formic acid solution in water (15%) / acetonitrile (85%). Flow rate: 0.3 ml/min. Injection volume: 7 μl. Separation was performed in isocratic mode. Column oven temperature: 25 ºC. The total analysis time was 30 minutes.

Spectrophotometric detection conditions:

Detection and acquisition of electronic absorption spectra in the range of 190–400 nm (with a step of 2 nm) were carried out using a diode array detector with an optical slit width of 4 nm and a response time of 2 s.

Mass spectrometric detection parameters:

Detection was performed in scanning mode for two ionization modes simultaneously in the m/z range of 70–2000. Resolution: 30,000 c.u.

Reagents:

Deionized water was prepared using a Milli-Q unit (Millipore, USA) from distilled water.

Formic acid (98%, reagent grade) and acetonitrile (all HPLC grade) (all from Panreac, Spain) were used to prepare the mobile phase. Gradient HPLC grade methanol (JTBaker, Poland, >99.8%) was used to dissolve the sample.

Preparing the sample for analysis:

A 1 mg sample was transferred to a plastic tube, and 500 µl of acetonitrile and methanol were added. After the sample was completely dissolved, the resulting solution was injected into the chromatographic system for HPLC-MS analysis.

The pharmaceutical substance Betulin, produced domestically, was used as a sample. The betulin sample was a finely crystalline white powder.

Using the developed method, the identity and quantitative content of betulin were determined. Figures 1 and 2 show chromatograms of experimental samples and a blank sample without a sample, along with a breakdown of the main components, obtained at a wavelength of 190 nm.

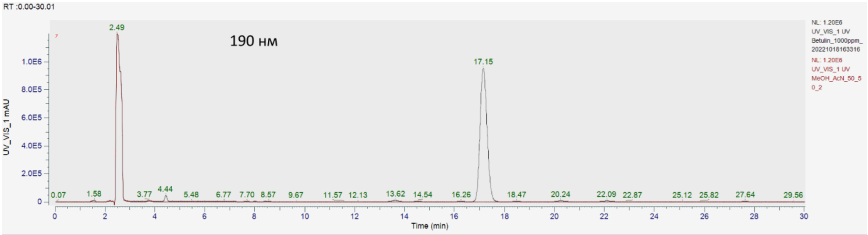

Figure 1. *Overlay of experimental chromatograms of the sample and the blank sample without sample, obtained at a wavelength of 190 nm.*

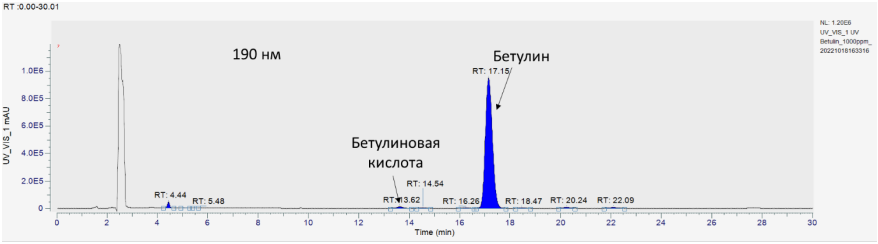

Figure 2. *Experimental chromatogram of the sample at a wavelength of 190 nm with marking of the main components.*

As can be seen from the spectra presented in the chromatogram in Fig. 2, the test sample contains a small amount of betulinic acid (0.9%), which presumably contributes to the enhanced therapeutic effect. Table 1 presents the results of peak area and component content calculations obtained using the internal normalization method.

Table 1.

Results of determination of quantitative content of betulin in the sample

No.	Compound	Start tR, min	End tR, min	Peak width, min	tR, min	Peak area, ye	Square, %	Peak height, µOpt	Height, %	S/N
1		4.22	4.64	0.425672	4.44	281526.4	1.45	43641.8	4.27	135.4677
2		4.93	5.27	0.341726	5.05	10622.81	0.05	030.518	0.1	3.148686
3		5.38	5.62	0.233333	5.48	10032.58	0.05	1385.428	0.14	4.225783
4	Betulinic acid	13.24	14.09	0.843194	13.62	175066.1	0.9	10163.3	0.99	31.22467
5		14.28	14.85	0.563739	14.54	34552.98	0.18	2048.424	0.2	6.231628
6		15.92	16:55	0.628052	16.26	27955.99	0.14	1398.724	0.14	4.277214
7	Betulin	16.64	17.84	1.198204	17.15	18551329	95.73	949782.2	92.87	2777.855
8		18.19	18.80	0.608032	18:47	36713.1	0.19	1785.991	0.17	5.466801
9		19.92	20.57	0.650906	20.24	133909.3	0.69	6226.125	0.61	19.20636
10		21.73	22.54	0.808967	22.09	118096.2	0.61	5244.821	0.51	16.37969

The obtained data indicate that the content of the main component (betulin) was 95.73%.

Conclusions

The developed method, based on the use of high-performance liquid chromatography, allows us to determine the authenticity and quantitative content of betulin in the Betadent dental product, intended for rinsing the oral cavity.

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关于组织老年人医疗和社会援助的一些事实
SOME FACTS ABOUT ORGANIZATION OF MEDICAL AND SOCIAL ASSISTANCE TO ELDERLY PEOPLE

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摘要：在包括俄罗斯在内的大多数经济发达国家，人口结构呈现出老龄化的特征，即老年人口数量和比例不断增加。这主要是由于预期寿命的延长。然而，这种看似积极的现象并非毫无意义。对大多数老年人来说，这并非一项社会成就，而是一种无趣、无助的生活，生活质量也较低。在俄罗斯，老年人的生活质量至今仍处于低迷状态。姑息治疗的可及性、及时性和质量是决定这一人群生活质量的重要因素。

关键词：老年人，生活质量，姑息治疗，治疗。

Abstract. *In most economically developed countries, including Russia, a demographic situation is characterized by an increase of the number and proportion of elderly people. This is primarily due to an increase in life expectancy. However, this seemingly positive phenomenon is far from unambiguous. For most elderly people, this is not a social achievement, but a joyless and helpless existence, accompanied by a low quality of life. In Russia, the quality of life of elderly people remains low to this day. An important factor determining the quality of life of this population group is the accessibility, timeliness, and quality of palliative care.*

Keywords: *elderly people, quality of life, palliative care, treatment.*

Population aging is the most serious medical, social, and economic problem in the world. Elderly people suffer from multiple, severe chronic diseases, accompanied by reduced compensatory capacity. According to R.S. Yatsemirskaya, the incidence rate of morbidity among people aged 60 to 74 is almost twice higher,

and among people aged 75 and older, it is six times higher than among younger people. Despite this, the volume of medical care provided to these individuals is lower than in other age groups [2].

Palliative care involves comprehensive support for patients and their caregivers. It includes addressing practical needs and consultation in case of mortality among relatives. It also provides support system that helps patients to maintain active lifestyle as possible before death. Modern hospices, as specialized medical institutions with their own unique characteristics, prioritize addressing the social and family needs of their patients. This is the fundamental difference between the care provided in a regular hospital and in a hospice. The level of development of hospice care varies significantly across countries. The World Health Organization's "Atlas of Palliative Care" presents a scale according to which 80 countries have been divided into four groups based on the level of palliative and hospice care provided. The top ten countries include, for example, the United Kingdom and the United States, where palliative care has been integrated into the healthcare system. The list of key quality indicators includes the level of education and competence of palliative care physicians, access to pain relief, the number of hospices per capita, and the degree of government support for this area. At the same time, there is a need for strategic integration of palliative care with programs aimed to the prevention, timely detection, and treatment of oncological diseases in children and adults [5]. In this scale, Russia ranks only 48th, occupying a place in the penultimate third group of countries with separate palliative care centers [1]. Significant organizational, economic, and political obstacles hinder the raising of hospice care to the required level and its transformation into a vital part of the modern healthcare system [3].

One of the fundamental factors influencing the quality of end-of-life care is an appropriate environment that can help to meet the physical, social, spiritual, and psychological needs of both patients and caregivers. [4] To create access to the highest quality services in this area, the National Palliative and End of Life Care Partnership published a six-year plan in 2021 [5]. In the United States, a measure (the only one to date) has been developed to assess healthcare professional workers attitude toward end-of-life care.

Based on the principles of hospice philosophy, this measure is called the Hospice Philosophy Scale (HPS) [6]. In many other countries, including Russia, the concept of "end-of-life care" will likely be included under the general term "palliative care." In our country, hospices are traditionally associated with a specific type of institution providing palliative care to patients suffering from severe oncological diseases. "Modern Russian hospices operate in much the same way as regular oncology clinics, but specialize in helping patients with particularly heavy cases" [7]. This circumstance is reflected in the Order of the Ministry of Health

and Social Development of the Russian Federation “On Approval of the Procedure for Providing Medical Care to the Population with Oncological Diseases” No. 944n dated December 3, 2009 // SPS “Garant”. Moreover, according to paragraph 2 of the Appendix to this document, hospices provide care primarily to incurable oncological patients in the terminal stage of the disease. This category is significantly more in need of medical care, social care, and drug provision than others.

Since population aging impacts virtually every aspect of life, affecting individuals, their families, and the population as a whole, a comprehensive approach is needed, encompassing healthcare, social services, education, policy, and ethical standards. This has led to a clear mismatch between the medical care received and the needs of patients in this age group. They associate the need for medical care with social support (care, communication, nutrition), meaning this group requires not only medical care but also social support.

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胃肠嗜酸性病变的诊治特点及文献综述
FEATURES OF DIAGNOSIS AND TREATMENT OF EOSINOPHILIC LESIONS OF THE STOMACH AND INTESTINES. LITERATURE REVIEW

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注释。嗜酸性粒细胞性胃肠疾病 (EGD) 是一组慢性免疫介导的胃肠道疾病，其特征是胃肠道症状和异常嗜酸性粒细胞浸润，而没有嗜酸性粒细胞增多的继发性原因。这类疾病包括嗜酸性食管炎、嗜酸性胃炎、嗜酸性肠炎和嗜酸性结肠炎。特别要注意不伴有嗜酸性食管炎的嗜酸性粒细胞性胃肠疾病。这些疾病的临床表现不具特异性且高度可变，取决于炎症过程的深度。不伴有嗜酸性食管炎的嗜酸性粒细胞性胃肠疾病的诊断需要结合临床表现、内镜检查结果和粘膜活检的组织学评估来确定。此类疾病的治疗主要经验性地采用排除饮食、糖皮质激素和生物制剂。目前尚无普遍接受的胃肠道嗜酸粒细胞病变治疗指南。

关键词：嗜酸粒细胞性胃肠道疾病、嗜酸粒细胞性胃炎、嗜酸粒细胞浸润、儿童、青少年。

Annotation. *Eosinophilic gastrointestinal diseases (EGDs) are a group of chronic immune-mediated gastrointestinal conditions characterized by gastrointestinal symptoms and abnormal eosinophilic infiltration in the absence of secondary causes of eosinophilia. This group includes eosinophilic esophagitis, eosinophilic gastritis, eosinophilic enteritis, and eosinophilic colitis. Particular attention is paid to eosinophilic gastrointestinal diseases without eosinophilic esophagitis. The clinical presentation of these diseases is nonspecific and highly variable, determined by the depth of the inflammatory process. The diagnosis of eosinophilic gastrointestinal disease without eosinophilic esophagitis is established based on a combination of clinical presentation, endoscopic*

examination results, and histological evaluation of mucosal biopsies. Elimination diets, glucocorticosteroids, and biologic agents are used empirically in the treatment of these diseases. There are no generally accepted guidelines for the treatment of eosinophilic lesions of the stomach and intestines.

Keywords: *eosinophilic gastrointestinal diseases, eosinophilic gastritis, eosinophilic infiltration, children, adolescents.*

Eosinophilic gastrointestinal diseases (EGIDs) are a group of chronic immune-mediated gastrointestinal (GI) disorders characterized by gastrointestinal symptoms and abnormal eosinophilic infiltration of specific GI sites in the absence of secondary causes of eosinophilia [1]. According to the 2022 international consensus on standardized nomenculation, a two-tier structure was adopted for EGIDs, in which the first tier is used to describe the relevant location in clinical practice, and the second tier is for clinical specificity and/or research purposes [2]. Involved GI tract segments should be specified and use the abbreviation “Eo” [3]. Thus, EGIS includes eosinophilic esophagitis (EoE) and EGIS without EoE, which include eosinophilic gastritis (EoG), eosinophilic enteritis (EoEn) and eosinophilic colitis (EoC) [4]. Cases of simultaneous or sequential damage to several parts of the gastrointestinal tract have been described.

Epidemiology. To date, there is insufficient data to understand the epidemiology of EGIS without EoE. The main reason is the rarity of these diseases in the population, and as a result, most publications are devoted to small studies or isolated cases.[3]. InIn 2016, Jensen ET et al. shared the results of a large study in which they analyzed the incidence among patients aged 0-65 years; the prevalence of EHG without EoE was 6.3 per 100,000 people for EoG; 8.4 per 100,000 people for EoG in combination with EoEn; 3.3 per 100,000 people for EoC [5]. A little later, Mansoor E et al. published the results of another large study, including more than 35 million electronic medical records (from 1999 to 2017), identifying 1820 patients with EoC in combination with EoEn and 770 patients with EoC, while the prevalence of EoG in combination with EoEn was 5.1 per 100,000 people, EoE - 2.1 per 100,000 people [6]. In 2020, Amelia Licari et al., having conducted the first systematic review and meta-analysis dedicated to the epidemiology of eosinophilic diseases of the gastrointestinal tract, not associated with the esophagus, in adults and children visiting outpatient clinics with gastrointestinal symptoms, showed that the overall prevalence of EGID without EoE, accounted for 1.9% of hospital patients with gastrointestinal symptoms [7]. Data reflecting an increase in the incidence of EoG in recent years is increasingly appearing [8,9]. EoG is more common in children than in adults: 10.7 cases per 100,000 in individuals under 20 years of age versus 7.1 cases per 100,000 in individuals aged 20 to 64 years, and the highest prevalence is found among children under 5 years of age (17.6

per 100,000 boys and 16.7 per 100,000 girls) [5]. There are also slight differences by gender: the frequency of EoG among males is 5.4 cases per 100,000, among females - 7.9 cases per 100,000, and with age, the prevalence of EoG in women increases to 14.4 cases per 100,000 at the age of 60-64 years [5]. EGIS can manifest at any age, but it is worth noting that 2 peaks of onset of EGIS without EoE have been demonstrated: 0-14 years and 50 years, and the average age at diagnosis was 7.3 (7.0 [0.5; 17]) years for children and 36 (32 [18; 77]) years for adults [10,11]. It is important to know that 57% of patients with EoH have at least 1 atopic disease (food allergy, dermatitis, bronchial asthma, allergic rhinitis, allergic reaction to drugs), and skin allergy tests in 7 out of 14 patients diagnosed with EoG give a positive result for food products or aeroallergens [3,8,12]. Moreover, it was found that eosinophilic infiltration of the gastric mucosa in children from 0 to 12 years old is secondary to food allergy (the main allergens are eggs, milk, shrimp, wheat and chicken) [13].

Pathogenesis. Currently, there is an active study of the pathogenesis of EGIS, not related to EoE, much remains unanswered, but it has been proven that the main place among the predisposing events is occupied by genetic factors, namely 7 genes recognized as the most important in the gene expression profiles of patients with EoG of the antrum: TXN, PRDX2, NR3C1, GRB2, PIK3C3, AP2B1 and REPS1[14]. These seven genes act as potential biomarkers [14].IN2020A diagnostic panel of the EoG transcriptome from 18 gastric genes, called the EoG diagnostic panel (EGDP18), was developed. Gastric biopsy and blood samples from 185 patients were taken for analysis, 74 of whom formed the main group - patients with EoG, which made it possible to develop diagnostic panels that can detect EoG from gastric mucosal biopsy samples and blood. In addition, CCL26/eotaxin-3 has proven to be a strong tissue biomarker for EoG [14]. In addition to genetic factors, an important role in the pathogenesis of EGID is assigned toTh2-mediated allergic reaction [15]. Food allergens activate T and B cells in the blood and tissues; under the influence of Th2-mediated cytokines (IL-4, IL-5, IL-13, etc.), the release, migration, and degranulation of eosinophils occurs. IL-5 promotes the release of eosinophils from the bone marrow, while eotaxin promotes chemotaxis and their migration into tissues. Activated B cells produce IgE, which, through the FceRI receptor (Fc epsilon I receptor) on eosinophils and mast cells, causes their degranulation [15]. The key cytokine in allergic reactions is thymic stromal lymphopoietin (TSLP), which has two isoforms - short and long. The long isoform is capable activate dendritic, mast and T cells by binding to the TSLP receptor (TSLPR), which allows it to exhibit pro-inflammatory functions [15]. It has been shown that in patients with EoH in combination with EoEeh Expression of the long isoform of TSLP has a significant positive correlation with the maximum number of eosinophils in the gastrointestinal mucosa [16].

Clinical manifestations. To the most common symptoms of EHG without EoE include abdominal pain (51%), nausea and/or vomiting (49%), and diarrhea (30%) [8]. EHG without EoE has been described with loss of appetite, weight loss, reflux/regurgitation, and rare development of ascites. For example, with EoG, a patient may complain of nausea, vomiting, early satiety, and abdominal pain [3]. Laboratory findings most often include eosinophilia (15-92%), anemia (15-54%), hypoalbuminemia (62%), and elevated IgE (62%) [3]. Specific clinical manifestations of EHG without EoE depend on the level of damage to the gastrointestinal wall, in other words, which layer is involved in the inflammatory process [17]. According to Klein's classification, all clinical symptoms of EoH combined with EoE depend on the location and depth of eosinophilic infiltration and are divided into mucous, muscular, or serous subtypes. The mucous subtype is more common than others and is characterized by complaints of abdominal pain, premature satiety, vomiting, flatulence, diarrhea, and gastrointestinal bleeding, and in severe cases, malabsorption and protein-losing enteropathy. The muscular subtype is characterized by symptoms of obstruction due to thickening of the intestinal walls and impaired peristalsis; intestinal perforation and intussusception, small intestinal diverticulosis, and intestinal volvulus may occur infrequently. The serous subtype is rare and is characterized by eosinophilic abdominal ascites combined with symptoms of the mucous and muscular subtypes; peritonitis and eosinophilic pleural effusion may occur [15]. In children and adolescents, the clinical picture of EoG in combination with EoE is supplemented by delayed growth and puberty, amenorrhea, and the absence of specific clinical features increases the period of diagnosis to 2 years or more [17, 18].

Endoscopic and morphological manifestations. Endoscopic picture EGIS without EoE has been described in a number of studies and most often represents a normal appearance of the gastrointestinal mucosa. For example, Pesek RD et al. in a multicenter retrospective study of 317 children and 56 adult patients showed that the normal appearance of the gastric mucosa is found in 66% of patients, the duodenum in 83%, the jejunum in 67%, and the ileum in 81% of patients; less common are ulcerations (6%), nodularity (3%), erythema (2%), and friability of the mucosa (2%) [11]. Another study showed that in 50 patients with EoC, a normal endoscopic picture was described in 74% of patients, and nodular lymphoid hyperplasia was detected in 26% of cases [19]. The main criterion for verifying EoG is the density of eosinophilic infiltration confirmed by morphological examination, which is reflected in the joint ESPGHAN/NASPGHAN guidelines for childhood (2024) (Table 2) [3]. In EoG, the eosinophil density in gastric mucosa biopsies is ≥30 eos/0.27 mm2 HPF [3]. Morphological data such as the presence of fibrosis and fibroblast proliferation in the basal and superficial parts of the lamina propria of the gastric mucosa, hemorrhages, thrombosis, and erosions are also taken into account [20].

Treatment. Therapy for EoH without EoE, given the lack of standardized recommendations, is currently empirical and is based on the severity of the disease and the presence of complications such as anemia, protein-losing enteropathy, gastrointestinal bleeding, intestinal obstruction, weight loss, and growth retardation [3]. Therapy should begin with an elimination diet, such as the "6-FED" diet, which excludes milk, soy, eggs, wheat, peanuts/tree nuts, and shellfish/fish [15, 21]. An alternative may be an elemental diet, in which only amino acids, medium-chain fatty acids, vitamins, and minerals are used in the diet [22]. A positive effect was achieved in 82% of children with EoH in the form of clinical improvement, and in 78% of patients in the form of a decrease in the eosinophil level to less than 10 eos /hpf against the background of dietary restrictions [3]. In this case, the return to a normal diet occurs gradually, according to the principle of "from the lowest to the highest risk" [15]. In addition to dietary correction, corticosteroids are used in patients with EoH in combination with EoEn, but only if the diet has proven ineffective or the course of the disease is severe and/or complicated [23]. Optimally, in the treatment of EoH in combination with EoEn, budesonide suspension or enteric-coated capsules, crushed and dissolved in water/juice, are used [24]. A multicenter study involving 142 children and adults with EoG showed that a combination of an elimination diet with topical steroids improves clinical symptoms in 75% of patients with EoG, in 65% of patients with EoG combined with EoE and in 54% of patients with EoC, and within 6 months after the start of the first course of treatment, the number of eosinophils in tissues decreases significantly (in the gastric mucosa, for example, from 145.4 eos / hpf to 50.8 eos / hpf after therapy) [8]. There are indications of the possibility of using proton pump inhibitors, mast cell inhibitors, montelukast, but as monotherapy, these drugs cannot provide clinical or histological remission [3,17,25]. Much attention is paid to the use of biological drugs in patients with EGIZ without EoE, the results of more than 30 clinical studies have been described, but a final decision the use of biological drugs as maintenance therapy has not yet been achieved [3]. The lack of professional consensus on the sequence and duration of EoG therapy in children does not allow for the development of a clear treatment algorithm, therefore, today, when choosing therapy, it is possible to rely on the recommendations of individual experts, which are based on several studies [15,17].

Conclusion. Eosinophilic gastrointestinal diseases without eosinophilic esophagitis are rare and little known to practicing physicians. Diagnosis of eosinophilic diseases of the stomach and intestines is difficult due to the nonspecific clinical and endoscopic presentation, as well as the lack of clear pathological diagnostic criteria. Treatment strategies, often focused on the recommendations of individual experts, includes the prescription of diet, corticosteroids, and biological therapy. All of this leads to a certain complexity in the management of patients and dictates the need for further study of the mechanisms of development of this pathology.

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肩部双侧不对称：青年人的几何形态测量研究
BILATERAL ASYMMETRY OF THE SHOULDER REGION: A GEOMETRIC MORPHOMETRIC STUDY IN YOUNG ADULTS

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摘要：本研究旨在利用几何形态测量方法评估右利手人群肩部形态不对称性。研究分析了32名右侧功能性不对称的年轻人（18-20岁）的数据。研究方法包括标准化摄影、使用TPS软件对肩部轮廓进行数字化处理以及使用MorphoJ 1.07a进行统计分析。Procrustes方差分析结果显示，在不存在尺寸差异（$p = 0.0854$）的情况下，形状方向性不对称具有统计学意义（$p < 0.0001$；$F = 13.81$）。主成分分析显示，第一个主成分（PC1）解释了52.27%的总体形态变异性，表明不对称性在所研究特征的结构中起主导作用。数据可视化采用95%置信度椭圆表示均值，证实了各组按体侧的清晰划分。所得数据表明，右利手个体肩部区域存在形态不对称的模式，这可能对制定临床和运动医学的规范参数具有重要意义。几何形态测量法已被证明可有效分析复杂的空间形状变化。

关键词：几何形态测量法、双侧不对称、肩部、MorphoJ、TPS、Procrustes 方差分析、主成分分析 (PCA)。

Abstract. *This study aims to assess morphological asymmetry of the shoulder region in right-handed individuals using geometric morphometric methods. The study analyzed data from 32 young adults (18-20 years) with right-sided functional asymmetry. The methodology included standardized photography, digitization of shoulder contours using TPS software complex, and statistical analysis in MorphoJ 1.07a. Results of Procrustes ANOVA revealed statistically significant directional asymmetry in shape ($p < 0.0001$; $F = 13.81$) in the absence of size differences ($p = 0.0854$). Principal component analysis showed that the first component (PC1) explains 52.27% of the total morphological variability, demonstrating the dominant role of asymmetry in the structure of the studied*

characteristics. Data visualization with 95% confidence ellipses for means confirmed clear separation of groups by body side. The obtained data indicate the presence of a pattern of morphological asymmetry in the shoulder region of right-handed individuals, which may be significant for developing normative parameters in clinical and sports medicine. The geometric morphometry method proved effective for analyzing complex spatial shape transformations.

Keywords: *geometric morphometry, bilateral asymmetry, shoulder, MorphoJ, TPS, Procrustes ANOVA, principal component analysis (PCA).*

Introduction. The study of bilateral asymmetry represents one of the fundamental problems of modern morphology, having substantial importance both for understanding general principles of biological system organization and for solving applied tasks in medicine and anthropology. The human upper extremity demonstrates pronounced structural polymorphism caused by complex interaction of genetic factors and functional loads [1]. The anatomical complexity of this region, including osseous, muscular and connective tissue components, makes it an ideal model for investigating the relationship between functional lateralization and morphological adaptations. The relevance of studying morphological asymmetry of the shoulder girdle is determined by several aspects. From a clinical perspective, understanding normal asymmetry parameters is necessary for developing objective diagnostic criteria for pathological conditions [2]. In sports medicine, asymmetry analysis allows optimization of training processes, design of specialized equipment, and development of individualized muscle imbalance correction programs [3]. Anthropological studies have revealed significant variability of upper extremity bone structure asymmetry among modern human populations, reflecting complex interaction of genetic factors and ontogenetic development features [4]. Traditional morphometric analysis methods based on linear measurements and angular characteristics have substantial limitations when studying complex spatial shape transformations [5]. In this context, geometric morphometry methods open new possibilities for quantitative analysis of integral morphological structure. The Procrustes coordinates superimposition method allows statistically reliable assessment of shape differences independent of size and position of objects [6]. Integrated software packages, such as TPS complex and MorphoJ, provide comprehensive analysis of morphometric data and visualization of spatial variability patterns [7]. Thus, comprehensive study of morphological asymmetry of upper extremity segments using modern geometric morphometric methods represents a relevant scientific task, the solution of which can contribute significantly both to fundamental understanding of bilateral asymmetry principles and to development of applied aspects in medicine and anthropology.

Aim. This study aims to comprehensively assess morphological asymmetry of the proximal upper extremity segment in right-handed individuals using modern geometric morphometry methods. The work aims to identify and quantitatively characterize patterns of bilateral variability in shoulder region shape, establish statistical significance of the identified differences, and determine their contribution to overall morphological variability. To achieve this aim, interconnected research objectives were sequentially addressed. The primary objective was development of a standardized methodology for digitizing morphological characteristics of the shoulder region based on photographic material with subsequent processing in specialized software. The next important objective was assessment of statistical significance of differences between right and left sides using multivariate analysis of Procrustes coordinates, allowing differentiation of directional and fluctuating asymmetry effects. The further objective was determination of the relative contribution of asymmetry to overall morphological variability using multivariate statistical analysis methods, particularly through principal component analysis. The final research objective was spatial visualization of the identified asymmetry patterns and their quantitative description, necessary for interpreting biological significance of the obtained results and their potential practical application in clinical medicine and anthropology.

Materials and Methods. The study voluntarily involved 32 young adults (18-20 years), ensuring minimization of age-related morphological changes associated with involutional processes while completing main growth processes. All participants provided informed voluntary consent for study participation. The gender composition included 24 females and 8 males. To exclude influence of motor dominance factor on morphological characteristics, only right-handed individuals were included, confirmed by standardized functional asymmetry questionnaire results. The image acquisition protocol involved shoulder region photography in lateral projection with natural upper extremity position along the torso with complete muscle relaxation. Considering the complex nature of shoulder region morphology, including anterior and posterior muscle groups, the chosen projection allowed fixation of the integral contour of the studied anatomical region. For each participant, separate right and left shoulder images were sequentially obtained under identical lighting conditions and shooting distance. The obtained digital images underwent standardization, including conversion to uniform spatial resolution and scale, which was a necessary condition for subsequent morphometric analysis. Data processing was performed using specialized geometric morphometry software: initial contour digitization was performed in TPS series programs (tpsUtil32 and tpsDig264), after which landmark coordinates were transferred to MorphoJ 1.07a program for statistical analysis. Application of this software complex ensured complete morphometric data processing cycle - from primary digitization to multivariate statistical analysis and result visualization.

Results. Initial data processing involved combining all photographic images into a single dataset using TPS software complex. On each shoulder region image, semilandmarks were sequentially placed along the external contour, which were subsequently converted to landmarks for statistical analysis. The formed TPS format file was imported into MorphoJ 1.07a, where data classification procedure was performed with allocation of groups corresponding to left and right shoulder, creating necessary conditions for statistical assessment of bilateral differences. The performed generalized analysis of Procrustes coordinates (Procrustes ANOVA) revealed statistically significant effects allowing differentiation of various variability components. The body side effect (Side) showed $p < 0.0001$ with F-statistic 13.81, indicating presence of pronounced directional asymmetry. The obtained numerical values demonstrate that systematic differences between right and left sides substantially exceed random shape fluctuations. Size analysis (Centroid Size) showed absence of statistically significant differences between sides ($p = 0.0854$; $F = 3.16$), indicating specificity of morphological differences limited exclusively to shape parameters. Significance of the Individual × Side interaction effect confirmed presence of fluctuating asymmetry, constituting a substantial component of overall variability. Principal component analysis allowed quantitative assessment of asymmetry contribution to overall morphological variability. The first principal component (PC1) explained 52.27% of variance, which is an exceptionally high indicator, testifying to the dominant role of asymmetry in the structure of morphological differences. The eigenvalue of PC1 was 0.00056080, substantially exceeding values of subsequent components. The second principal component (PC2) with eigenvalue 0.00021955 explained additional 20.46% of variance, and the third component (PC3) - 7.60%. Cumulative variance proportion explained by the first three components reached 80.33%, indicating high structuredness of morphological variability in the studied sample. Result visualization in principal component space showed clear sample separation into two non-overlapping clusters corresponding to right and left sides. Construction of 95% confidence ellipses for means demonstrated their complete separation along PC1 axis with insignificant overlap along PC2 axis (Appendix, Fig. 1). Ellipse centers were located at approximately 0.09 conventional units distance along PC1 axis, visually reflecting the magnitude of morphological differences between sides. Absence of ellipse overlap along the main asymmetry axis (PC1) statistically confirms presence of the identified asymmetry pattern at the entire sample level. Analysis of principal component coefficients revealed complex spatial organization of asymmetry. The greatest contribution to PC1 was made by landmarks located in the deltoid muscle region and upper shoulder contour, with coefficients ranging from 0.136279 to -0.113158, indicating coordinated displacements of these areas in opposite directions for right and left sides. The obtained data allow concluding that

morphological shoulder asymmetry in right-handed individuals is characterized by a complex spatial pattern of shape transformations, statistically reliably reproduced in the studied group and constituting the main component of overall morphological variability.

Conclusions. The conducted study established presence of statistically significant morphological asymmetry of the proximal upper extremity segment in young adults with right-sided functional asymmetry profile. Geometric morphometry methods confirmed qualitative nature of the identified differences, manifested in stable spatial patterns of shape transformation in the absence of statistically significant differences in absolute sizes. The directional asymmetry component demonstrates dominant contribution to overall morphological variability, confirmed by 52.27% of variance explained by the first principal component. Presence of fluctuating asymmetry was established, reflecting individual variations in manifestation of bilateral differences. Application of geometric morphometry method complex proved effective for quantitative analysis of complex spatial transformations of shoulder region shape. A promising direction for further research is sample expansion for assessing age dynamics of morphological asymmetry and inclusion of additional muscle tone and biomechanical parameters. Methodology improvement may include application of three-dimensional scanning for more accurate reconstruction of shoulder region spatial configuration. The obtained normative asymmetry parameters may find application in developing objective diagnostic criteria in sports medicine and rehabilitation, though this requires additional studies with inclusion of clinical groups.

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Appendix

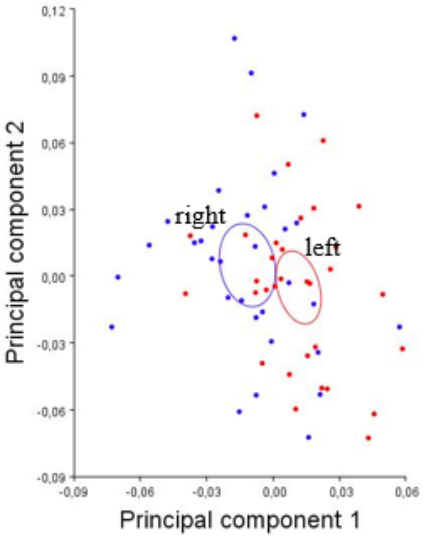

Figure 1. *Distribution of objects in principal component space PC1 and PC2 with 95% confidence ellipses for means, grouped by body side (left/right).*

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大隐静脉主干非逆行段自体静脉假体置换腘动脉
AUTOVENOUS PROSTHETIC REPLACEMENT OF THE POPLITEAL ARTERY WITH A NON-REVERSED SEGMENT OF THE GREAT SAPHENOUS VEIN TRUNK

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A popliteal artery (PA) aneurysm, in practical terms, is defined as an artery dilation greater than 2 cm.

The prevalence of patients with PA aneurysms, given the largely asymptomatic and unverified nature of the disease, is approximately 1% of the total population, according to several sources. Older men, aged 60-80 years, are most often affected.

PA aneurysms account for 70-80% of all peripheral arterial aneurysms and are associated with aortic aneurysms in 40-50% of cases.

Ultrasound is a screening method.

Timely verification of SCA aneurysms and planned surgical treatment (before complications such as rupture, embolism, or thrombosis) are necessary to reduce the risk of limb loss.

Depending on the extent and size of the SCA aneurysm, the presence/absence of concomitant involvement of adjacent arteries and compression of surrounding structures (veins, nerves), the reconstructive surgery method is determined. These include:

- arthroplasty or bypass: femoropopliteal, femorotibial, popliteal-tibial, SCA arthroplasty.

- stent graft implantation is an alternative to open reconstructive surgery. The choice of surgery should be based on the clinical and anatomical characteristics of the patient. Careful patient selection (suitable vascular anatomy and availability of outflow tracts), proper surgical technique, and correct stent graft selection are necessary.

-aneurysmorrhaphy—tight suturing of the aneurysm walls with a significant reduction in its volume.

Ligation of the arteries above and below the aneurysm is recommended to prevent peripheral embolism in the postoperative period and to prevent continued aneurysm growth after reconstruction.

In cases of popliteal vein, sciatic, tibial, or peroneal nerve compression by an aneurysm, excision of the aneurysm and suturing of the arterial orifices of the knee joint network, which open into the aneurysm cavity and often cause aneurysm growth, are recommended.

The choice of conduit is a pressing issue, which is directly related to the duration of prosthesis/bypass function and the risk of limb loss.

As a conduit, an autologous vein has advantages over a synthetic graft (polytetrafluoroethylene, knitted synthetic dacron graft impregnated with silver, knitted polyester graft) or stent graft implantation:

- the presence of an endothelial layer in the lumen. The endothelium is the prototype of an athrombogenic surface (cell membrane), which secretes thromboresistant glycoproteins and antithrombotic substances, including prostacyclins;
- mechanical compatibility - elasticity, similar to arteries with subsequent histological changes – "arterialization";
- the risk of thrombosis and infection is comparatively lower in the postoperative and long-term periods.

The physical properties of the foreign material (synthetic prosthesis/bypass, stent graft) are complicated by kinking, reduced blood flow, and an increased risk of thrombosis when flexing the operated lower limb at the knee joint.

Given that the normal diameter of the SCA is 0.5-1.1 cm, in most cases, autovenous material of a suitable diameter is not available for prosthetic replacement. Data obtained from literature review and our experience show that a mismatch between the diameter of the autologous vein and artery leads to turbulent blood flow (associated with endothelial dysfunction and neointimal hyperplasia), the development of pre- and poststenotic dilations, and thrombosis of the autologous vein graft.

Case Study No. 1

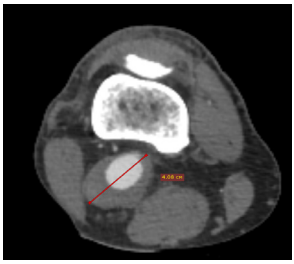

Figure 1.

Patient V., 72, sought routine medical attention complaining of a large, pulsating mass in the right popliteal region. Based on ultrasound imaging of the lower extremity arteries, a diagnosis of a popliteal artery (PA) aneurysm measuring approximately 40 mm was made. As part of the preoperative examination, visualization of the arterial bed of the lower extremities was performed – computed tomography of the arteries of the lower extremities (conclusion – aneurysm of the popliteal artery of the right lower

extremity, maximum diameter – 4.08 cm, mural thrombosis, compression of the popliteal vein) (Figs. 1, 2). The diameters of the popliteal artery proximal and distal to the aneurysm are 10 mm.

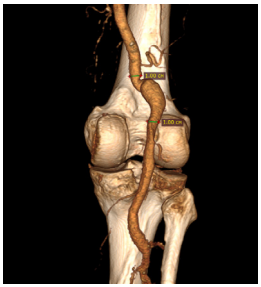

Figure 2.

Given the isolated aneurysmal lesion of the popliteal artery (SCA) and concomitant compression of the popliteal vein, a decision was made to perform surgical treatment: resection of the SCA aneurysm followed by autologous vein grafting through a posterior approach.

The surgical stages are illustrated in Figs. 3-9:

- a posterior approach was performed, the popliteal artery aneurysm was isolated, and the proximal and distal aneurysm-intact fragments of the SCA were secured with holders.

- the trunk of the great saphenous vein (GSV) was isolated on the leg (length = aneurysm length x 2 + reduction in vein length during isolation and removal).

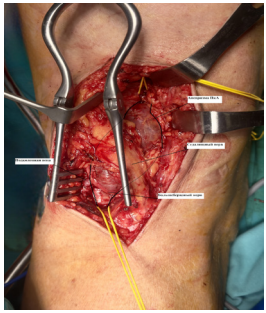

Figure 3.

- an autologous vein conduit was prepared using hydraulic bougienage, valvulotomy, and longitudinal and transverse dissection of the vein. - Formation of an autogenous venous neoconduit from two semicircles of the GSV using 6/0 Prolene suture in a continuous, twisted suture. The neoconduit diameter is 10 mm.

- Resection of the aneurysm, suturing of the arterial orifices of the knee joint network.

- Formation of a distal anastomosis

- Formation of a proximal anastomosis

- Blood flow initiation, hemostasis, drainage, wound closure.

Figure 4.

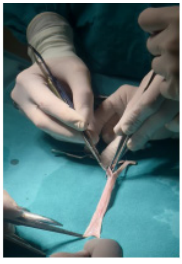

Figure 5.

Figure 6.

Figure 7.

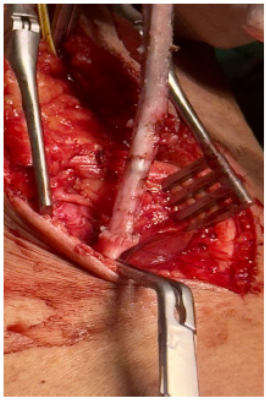

Figure 8.

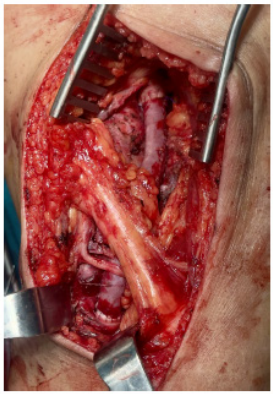

Figure 9.

The postoperative period was uneventful, and the patient was discharged on the fifth postoperative day. Lower extremity artery angiography was performed for dynamic monitoring one month after surgery, and the autovenous graft was patent (Fig. 10). The patient had no complaints.

This method of SCA replacement allows for the production of an autovenous graft of appropriate diameter, maintaining laminar blood flow, and, consequently, preventing the development of pre- and poststenotic dilation, intimal hyperplasia, and occlusion of the autovenous graft.

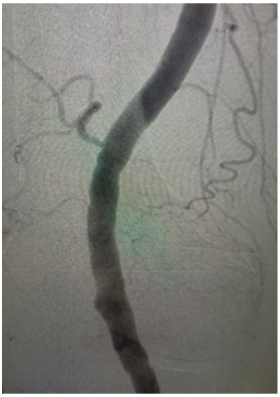

Figure 10.

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反应磁控溅射沉积复合氮化物薄膜金属组分含量预测
PREDICTION OF THE CONTENT OF METAL COMPONENTS OF COMPLEX NITRIDE FILMS DEPOSITED BY REACTIVE MAGNETRON SPUTTERING

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注释：本文提出了一个模型，用于预测在氩气/氮气工作气体环境下，采用双组分复合靶材进行反应磁控溅射沉积的复杂氮化物薄膜的金属含量。该模型考虑了溅射金属及其氮化物的溅射产额和离子电子发射、靶材上的离子流密度分布以及形成这些金属氮化物的化学反应速率。为了验证所提出的模型，研究了在氩气和氩气/氮气工作气体环境下，采用Cu-Mo复合靶材进行磁控溅射沉积在钛基体表面的氮化物薄膜的元素组成。

关键词：反应磁控溅射，复合靶材，薄膜，元素组成，反应溅射模型，氮化物。

Annotation. *This article proposes a model for predicting the metallic content of complex nitride films deposited by reactive magnetron sputtering of a two-component composite target in an Ar/N_2 working gas environment. The model takes into account the sputtering yields and ion-electron emission of the sputtered metals and their nitrides, the ion current density distribution on the target, and the rates of the chemical reaction that forms these metals' nitrides. To verify the proposed model, the elemental composition of nitride films deposited on the surface of a titanium substrate by magnetron sputtering of a Cu–Mo composite target in Ar and Ar/N_2 working gas environments was studied.*

Keywords: *reactive magnetron sputtering, composite target, thin films, elemental composition, reactive sputtering model, nitrides.*

Composite materials based on immiscible component systems, particularly the Cu–Mo system, are used as antifriction materials in friction units of machines and mechanisms [1]. In addition to the metals themselves, thin-film coatings based on copper and molybdenum, with inclusions of nitrides of these metals, are promising for reducing the coefficient of friction and increasing wear resistance in components operating under dry friction [2].

However, the properties of these materials are highly sensitive to the chemical composition of the elements and structural features. This circumstance imposes strict limitations on thin-film manufacturing technology. The deposition method must ensure stable reproduction of the crystalline structure, chemical composition of the components, and phase states of the formed layers.

Reactive magnetron sputtering of composite targets is a promising technology for forming complex nitride films [3]. This method utilizes targets comprising a matrix of the base metal with embedded fragments of other metals, enabling the production of multi-component coatings with a specified number and concentration of elements using a single magnetron. The main limitation of this approach is the difficulty in selecting the optimal size of the metal inserts to achieve the desired component composition of the film coating.

Experience shows that during magnetron sputtering of composite targets, the structure of the resulting films is determined by a multitude of variables (the size of the inclusion regions of individual components, the erosion rates of each element, the distribution of the ion flux density on the target surface, the energy of the ions impacting the target, and other factors) [4].

During reactive sputtering, significantly more complex processes occur within the chamber, resulting in the composition of the resulting films being further determined by the chemical activity of the target material and the pressure of the reactant gas. In such situations, the use of computer modeling techniques becomes the only way to determine the most appropriate dimensions of the composite target components and the sputtering process conditions that enable the synthesis of a film of the desired composition [5].

The model under consideration assumes that a composite planar target is sputtered using an axial magnetron sputtering system (AMS). The target consists of two metals, A and B, and is sputtered in an Ar/N2 working gas environment at a chamber pressure of less than 0.1 Pa.

Due to the low ion energy, sputtering occurs only from the outermost atomic layers and only in the form of atoms. The emission of higher-order particles (Me_2N, MeN clusters, etc.) is two orders of magnitude slower than the atomic

sputtering rate and is therefore not considered in the model. Target sputtering occurs only within the sputtering zone.

In MRS, the sputtering zone is determined by the magnetic trap configuration and, for axial planar magnetrons, is a ring bounded by two radii, Rmin and Rmax. With a uniform density distribution of ions bombarding the target in the sputtering zone, the sputtering rate of each material should be proportional to the areas occupied by the target parts within the sputtering zone. However, in MRS, the density distribution of ions bombarding the target is non-uniform.

Chemical reactions that form nitrides occur on all surfaces involved (target, substrate, chamber walls). However, the metal content of the film is only affected by processes occurring on the target. As a result of the chemical reaction, an oxide film forms on the target surface. However, simultaneously with the film's formation, it is removed from the target by sputtering.

To verify the proposed model, studies were conducted on the deposition of copper and molybdenum nitride films using magnetron sputtering of Cu–Mo composite targets in Ar and Ar/N2 working gas environments.

The experimental vacuum chamber was equipped with a magnetron with a 50 mm diameter target. Cu–Mo targets with varying molybdenum content were used for sputtering. The composite targets consisted of a Cu base (99.5% pure) with a diameter of 50 mm and a thickness of 5 mm, into which molybdenum sectors (99.9% pure) were pressed. By varying the angle of the molybdenum sector, the ratio of the sputtered copper to molybdenum areas was varied. A 3 mm thick VT6 titanium alloy plate was used as the sputtering substrate. During the experiments, a VT6 titanium alloy substrate was mounted on a substrate holder 70 mm from the magnetron target surface. The vacuum chamber was evacuated to a pressure of 10–3 Pa, and the substrates were ion-cleaned. Ar was supplied to the ion source at a flow rate of 20 ml/min. The cleaning time, discharge voltage, and discharge current were constant throughout the experiments: t = 2 min, Ud = 85 V, Id = 5 A.

The films were then deposited. Cu–Mo targets were sputtered in an Ar/N_2 gas mixture at a total gas flow rate of 60 ml/min and a nitrogen concentration in the gas mixture (N_2) ranging from 0 to 10%. All experiments were performed using a magnetron discharge current stabilization mode of It = 1.25 A (pulse repetition rate F = 9.5 kHz, duty cycle 70%). The film thickness was approximately 80–85 nm and was controlled by deposition time.

The elemental composition of the films was analyzed using atomic emission spectroscopy on a GD-Profiler 2 glow discharge optical emission spectrometer (HORIBA). Initially, the elemental composition of the films deposited by sputtering Cu–Mo composite targets in an argon (Ar) environment was studied.

During sputtering of Cu–Mo composite targets, the magnetron discharge voltage varied from 276 to 328 V, corresponding to an average ion energy of about Ei

= 180–210 eV. At these ion energies, the sputtering yields of copper and molybdenum are YCu = 0.33 and YMo = 0.22. The ratios of these coefficients are YCu/YMo = 1.50 for Ei = 300 eV and YCu/YMo = 1.75 for Ei = 200 eV. Therefore, using formulas (1)–(6) and the values YCu = 0.33 and YMo = 0.22, refined calculations of the metal content in the films were performed. The modeling error did not exceed 5%, and these coefficients were subsequently used in modeling reactive sputtering processes. The dependences of the elemental composition of films on the nitrogen content in the Ar/N_2 gas mixture during reactive sputtering of Cu–Mo targets were obtained. When nitrogen was added to the chamber, a sharp increase in its content in the film was observed. When the nitrogen concentration GN2 in the Ar/N2 gas mixture reached 7%, its content in the films reached 42%. With a further increase in GN2 to 12%, the nitrogen content in the films increased to 48% and then remained virtually independent of the nitrogen concentration in the Ar/N_2 gas mixture.

However, of particular interest for modeling is the metal content in the deposited films without taking nitrogen into account (Fig. 3). As can be seen from Fig. 3, a sharp decrease in the molybdenum content in the film occurred when the nitrogen flow into the chamber QN2 was greater than 6 sccm, and at QN2 = 7.5 sccm, the minimum aluminum content was observed – CMo = 26 at.%. In the case of a further increase in QN2, the molybdenum content in the films increased almost linearly and reached its initial value at QN2 = 15 sccm. This behavior is associated with the processes of nitride film formation on the surface of the copper and molybdenum parts of the target and the difference in the nitriding rates of copper and molybdenum. At QN2 < 6 sccm, only a small fraction of the copper and molybdenum parts of the target is covered with a nitride film, and the resulting nitride films are effectively removed by sputtering. In case of further increase of QN2, oxidation of molybdenum occurs first, which leads to a decrease in the rate of its sputtering and, as a consequence, to a decrease in its content in the film.

Copper absorbs virtually no nitrogen, and intensive nitriding of molybdenum begins. This leads to the surface of the molybdenum portion of the target also becoming coated with a nitride film, and the sputtering rate slows. Further changes in the copper and molybdenum concentrations in the film are determined by the sputtering yields of their nitrides.

The proposed model accurately describes the change in elemental content in the film with varying nitrogen flow into the chamber. Similar results were obtained when predicting the metallic components in films during sputtering of CuMo-10, CuMo-25, and CuMo-60 targets. The modeling error is no more than 10%. Significant deviations were observed at low nitrogen flows into the chamber, which is most likely due to the model not accounting for the decrease in the partial pressure of the reactive gas in the chamber due to its absorption by the target and growing film surfaces at low target and film surface coverages.

The results presented in the article were obtained within the framework of the project under State Assignment No. FZRR-2023-0005 "Development of fundamental technological principles for the use of concentrated energy flows to obtain new import-substituting composite materials for special purposes based on systems of immiscible components".

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研究植物油的成分以生产富含多不饱和脂肪酸的混合油

INVESTIGATION OF THE COMPOSITION OF VEGETABLE OILS FOR THE PRODUCTION OF BLENDED OILS ENRICHED WITH POLYUNSATURATED FATTY ACIDS

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注释：基于对中亚地区人口膳食中主要使用的棉籽油和葵花籽油的脂肪酸组成及其相关物质的研究，开发了双组分和三组分混合植物油的配方。通过将这些油与必需脂肪酸来源菜籽油混合，优化了配方，使健康膳食中ω6:ω3脂肪酸的比例达到4:1，日常食用中ω6:ω3脂肪酸的比例达到10:6:1。

关键词：棉籽油和葵花籽油、菜籽油、脂肪酸平衡、必需脂肪酸、混合、ω6:ω3脂肪酸比例。

Annotation. *Based on a study of the fatty acid composition and associated substances of cottonseed and sunflower oils, which are predominantly used in the diets of the population of Central Asia, formulas for two- and three-component blended vegetable oils were developed. By mixing these oils with rapeseed oil, a source of essential fatty acids, the composition was optimized, achieving an ω6:ω3 fatty acid ratio of 4:1 for a healthy diet and 10-6:1 for daily consumption.*

Keywords: *Cottonseed and sunflower oils, rapeseed, fatty acid balance, essential fatty acids, blending, ω6:ω3 fatty acid ratio.*

As is well known, individual vegetable oils do not have a balanced fatty acid composition fully consistent with the human diet. That is, the ratio of saturated, unsaturated, and polyunsaturated fatty acids, including ω9, ω6, and ω3 groups, is insufficient to support healthy body function [1-3]. However, blending can produce oils from two- and multi-component mixtures with a desired composition and properties [4].

Cottonseed oil is highly nutritious, containing 884 calories per 100 grams. It is rich in vitamins A, E, and PP, as well as saturated and unsaturated fatty acids. Sunflower oil is also rich in unsaturated fatty acids. Physiologically, omega-3 fatty acids, including linolenic acid, are essential fatty acids that regulate lipid metabolism. The recommended dietary ratio of saturated, unsaturated, and polyunsaturated fatty acids is 3:6:1, and the omega-6:omega-3 ratio is 5:1 to 3:1. Cottonseed and sunflower oils account for 99.1% of the vegetable oil consumption in the Republic of Uzbekistan, and the above-mentioned ratios are not met. As a solution, we propose enriching cottonseed and sunflower oils by blending them with rapeseed oil, which is rich in omega-3 fatty acids.

As a solution to this problem, we propose enriching cottonseed and sunflower oils by blending them with rapeseed oil, which is rich in omega-3 fatty acids. The fatty acid composition of the vegetable oils we used is shown in Figure 1.

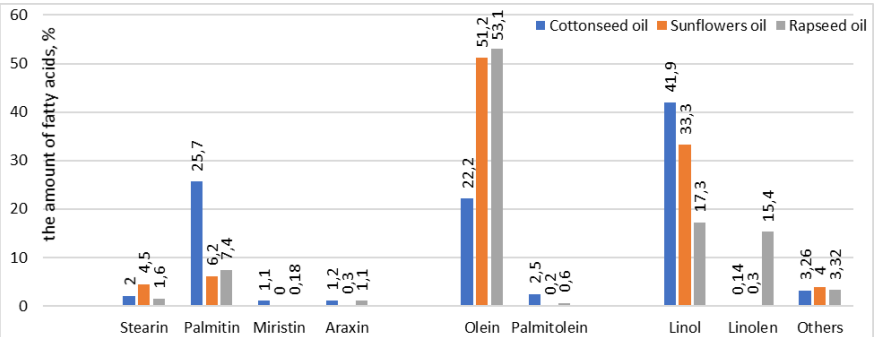

Fig. 1. Fatty acid composition of used oils

As can be seen from Fig. 1, cottonseed oil has the highest content of saturated fatty acids. The total amount of saturated fatty acids in sunflower oil is 10.7%, with the main fatty acid consisting of monounsaturated olein (51.2%). Rapeseed oil has an advantage in the content of polyunsaturated fatty acids linoleic acid (17.3%) and linolenic acid (15.4%). The amount of linolenic acid in cottonseed oil is 0.14%, and in sunflower oil 0.3%. Meanwhile, the ratio of saturated to unsaturated fatty acids in cottonseed oil is 1:2.3, indicating its resistance to oxidation and its excessively high nutritional value, which physiologically negatively saturates

the body. Rapeseed oil has the highest level of unsaturation and is 1:8.7, indicating its tendency to oxidize. By blending oils with such a composition, it is possible to increase their biological activity and ensure resistance to oxidation.

In our research, we created two-component cottonseed:rapeseed and sunflower:rapeseed oils by blending them in ratios ranging from 80:20 to 20:80. Increasing the proportion of rapeseed in the blend from 20 to 80% optimized the linolenic acid content. The changes in the ratio of saturated, mono-, and polyunsaturated fatty acids depending on the rapeseed oil content in the cottonseed:rapeseed blend are shown in Figure 2.

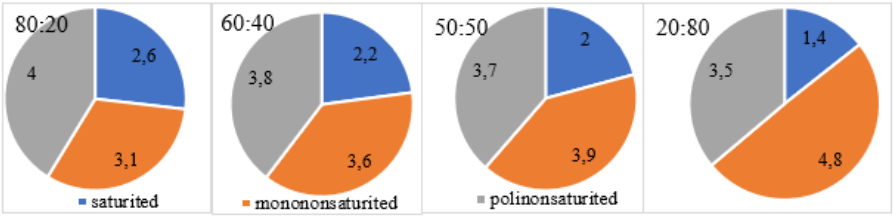

Figure 2. *The effect of changes in proportions on the fatty acid balance of cottonseed:rapeseed oil*

According to nutritionists' recommendations, the ω6:ω3 fatty acid ratio should be 3-5:1. The optimal cottonseed:rapeseed oil ratio is achieved when the proportion of rapeseed oil in the blend is in the range of 40-50%. Similar results were obtained with sunflower:rapeseed oil ratios from 80:20 to 20:80. Satisfactory results for the linoleic acid to linolenic acid ratio were obtained by changing the proportion of sunflower and rapeseed oils from 60:40 to 20:80. However, a positive balance of polyunsaturated fatty acids was achieved at a ratio of 60:40. Figure 3 shows the effect of changing the proportions on the fatty acid balance in a sunflower:rapeseed oil blend.

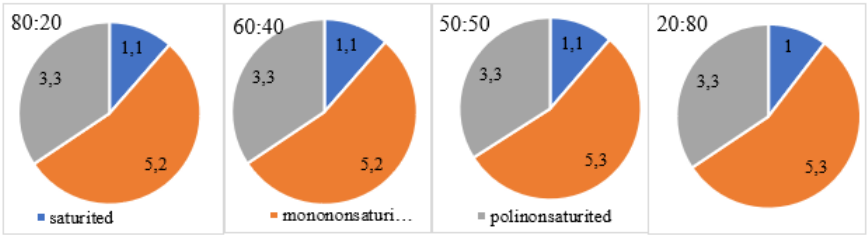

Figure 3. *The effect of changes in proportions on the fatty acid balance of sunflower:rapeseed oil*

In subsequent studies, three-component blended oils (cottonseed:sunflower:rapeseed) were created and their changes in fatty acid content were examined. As can be seen from the data in Figure 4, when sunflower oil is added to the three-component blend, optimal conditions are achieved at a ratio of 40:20:40 (Table 1).

Table 1

The composition of the blend is cottonseed:sunflower:rapeseed oils in a ratio of 40:20:40

No.	Fatty acids	Amount of fatty acids, %			Content in the blend			
		cotton.	sun-flower	rape-seed.	cotton.	sun-flower	rape-seed.	total
saturated								18.3
1	Stearic	2.00	4.50	1.60	0.8	0.9	0.6	2.3
2	Palmitic	25.7	6.20	7.40	10.3	1.2	3.0	14.5
3	Myristic	1.10	0.00	0.18	0.4	0.0	0.1	0.5
4	Arachidic	1.20	0.30	1.10	0.5	0.1	0.4	1.0
monounsaturated								41.6
1	Oleic	22.2	51.2	53.1	8.9	10.2	21.2	39.4
2	Palmitol-aya	2.50	0.20	0.60	1.0	0.0	0.2	1.3
polyunsaturated								37.6
1	Linoleic	41.9	33.3	17.3	16.8	6.7	7.9	31.3
2	Linolenic	0.14	0.30	15.4	0.1	0.1	7.2	6.3
	Other	3.26	4.00	3.32	1.3	0.8	1.3	3.4

Moreover, the content of saturated fatty acids in the fatty acid balance was 1.8/10 (Fig. 4), the ratio of saturated and unsaturated fatty acids reached 1:5.5.

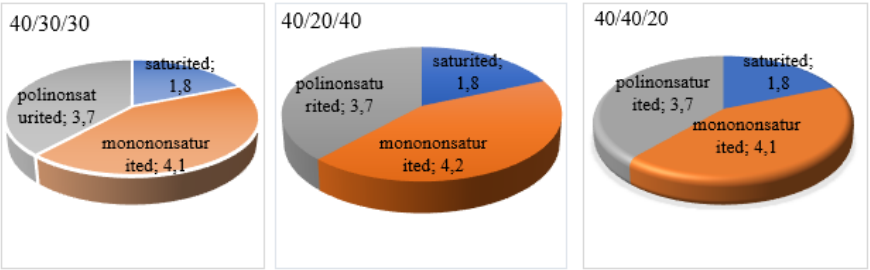

Figure 4. *The ratio of saturated/unsaturated fatty acids in a three-component blend of cotton:sunflower seeds:rapeseed oil*

In the proportion of 40:20:40, respectively, oils, and the ratio of linolenic acid to linoleic ω6:ω3 to 5:1 is achieved (Fig. 5).

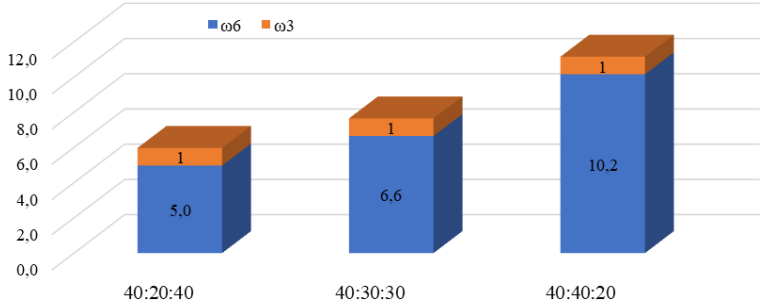

Fig. 5. The effect of changes in proportions on the content of ω_6:ω_3 fatty acids in cotton:sunflower seeds:rapeseed blend

Thus, experimental research shows the possibility of obtaining rapeseed oil blends that are balanced in fatty acid composition and enriched with essential ω3 fatty acids.

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俄罗斯城市塑料预处理带来的生态效应
THE ECOLOGICAL EFFECT FROM PLASTIC PRE-TREATMENT IN RUSSIAN CITIES

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注释：本文探讨了俄罗斯城市居民预处理塑料垃圾对环境和经济的影响。提出了一个降低运输成本和污染物排放的简单解决方案：居民粉碎塑料瓶和包装，然后拧紧瓶盖。本文利用八个人口规模各异的城市的数据，计算了运输影响，包括节省柴油以及减少二氧化碳和氮氧化物排放。结果表明，居民通过粉碎塑料瓶来提高塑料的容重，可使城市固体废物收集的燃料消耗减少5–8%，并减少大城市每年数百吨的温室气体排放。开展此类活动无需任何资本投入，仅依靠公众的环境教育。引入预压实塑料垃圾可以成为城市固体废物管理战略的有效组成部分，带来环境和经济效益。

关键词：塑料垃圾、压实、城市固体废物、容重、瓶子和包装粉碎、燃油经济性、二氧化碳排放、氮氧化物、废物回收、社区参与。

Annotation. *This article examines the environmental and economic impact of pre-processing plastic waste by residents in Russian cities. A simple solution to reducing transportation costs and pollutant emissions is proposed: crushing plastic bottles and packaging and then screwing the caps on them by residents. Using data from eight cities with varying population sizes, the transport impact is calculated, including diesel fuel savings and reduced carbon dioxide and nitrogen oxide emissions. The results show that increasing the bulk density of plastic through bottle crushing by residents reduces fuel consumption for municipal solid waste collection by 5–8% and reduces annual greenhouse gas emissions by hundreds of tons in large cities. Implementing such a campaign requires no capital investment and relies solely on environmental education of the public. The introduction of pre-compacting plastic waste can become an effective element of a municipal solid waste management strategy, providing environmental and economic benefits.*

Keywords: *Plastic waste, compaction, municipal solid waste, bulk density, bottle and packaging crushing, fuel economy, carbon dioxide emissions, nitrogen oxides, waste recycling, community involvement.*

The volume of plastic waste worldwide is constantly growing, and its low bulk density means that waste containers are filled with air rather than material. According to various estimates, the mass fraction of plastic in the morphological composition of municipal solid waste (MSW) ranges from 5 to 16%. According to the Russian Ministry of Natural Resources, plastic accounts for approximately 10% of MSW by weight [1]. In large Russian cities, such as Moscow, the proportion of plastic reaches 14–16% by weight, equivalent to approximately 44 kg of plastic per person per year [2]. Due to its low density, plastic can account for up to 20–30% of the total volume of MSW. As a result, regional operators are forced to remove containers more frequently, which increases diesel fuel consumption by garbage trucks and leads to increased CO_2 and nitrogen oxide (NO_x) emissions [3].

The problem can be solved by increasing the bulk density of plastic waste in municipal solid waste. One solution is to involve the public in the pre-processing of plastic waste. To this end, an information campaign should be conducted for the public, such as the nationwide “Crush a Bottle – Protect Nature” campaign. It is recommended to crush plastic bottles and packaging and tighten the lids to prevent air from returning and minimize the volume.

According to the UK’s Waste & Resources Action Programme (WRAP), the bulk density of empty PET bottles without compaction is approximately 16 kg/m³, whereas with moderate crushing and subsequent screwing of the cap, it increases to 20–26 kg/m³—i.e., by approximately 25–60% [4]. Importantly, such moderate compaction does not interfere with subsequent sorting and recycling of the plastic [4]. Increasing the bulk density allows waste trucks to be loaded more efficiently, reducing the number of trips required to remove the same amount of waste. This directly leads to fuel savings and a reduction in emissions from MSW transportation.

In this paper, we evaluate the environmental impact of pre-compacting plastic waste by residents (crumpling bottles and screwing on caps) in cities of varying sizes. The primary calculation indicator is the transport effect, i.e., savings in diesel fuel used by garbage trucks and the associated reduction in CO_2 and NO_x emissions with an increase in the bulk density of plastic. Cities with varying population sizes and typical MSW generation indicators are selected as examples: Moscow, St. Petersburg, Kazan, Perm, Rostov-on-Don, Donetsk, Luhansk, and Alchevsk. For the calculations, we use a methodology that utilizes available initial data from open sources.

The volume of MSW generation is determined by the city’s population size N and the waste generation standard per capita per year (q, kg/person year). For example, the average Russian generates approximately 325–440 kg of waste per year [3, 5]. For each city, the current population size and an estimated value of q are taken into account, taking into account regional data. The total MSW generation for the city will be $M_T = N \cdot q$.

The mass of plastic waste is estimated based on the mass fraction of plastic (Pm) in the morphological composition of MSW. Thus, in large Russian cities, plastic accounts for approximately 10% of the mass of MSW, while in Moscow it reaches 14–16% [2]. In the other cities considered, the proportion of plastic is estimated at 5–10%, based on consumption levels and available data.

The volume of plastic waste before the campaign (without crushing) is calculated as $V_{P1} = M_P / \rho_1$, Where ρ_1 – initial bulk density of plastic (16 kg/m³).

As a result of the information campaign, the population of cities begins to crush plastic waste, which leads to an increase in the bulk density of plastic in a moderate scenario up to $\rho_2 = 22$ kg/m³[4].

Volume of plastic after the campaign $V_{P2} = M_P / \rho_2$ Thus, public participation reduces the volume occupied by plastic by approximately $\Delta V_P = V_{P1} - V_{P2}$.

Total volume of MSW before the campaign $V_1 = V_{P1} + V_{oth}$, Where V_{oth} – the volume of remaining waste. After the campaign $V_2 = V_{P2} + V_{oth}$ (It is assumed that the volume of other waste will not change). The relative reduction in the total volume of transported waste is $\Delta V = (V_1 - V_2) / V_1$.

Fuel savings are estimated proportionally to the reduction in traffic volume. $\Delta F = F_0 \cdot \Delta V$, Where F_0 – the initial annual consumption of diesel fuel for the collection and removal of solid municipal waste. For the assessment F_0 Data from regional operators is used. For example, in Perm (1 million residents), garbage trucks consume approximately 51,226 liters of diesel fuel per month.[6], which amounts to 614 thousand liters per year. The initial fuel consumption for other cities is scaled depending on the volume of waste.

Reductions in greenhouse gas and pollutant emissions are calculated based on fuel savings. Burning one liter of diesel fuel produces 2.68 kg of CO_2. NO_x emissions from diesel garbage trucks range from 20–50 g/l.[7]For estimates, an average value of 30 g NO_x per 1 liter of fuel is assumed. Emission reduction is calculated accordingly: $\Delta CO_2 = \Delta F \cdot f_{CO_2}$, $\Delta NO_x = \Delta F \cdot f_{NO_x}$, Where f_{CO_2} And f_{NO_X} — emission of carbon dioxide and nitrogen oxides during combustion of 1 liter of diesel fuel.

For each of the selected cities, up-to-date data on the population and waste generation volumes were collected. For example, for Moscow (population 12.6 million), q = 440 kg/person year [5] is adopted, which corresponds to 5.5 million tons of MSW per year, of which up to 0.9 million tons is plastic (16% by weight). In smaller cities (for example, Alchevsk with 110 thousand residents), the total waste volume is approximately 33 thousand tons/year, plastic 5% (1.7 thousand tons). The basic fuel consumption of garbage trucks varies from 8 million liters/year in Moscow to 50 thousand liters/year in Alchevsk (estimated proportional to the amount of MSW). The environmental impact indicators are estimated with an increase in the bulk density of plastic waste from 16 to 22 kg/m³ in all cities (mod-

erate compaction scenario) using the above-described methodology. The results are summarized in Table 1.

An analysis of the obtained results shows that absolute fuel savings and, consequently, the reduction in harmful emissions are proportional to the city's population size and waste volume. The effect is most significant in the largest metropolitan areas: for example, in Moscow, savings reach 662,000 liters of diesel fuel per year, which reduces CO_2 emissions by approximately 1,775 tons per year and NO_x by almost 20 tons per year. For St. Petersburg, annual savings are estimated at 169,000 liters of fuel, reducing CO_2 emissions by 454 tons. A city with a population of over a million can save approximately 33,000-47,000 liters of fuel and reduce CO_2 emissions by 90-125 tons annually thanks to pre-crushing of plastic by residents. In medium-sized and small cities, the absolute figures are more modest: for example, in Alchevsk, fuel savings will amount to approximately 1,300 liters per year, while emissions reductions will amount to 3.5 tons of CO_2 and 0.04 tons of NO_x per year. In relative terms (per capita), the contribution of small cities is comparable to that of large cities; the overall impact in these cities is limited by the small scale of waste generation.

Table 1

Estimated annual transport effect of pre-compacting plastic waste

City	Population, million people	Solid municipal waste generation, thousand tons/year	Fuel economy, thousand liters/year	Reduction of CO2 emissions t/ year	Reduction of NOx emissions, t/ year
Moscow	12.6	5544	662.3	1775	19.9
Saint Petersburg	5.6	3128	169.5	454	5.1
Kazan	1.3	585	46.6	125	1.4
Rostov-on-Don	1.13	452	36.0	97	1.1
Permian	1.0	420	33.4	90	1.0
Donetsk	0.9	315	18.8	50	0.6
Lugansk	0.4	120	7.2	19	0.2
Alchevsk	0.11	33	1.3	3.5	0.04

It's also worth noting that the relative reduction in fuel consumption is approximately 5-8% of the baseline. For example, for a city with a population of 1 million (like Perm), the expected reduction in diesel fuel consumption is approximately 5.5% (33,000 out of 614,000 liters per year). In Moscow, due to the higher proportion of plastic (up to 16% of the mass), the potential is relatively higher – an 8% fuel savings. These figures suggest a significant reduction in transporta-

tion costs and a corresponding reduction in greenhouse and toxic gas emissions, thereby reducing the anthropogenic impact on the environment.

Increasing the bulk density of plastic waste clearly has a positive impact on transport infrastructure. This will reduce the need for container collection, reducing the load on the waste collection fleet (fewer trips and engine hours) and the road network. In the long term, this can slow down equipment wear and tear and reduce maintenance costs. For regional operators, reducing the number of trips also means increased logistics efficiency and lower variable costs (fuel, depreciation, driver salaries, etc.). These savings can be redirected toward improving waste collection infrastructure or recycling programs.

It's important to emphasize that the proposed measure doesn't require large capital investments; it relies solely on public engagement. Information campaigns and public education on simple actions with significant environmental impact are essential. Properly conducted public awareness campaigns can significantly change citizens' waste management behavior. Improving public environmental awareness will also bring collateral benefits: people accustomed to crushing bottles will generally be more responsible in sorting their waste, which increases the efficiency of subsequent recycling.

Adopting this practice nationwide could yield a significant cumulative effect. It is estimated that for Russia's 146 million people, compacting plastic through simple household actions would save approximately 4,895 cubic meters of diesel fuel per year. This is equivalent to the volume of 70 60-ton railway tank cars. In terms of emissions, this equates to a reduction of approximately 13,000 tons of CO_2 and 147 tons of NO_x annually. Even though the transport waste management sector is not the largest source of harmful emissions, the reduction in environmental impact will be significant, especially in cities with stressed environmental conditions.

The results obtained allow us to draw the following conclusions. Pre-crushing plastic containers by the public is a simple measure that yields significant environmental and economic benefits. By reducing the volume of plastic waste in municipal solid waste, the number of garbage truck trips is reduced, resulting in fuel savings (5-8% annually) and a proportional reduction in greenhouse and toxic gas emissions. In large cities, implementing this practice will save hundreds of thousands of liters of diesel fuel annually, reducing carbon dioxide emissions by hundreds of tons. Additional benefits include reducing the burden on waste collection infrastructure, reducing costs for regional operators, and raising environmental awareness among the population. Thus, a campaign to compact plastic waste on a large scale can become an effective element of a municipal solid waste management strategy, bringing tangible benefits to both the environment and the economy.

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杂交牡丹与脊椎动物止血功能的体外关系
BIOFUNCTIONAL RELATIONSHIPS OF HYBRID PEONIES WITH VERTEBRATE HEMOSTASIS IN VITRO

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注释杂交牡丹根提取物含有各种感兴趣的化合物，可作为具有抗凝和抗血栓作用的新型活性药物成分的来源。我们的目标是确定莫斯科国立大学彼得大帝科学教育中心收藏的草本牡丹品种‘Tenderness’和‘Chameleon’的水根提取物的潜在体外抗凝和抗血栓活性。为此，我们研究了杂交牡丹‘Tenderness’和‘Chameleon’的水根提取物的体外抗凝活性。我们评估了测试样品对内在、外在和一般凝血机制的凝血因子活性的影响，以及对纤维蛋白原浓度和纤维蛋白聚合程度变化的影响。‘Tenderness’和‘Chameleon’的水根提取物表现出明显的抗凝活性。提取物对所有研究的凝血参数均有不同程度的影响，在体外表现出抗血栓和抗凝血酶活性，并对各种凝血参数具有统计学显著影响。“涅日诺斯特”品种在降低纤维蛋白聚合度方面略优于“变色龙”。所得数据表明，这些杂交品种的提取物值得进一步研究，以开发用于心血管疾病的功能性药物以及抗血栓药物。

关键词：牡丹根提取物、“柔嫩”品种、“变色龙”品种、抗凝活性、类肝素、抗血栓药物。

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Annotation *Hybrid peony root extracts contain various compounds of interest as a source of new active pharmaceutical ingredients with anticoagulant and antithrombotic effects. Our objective was to determine the potential in vitro anticoagulant and antithrombotic activity of aqueous root extracts of the*

herbaceous peony varieties 'Tenderness' and 'Chameleon' from the collection of the Peter the Great Scientific and Educational Center of Moscow State University. To this end, we studied the anticoagulant activity of aqueous root extracts of the hybrid peonies 'Tenderness' and 'Chameleon' in vitro. We assessed the effects of the test samples on the activity of coagulation factors of the intrinsic, extrinsic, and general coagulation mechanisms, as well as on changes in fibrinogen concentration and the degree of fibrin polymerization. Aqueous root extracts of 'Tenderness' and 'Chameleon' were shown to exhibit pronounced anticoagulant activity. The extracts exert varying degrees of influence on all studied coagulation parameters, demonstrating antithrombotic and antithrombin activity in vitro and exerting statistically significant effects on various blood coagulation parameters. The 'Nezhnost' variety exhibits a slight advantage over 'Chameleon' in reducing the degree of fibrin polymerization. The obtained data allow extracts from these hybrids to be recommended for further study to develop functional drugs for cardiovascular diseases, as well as for the creation of antithrombotic drugs.

***Keywords**: extracts from peony roots, variety 'Tenderness', variety 'Chameleon', anticoagulant activity, heparinoid, antithrombotics.*

***Financing.** The study was carried out in connection with the assignment of the Moscow State University named after M.V. Lomonosov.*

According to botanical taxonomy, peonies are classified in a separate family, Paeoniaceae Rudolph, which includes only one genus: peony (Paeonia L.). The classification within the genus has been repeatedly revised and remains undecided. Peony comprises 33 species (Hong, 2011), which arose through the natural evolution of plants. This genus includes both deciduous shrubs and rhizomatous herbs, the latter of which we commonly call herbaceous peonies. Shrub species are not widely distributed in our country.

During a routine inventory of the peony collection at the Peter the Great Scientific and Educational Center, our attention was drawn to two super-early blooming herbaceous peony varieties: 'Tenderness' and 'Chameleon.' As is well known, all peony species are highly ornamental, and many are used in folk medicine or serve as raw materials for industrial pharmaceuticals.

The relationship between plant and animal components is poorly understood and is of great interest both for the rational use of natural resources, environmental protection, and from a medical perspective aimed at preserving the health of humans and animals. One promising and important area is the study of peony consortia, which represent a highly complex and diverse natural phenomenon. There is a need for a clearer interpretation of this concept and a classification of consortia for their detailed study. As is known, the normal functioning of the hemostatic system depends on the regulatory interactions of the coagulation and anticoagulation sys-

tems of the blood, which are part of the general hemostatic system of mammals. Disruptions in the functioning of this system lead to various diseases, including life-threatening conditions such as thrombosis or uncontrolled bleeding (Lyapina et al., 2012) Blood coagulation is an important biochemical process aimed at the formation and subsequent lysis of fibrin clots (Berkovsky et al., 2015).

To date, various medications have been developed that prevent the formation of blood clots or promote their dissolution. These include thrombolytic (fibrinolytic) agents (alteplase, tenecteplase, urokinase, and others) and various anticoagulants (glycosaminoglycans, flavonoids, etc.) and their analogs. The use of these drugs is associated with a number of negative side effects, including the development of immunogenicity and systemic fibrinolysis (Ling Hua Wei et al., 2019). The search for alternative drugs, including plant extracts with anticoagulant and antithrombotic effects, remains relevant to this day.

According to published data, extracts from peony roots contain heparin-type anticoagulants that exhibit sufficient activity in the bloodstream (Lyapina M.G. et al., 2016; Zhang, 2016; Wang et al., 2023), which are capable of preventing fibrin formation and its subsequent transformation into a thrombus. This suggests that peonies may have applications, for example, as active pharmaceutical ingredients for the development of drugs for the treatment of thrombosis or for the development of functional preventive agents for cardiovascular diseases.

The lactiflora peony is represented in cultivation by many garden forms and hybrids, one of which is the 'Tenderness' variety. In Chinese medicine, the biological activity of dried, parboiled, and peeled roots of this peony is well known. It has long been used in folk medicine for diseases of the central nervous system, posthemorrhagic anemia, retinal hemorrhage, infectious hepatitis, cancer, diabetes, nephritis, hypertension, loss of appetite, spastic colitis, gastralgia, and delayed lactation. In Tibetan medicine, it is used for tuberculosis, bronchitis, pneumonia, colds, and many other ailments. Analysis of the chemical composition of the roots revealed the presence of monoterpenoids (paeoniflorin, paeoniflorigenin, albiflorin, oxypeoniflorin, 6'-O-benzoylpeoniflorin), benzoic acid, a steroid (β-sitosterol), tannins (penta-O-galloyl-β-D-glucose), carbohydrates and related compounds (starch, pectin, etc.), triterpenoids, quinones, essential oils, traces of coumarins and alkaloids, flavonoids (peonidin, peonin, peonoside, astragalin). The petals contain pyrethrin, and the leaves contain the flavonoid kaempferol. According to the requirements of the Chinese Pharmacopoeia (2000), the content of paeoniflorin ($C_{23}H_{28}O_{11}$) in the roots of the milky-flowered peony should not be less than 0.8% (Shreter A.I. et al., 2004).

When using high-molecular-weight heparins derived from porcine intestinal mucosa or bovine lungs, patients develop a number of serious side effects associated with high levels of anticoagulant in the blood, which can cause bleeding

or a “rebound effect.” Therefore, studying low-molecular-weight anticoagulant components from the roots of hybrid peonies, which exhibit enhanced anticoagulant activity by crossing two or more peony species with anticoagulant properties, is promising. **Previously, work was carried out to identify heparinoids in tree and herbaceous peonies that have anticoagulant and fibrin depolymerization activity** (Zhang, 2016; Wang et al., 2023). Based on these heparinoids, it is possible to create medicinal preparations.

The aim of this work is to determine the potential anticoagulant and antithrombotic activity in vitro of aqueous extracts of peony roots: 1)’Tenderness’, 2)’Chameleon’. Low molecular weight heparin (LMWH) from Celsus (USA) was used for comparison.

To evaluate the pharmacological activity of objects in vitro, the following coagulation parameters were selected (Lyapina et al., 2012): anticoagulant activity of blood plasma (according to tests of activated partial thromboplastin time (APTT), thrombin time (TT), prothrombin time (PT); degree of fibrin polymerization; fibrinogen concentration.

Materials and methods of research

The objects of study are aqueous extracts obtained from the roots of peonies of the following species:1)’Tenderness’*, 2)* ‘Chameleon’3) commercial LMWH of animal origin. KoPeony seeds were collected in the Botanical Garden of Moscow State University between August and September 2024 and in spring (March) 2025.

Method for obtaining aqueous extracts of peonies

To obtain extracts, peony roots were washed several times with distilled water, then dried for 24 hours at 40°C to a residual moisture content of 10-15% and ground to a particle size of no more than 2.5 mm. Powdered root samples were then successively extracted with ethyl alcohol (5%, Russia) and then with distilled water to obtain aqueous extracts. The aqueous extracts were centrifuged at 2,000-3,000 rpm for 20-30 minutes. The supernatant was separated, frozen at a temperature no higher than -18°C, and freeze-dried. The lyophilized aqueous root extracts were a powdery mass of varying yellow color. The samples were then stored at 2-8°C.

Methods for assessing coagulation parameters in vitro

To assess the influence of objects on hemostasis parameters in vitro, commercially available reference normal pooled rat blood plasma with hemostasis parameters within the normal range was used.

Preparation of stock solutions and model mixtures of test objects.

A sample of the test objects, weighed to an accuracy of 0.001 g, was dissolved in distilled water at a rate of 100 μg of the substance per 1 ml of solution, resulting in stock solutions with a test object concentration of 1 mg/10 ml. Then, using a series of serial dilutions in distilled water, stock solutions with concentrations

ranging from 0.001 mg/ml to 0.1 mg/ml were prepared. To conduct the study, stock solutions with concentrations of test objects No. 4 - 0.001, No. 3 - 0.01, No. 2 - 0.1, and No. 1 - 1 mg/ml were used as test solutions. 0.05 ml of the studied extracts were added to 0.2 ml of plasma, incubated at 37°C for 10-16 minutes, after which determinations were carried out according to the methods.

Model mixtures of objects with blood plasma were used for further analysis to determine hemostasis parameters (thrombin time - TT, prothrombin time - PT and activated partial thromboplastin time (APTT) using the reagent kits "Technology-standard", Russia). These parameters were studied on a semi-automatic coagulation analyzer Astra-2-01 (Russia).

The study of the influence of the test objects on the concentration of fibrinogen was carried out using the Bidwell method, a detailed description of which is available in the methodological manual (Lyapina et al., 2012). The functional analysis for determining fibrinogen concentration is based on the formation of a fibrin clot: the concentration of fibrinogen in rat blood plasma is measured after adding an excess of thrombin to it. The method for determining fibrin polymerization (in %) on unstabilized fibrin (with weak hydrogen bonds) is based on the ability of the test substances to delay or enhance fibrin formation using a test for determining fibrin polymerization on unstabilized fibrin. To determine the degree of fibrin polymerization, unstabilized fibrin films were prepared (Lyapina et al., 2012). Blood plasma from control and experimental rats was applied to the prepared films in an amount of 0.05 ml in the presence of an equal amount of 0.3% EACA. Incubated at 37°C for 2 hours, after which the lysis zones were measured. 100% fibrin polymerization was taken as the control, lysis zones - A. In the experiment, lysis zones B. There is an inverse proportional relationship between the lysis zones and the % of fibrin polymerization, which was calculated according to the formula: % polymerization in the test sample (B) = (A: B) x 100%.

Data processing

Statistical analysis of the data was performed using the Statistic 8 statistical software package (StatSoft Inc., USA). NormalityData distributions were assessed using the Shapiro-Wilk test, and pairwise comparisons of independent groups were assessed using the nonparametric Mann-Whitney test. Differences were considered statistically significant at $p < 0.05$.

Results

Blood coagulation and fibrinolysis are multistage processes. In vitro studies assessed the effects of extracts on a number of parameters characterizing hemostasis and fibrin polymerization.

The roots of the hybrid peonies 'Tenderness' and 'Chameleon' were used in this study. Anticoagulants were obtained at a concentration of 0.5-0.6 mg, dis-

solved in 0.5 ml. A commercial LMWH preparation from Celsus (USA) was used for comparison. All anticoagulants were dissolved in 0.85% saline.

As can be seen from Table 1, peony extracts demonstrated a dependence of their anticoagulant effect—based on APTT and PT—on the concentration used in the sample. According to the APTT test, 'Chameleon' demonstrated a higher effect than 'Tenderness'. No clear concentration dependence was revealed for the fibrin polymerization test, as both peonies demonstrated virtually identical reductions in the degree of fibrin polymerization (by 24-20%). However, the 'Tenderness' peony had a slight advantage over the 'Chameleon' peony in reducing the degree of polymerization.

Table 1.

Dose-dependence of the effects of extracts from peonies 'Tenderness' and 'Chameleon' according to the tests of APTT, PT and degree of fibrin polymerization

The indicators studied	Concentrations (mcg/ml)	Peony 'Chameleon'	Peony 'Tenderness'
APTT	10-1	46.1	40.4
Control with NaCl - 33.0	10-2	45.0	40.0
	10-3	40.3	38.7
	10-4	35.3	34.3
PV	10--1	31.7	32.3
Control with 0.85% NaCl - 28.5	10-2	29.9	32.0
	10-3	29.5	29.1
	10-4	28.9	29.0
Degree of fibrin	10-1	83.6	76
polymerization	10-2	83	80
Control with NaCl – 100%	10-3	83	80

Note for Tables 1 and 2: * $p < 0.05$ – significant difference from control (100%). M ± m – mean ± standard error of the mean.

Subsequently, the effect of peony extracts and, for comparison, the commercial LMWH preparation on coagulation time intervals, fibrinogen concentration, and plasma fibrin depolymerization activity was studied (Table 2).

Table 2.

The effect of extracts from peonies 'Tenderness' and 'Chameleon' at a concentration of 10-1 mg/ml on activated partial thromboplastin time (APTT), thrombin time (TT), prothrombin time (PT), fibrin depolymerization activity (FDPA) and the degree of fibrin polymerization

The roots under study	APTT, sec	TV, sec	PV, sec	Fibrinogen concentration (mg%)	FDPA, mm2	Fibrin polymerization %
From the peony 'Tenderness'	40.4±1.3*	21.4±0.9*	32.3±1.0*	248.3±10.2*	22.3±0.8*	76±4.4*
From the peony 'Chameleon'	46.1±1.1*	20.3±1.0	31.7±1.0	286±7.0	19.0±2.1	83.6±4.9*
NMG «Celsus»	38.2±1.0*	19.0±0.5	30±0.5	290±9 6	15.1±0.3	100±1.2
Control -0.85% NaCl	30.0±1.0	18.3±0.8	28.5±0.8	341±8.5	14.3±0.5	100±0.2

As shown in Table 2, root extracts from the 'Tenderness' and 'Chameleon' peonies, as well as commercial LMWH, influenced the intrinsic blood coagulation mechanism, as evidenced by a significant increase in APTT compared to the control. It should be noted that 'Tenderness' peony, unlike commercial LMWH and 'Chameleon', increased PT, indicating its effect on the extrinsic coagulation pathway. It also exhibited anti-factor IIa activity, increasing TI, and significantly reduced fibrinogen concentration.

Discussion

Herbaceous peony 'Tenderness' The earliest-blooming hybrid. It blooms at the same time as species peonies, sometimes right during spring frosts and snowfalls. The flower shape is simple, the petals are usually white (in some years, slightly pinkish). The diameter of the flower is 14 cm. The bush during budding and flowering is semi-spreading, reaching a height of 75-80 cm. The foliage is bluish-gray, very large. The flower has a pleasant fragrance. This is a species peony (Paeonia mlokosewitschii Lomakin). obtained by M.S. Uspenskaya from irradiated seeds and registered in 2006 in Russia (patent 3249, 2006).

The early-flowering herbaceous peony 'Chameleon' was also selected by M.S. Uspenskaya in the Moscow State University Botanical Garden and is a natural hybrid between P. Mlokosevichii and P. caucasica. Not to be confused with the hybrid peony (P. tenuifolia L.), the cultivar 'Chameleon', which was registered in 2001 by William Krekler-Roy G. Klehm, a member of the board of directors of the American Peony Society (APS) in the USA. (Myron D. Bigger et al., 1962, p. 38).

The varieties described above, as we have found, have anticoagulant properties and affect the internal mechanism of blood clotting. 'Tenderness', in addition, it affects the external mechanism of blood clotting, blocking factors of this pathway,

for example, tissue factor, which is involved in the formation of increased blood clotting. It is noteworthy that peony 'Tenderness' reduces the activity of the main blood coagulant, thrombin. Fibrinogen, a protein circulating in the bloodstream (molecular weight 340 kDa), is the only substrate for the formation of a fibrin blood clot (thrombus) (Lyapina et al., 2012). In addition to the hemostatic function, fibrinogen is involved in the regeneration of damaged areas of the skin, mucous membranes and in fibrinolysis to dissolve blood clots during the restoration of damaged areas in order to normalize blood supply Components of peony root extracts in vitro have little effect on the time of fibrin clot formation and reduce the concentration of fibrinogen in blood plasma by 20-24% in the concentration range of 10 to 100 μg/ml.

When comparing the obtained effects for various ions with commercial LMWH, it should be noted that the polysaccharide components contained mainly in the aqueous part of the roots of the peony 'Tenderness' have a pronounced effect on the anticoagulant activity according to the APTT test in vitro.

Conclusion

An in vitro study examined the antithrombotic activity of aqueous extracts from the roots of the herbaceous perennial peonies 'Tenderness' and 'Chameleon.' The effects of aqueous extracts of these peony species on individual hemostatic parameters (antifactor II activity, fibrin polymerization, and fibrinogen concentration) have not previously been studied. Fractions isolated from the roots of these peonies exhibit pronounced antithrombotic activity and exert varying effects on all studied blood coagulation parameters, exhibiting anticoagulant and fibrin-depolymerizing effects, as well as reducing fibrin polymerization. Of the two peony species, the 'Tenderness' peony exhibited the greatest effect.

Extracts we isolated from the roots of the herbaceous peonies 'Tenderness' and 'Chameleon' did not affect the studied fibrinogen concentration parameters. These data allow us to recommend aqueous extracts from the roots of these peonies for further study, including in vivo studies, for example, to create an antithrombotic drug or develop functional foods for cardiovascular diseases.

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贝加尔湖水域和沿岸带的大鸬鹚Phalacrocorax carbo：种群密度、数量、分布和生态特征

GREAT CORMORANT *PHALACROCORAX CARBO* IN THE WATERS AND COASTAL ZONE OF LAKE BAIKAL: POPULATION DENSITY, ABUNDANCE, DISTRIBUTION, AND ECOLOGICAL CHARACTERISTICS

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注释：基于2025年的研究，本文展示了贝加尔湖水域和沿岸地区大鸬鹚种群数量和分布的变化。强劲且常伴有暴风雨的西北风导致鸟类聚集，主要集中在湖的东岸。东岸的种群密度为15.7只/平方公里，而西岸为1.7只/平方公里，即西岸的9.2倍。同时，值得注意的是，东岸的自然生产力较低，尽管该物种在那里形成了大量的觅食、筑巢和飞行前的聚集。2025年贝加尔湖大鸬鹚的总种群密度为9.6只/平方公里，总数为52,380只。在色楞格河三角洲（卡尔加）边缘，该物种飞行前聚集的数量有所减少，降至3.05万只，而去年该地记录的鸟类数量超过7.3万只。主要原因很可能与2024年观察到的邻近地区鸟类迁徙减少有关。与以往一样，该物种最大的聚居地位于赤乌尔奎斯基湾。已确定巴尔古津湾没有该物种的大型聚居地，因为该湾入口宽阔，经常受到贝加尔湖主要风暴风的影响。然而，在海湾的最尽头，在中等风力下，可以形成大型的觅食聚集地，数量从200只到2700只不等。贝加尔湖的大鸬鹚仍然是湖面上的主要鸟类，在8月初（贝加尔湖鸟类迁徙强度急剧下降的时期），其数量占湖面上所有滨鸟和水禽总数的36.4%至77.0%。

关键词：贝加尔湖，大鸬鹚，分布，种群密度，丰度，繁殖前聚集，生态学。

Annotation*. Based on the 2025 studies, changes in the population size and distribution of the Great Cormorant in the waters and coastal area of Lake Baikal*

are shown. Strong, often stormy northwestern winds led to a concentration of birds, primarily on the eastern coast of the lake. Their population density there was 15.7 birds/km², compared to the western shore – 1.7 birds/km², i.e., 9.2 times higher. At the same time, it should be noted that the natural productivity of the eastern shore is lower, although very large feeding, nesting, and pre-flying gatherings of birds of this species form there. The overall population density of the great cormorant on Lake Baikal in 2025 was 9.6 birds/km², with a total number of 52,380 birds. A decrease in the number of pre-flight gatherings of the species along the edge of the delta of the Selenga River (karga) has been noted, down to 30.5 thousand individuals, although last year more than 73.0 thousand birds were recorded here. The main reason for this is most likely associated with the absence of birds arriving from adjacent areas, which was observed in 2024. As before, the largest colonies of the species are located in the Chivyrkuisky Bay. It has been established that there are no large colonies of the species in the Barguzinsky Bay, which has a wide entrance and is constantly exposed to the main storm winds of Lake Baikal. However, at the very end of the bay, under moderate winds, large feeding aggregations of the species can form – ranging from 200 to 2,700 birds. The Great Cormorant on Lake Baikal remains the dominant bird species, accounting for 36.4% to 77.0% of the total number of shorebirds and waterfowl present directly on the lake in early August (a period of a sharp decline in the intensity of bird migrations on Lake Baikal).

Keywords: *Lake Baikal, Great Cormorant, distribution, population density, abundance, pre-breeding gatherings, ecology.*

Introduction. Due to the current pronounced climate warming, the optimal range of the Great Cormorant, *Phalacrocorax carbo*, has shifted far north, and its population at the northern boundary has now sharply increased. The extreme points of the species' sightings, where previously only occasional occurrences were recorded, have reached Central Yakutia. At the same time, the ecological characteristics of the species in the new areas of its range remain unknown. This issue has not been resolved even in the specialized monograph on this species (Yelaev et al., 2024). Our data on the characteristics of the great cormorant's colonization of a new part of its range at its northern boundary are undoubtedly of interest. The work was carried out on Lake Baikal (2018–2025), where a relatively independent large population of the species has currently formed, reaching a high number. It should be noted that each year of research has brought new adjustments to our knowledge of this species. First and foremost, this concerns the features of its distribution across Lake Baikal. To date, a high dependence of this species on strong storm winds (Mel'nikov, 2023; Mel'nikov et al., 2023), as well as on the water level in Lake Baikal and its inflowing rivers and the distribution of food re-

sources, has been established (Mel'nikov, 2024; Mel'nikov et al., 2023). In recent years, a large pre-breeding aggregation of the species has been forming along the edge of the Selenga River delta, which, judging by its numbers, unites not only the birds from the lake but, in some years, also from the surrounding areas. All of these issues require special consideration and discussion. In this case, we examine the characteristics of the species' biology and ecology in 2025, which is distinguished from previous years by a strong prevalence of northwestern winds and a high water level in the major rivers flowing into Lake Baikal.

Area of work, material, and methodology. In 2025, a comprehensive survey of the Baikal Lake water area and its coastal zone was carried out, and a census of all species of shorebirds and waterfowl was conducted. The work was carried out using the research vessel "Professor A.A. Treskov." Lake Baikal is characterized by unique conditions that make it a unique ecosystem, formed under the conditions of increased seismicity of the area – the Baikal rift zone. The location of the lake in the central region of Inner Asia determines many of its climatic characteristics. First of all, they are influenced by the orographic barriers of this region (Naprasnikov, 2003; Berezhnykh et al., 2012; Latysheva et al., 2013).

The main air currents determining the climatic features of Eastern Siberia are associated with northwestern (North Atlantic) and southeastern (Pacific monsoon) opposing flows, rich in oceanic moisture. A significant weakening of the northwesterly flow disrupted the East Asian hydrological system (Berezhnykh et al., 2012). It is well known that the advection zone of westerly and eastern air masses in Inner Asia determines the locations of heavy precipitation (the Siberian frontal zone) (Koshelenko, 1983; Naprasnikov, 2003; Levi et al., 2004; Shimaraev, Starygina, 2010; Zherebtsov et al., 2011; Berezhnykh et al., 2012; Latysheva et al., 2013; Latysheva et al., 2022). Due to the shift of this zone to the peak of climate warming at the level of Southern Yakutia, Eastern Siberia experienced very severe and widespread droughts, followed by prolonged dry periods (Koshelenko, 1983; Levi et al., 2004; Zherebtsov et al., 2011; Berezhnykh et al., 2012). This is why there was a mass migration of birds from the southern regions of Asia to the northern boundaries of their ranges.

Due to the complex climatic conditions and the large expanse of the Lake Baikal basin, three regions are distinguished within it: the South-Baikal, Central-Baikal, and North-Baikal climatic districts. From south to north, the climate becomes harsher—the climate severity coefficient (according to Tsenker) increases from 62 to 64. The mountainous surroundings of the lake, on one hand, reduce the impact of external conditions on the basin's climate, and on the other hand, limit the climatic influence of the lake itself on the surrounding areas (Baikal…, 1993). The actual influence of Lake Baikal on the coastal climate can be traced up to the ridges of the surrounding mountains, while in the river valleys it is recorded at weath-

er stations 40.0 km from the coast (Galaziy, 2012; Shimaraev, Starygina, 2010). Due to these features, the lake is characterized by a milder maritime climate and a warm, prolonged autumn, favorable for birds to stop and rest (Baikal…, 1993).

The main focus was on surveying the shores of Lake Baikal, as birds are very rarely found in the open lake. They were recorded here when crossing the lake from one shore to the other while searching for suitable places to stop during strong storms. Observations were made using 12x and 35x binoculars and a 75x spotting scope throughout the entire period of the vessel's journey along the shore. The coastal strip from 2.0 to 3.0 km was surveyed (500 m on one side for a detailed inspection of the shore, and 1500 m on the other side of the Lake Baikal water area). According to its indicators, the count was practically absolute (Mel'nikov, 2022). Sightings of birds at long distances during this time were rare and were observed only when crossing Lake Baikal from one shore to the other (3 times in 17 crossings) before the storm.

The calculation of the average bird population density was carried out based on general recommendations for bird surveys using the transect method (Ravkin, Chelintsev, 1990). The width of the survey strip was determined based on the geometric mean of all sighting distances of the Great Cormorant, separately for sitting and flying birds (Ravkin, Chelintsev, 1990; Mel'nikov, 2022). The proposed formulas for calculating bird population density include a conversion factor that compensates for differences in the width of the survey strip and the area of the surveyed territory (in the numerator), equal to 50 (instead of 500). Since weather conditions and the length of the daytime route could vary significantly, the population density of the Great Cormorant for each route was calculated separately. The average bird population density across Lake Baikal was determined as a weighted average based on the lengths of routes with varying bird population densities.

The movement speed of the research vessel, depending on the strength of storms and the nature of the coastline, ranged from 16 to 22 km/h. It was higher in calm seas and decreased in rough waves. It should be noted that in rough seas the passage of birds of this species increases. The Great Cormorant sits very low on the water, and already at a distance of about 100 meters only the head and neck of the bird are visible, which against the dark waves sharply reduces the possibility of detecting it. The total length of the survey routes during the work period amounted to 1,850 km.

Results and Discussion. Only two groups of stations are distinguished in Baikal itself: the open deep-water part of Baikal (which covers the part of the lake with depths greater than 10.0 m) and the coastal shallows with the adjacent shoreline (Skryabin, 1975; Melnikov, 2025). The second group of stations includes three habitats (stations): a) the coastal open waters of Baikal – a strip of shallows with depths less than 10.0 m around the deeper areas of the lake, poor in plant

food but rich in animal food; b) shallow shores and bays in terms of bird habitats, resembling lakes or salt flats; c) coastal areas with rocky, steep cliffs descending sharply to the water (Skryabin, 1975; Melnikov, 2025). The specificity of such sites is evident – they are favorable only for birds that obtain food by diving.

The distribution of the Great Cormorant across the waters and coastal zone of Lake Baikal is very uneven. Areas with very high bird density and population stand out clearly. As a rule, they are located in places of mass bird nesting – these are the deltas of large rivers, large bays, and the Maloye More Strait. At the same time, there are no large bird nesting sites in the Barguzin Bay. The main reason for this is the very wide entrance. Here, with any wind direction, there is strong wave activity, and in terms of bird habitats, it differs little from the main shore of the lake. At the same time, with relatively calm waters, large feeding gatherings of birds form here—from 200 to 2,700 birds on August 9, 2025. The size of these feeding gatherings can vary greatly and clearly depends on the abundance of fish in different parts of Lake Baikal. The most common gatherings range from 40-50 to 500 birds, although there are known gatherings of up to 3,000 birds (Sosnovka Bay, August 2018) and 8,000 individuals (entrance to Chivyrkuysky Bay, August 2023).

In recent years, marked by high water levels in the estuaries of major rivers at the end of summer, birds have begun forming large pre-flight gatherings of Great Cormorants along the edge of the Selenga River delta – the karga (a sandbank separating shallow bays from the deeper part of Lake Baikal). Here, not only birds that fly and nest on Baikal gather, but also those arriving from neighboring areas, particularly from the cascade of Angara reservoirs (a well-defined migration route near the city of Irkutsk). In such years, the number of birds along the Selenga Delta sharply increases – up to 73,000 or more (Melnikov, 2024). At the same time, in 2025, birds nesting in Baikal gathered here – 30,531 individuals. This is also highlighted by a sharp decrease in non-breeding birds in the species' nesting colonies. It should be noted that the first pre-migration gatherings are formed by non-breeding birds (young) of the previous year, adult birds with an unsuccessful breeding season, and young from early broods that managed to take flight.

The highest population density (though not the total number) in 2025 was characteristic of the Chivyrkuysky Bay – 42.3 birds/km². It was noticeably lower in the delta of the Selenga River, which is associated with its large area, about 30.5 birds/km². Despite the large number of colonies located on the islands and capes of the Maloye More Strait, the population density of the great cormorant here was relatively low, about 4.6 birds/km². All colonies were small in number, with only Shargadagon Island (376 birds) and Bolshoy Toynik Island (237 birds) having a higher abundance of birds. At the same time, it should be noted that on the latter island, the population of the Mongolian gull *Larus (vegae) mongolicus* was high

– 900 birds. In other areas of Lake Baikal, the population density of the Great Cormorant was low, ranging from 0.3 to 1.8 birds/km².

The population density and bird numbers were fairly high in the North-Baikal climatic district – 3.7 birds/km². Undoubtedly, this is due to the fact that the Chivyrkuisky Bay is part of this climatic district. The highest population density of the Great Cormorant is found in the Middle-Baikal climatic district, which includes two large nesting concentration areas for this species (the Selenga River delta and the Maloye More Strait) – 5.3 birds/km². It covers areas with relatively shallow depths and includes the main part of the district. Here are located the sites most suitable for nesting of the Great Cormorant (rocky islands and large capes among shallow waters), as well as areas for the formation of large feeding grounds (Proval Bay and Posolsky Sor) and pre-flying gatherings of the species (along the edge of the Selenga River delta). The lowest population density and species abundance are characteristic of the South Baikal climatic district – 0.7 birds/km². Within this area, there are no colonies of the Great Cormorant, nor locations of its mass feeding concentrations. However, individual pairs of this species may nest in colonies of the Mongolian gull.

It is well known that more favorable conditions for the habitation of the Great Cormorant are formed on the eastern shore of Lake Baikal. Here, the river mouths flowing into Baikal have a more lowland character, and the sediment deposition cones are more pronounced, providing higher productivity of sedimentation areas. As a result, a larger number of birds are found here, in particular the Red-Breasted Merganser *Mergus serrator*. All major bays of Lake Baikal are located on the eastern shore – the Barguzin and Chivyrkuisky bays, the delta of the Selenga River with the Posolsky Sor and Proval Bay, as well as other smaller bays that play a significant role in the lives of birds. Therefore, the population density of the Great Cormorant on the eastern shore is much higher – 15.7 birds/km² compared to the western coast, where it is 1.7 birds/km². At the same time, it should be borne in mind that during strong winds many birds take shelter in the bays of the eastern shore, and therefore the observed density of their population does not reflect its true productivity. This characteristic is also typical for the 2025 season – strong northwesterly winds led to an increased concentration of birds in the bays of the eastern shore, and this was also facilitated by the formation of a large pre-migration aggregation of birds in the Selenga River delta. The overall population density of the Great Cormorant on Lake Baikal in 2025 was 9.6 birds/km².

Of particular interest is the discovery of a large pre-breeding aggregation of Great Cormorants in the delta of the Selenge River. It has formed only in the past two years and coincides with a period of increased water levels in the delta. Long-term studies in this region show that during such periods its productivity sharply increases due to the flooding of the middle delta and the significant expansion

of flooded meadows. The extensive area of rich shallow waters greatly increases the number of sites favorable for carp fish feeding. This attracts many species of fish-eating birds here for feeding, whose numbers increase sharply but temporarily. This is precisely what causes the formation of a large pre-flight congregation of the Great Cormorant, whose feeding intensity increases in connection with the preparation for a long migratory flight to intermediate stopover sites for rest (from 500 km and more) in northeastern China. The main wintering areas of this species are located in Southeast Asia.

The very process of forming such aggregations requires special study. They are known for many species of shorebirds and waterfowl and have been noted by us previously (Mel'nikov, 2023). It should be noted that before the start of the pre-flight aggregation in previous years, in mid-summer we observed flocks of birds freely moving across Lake Baikal and forming large feeding aggregations in convenient areas. A large number of non-breeding birds were also noted in colonies of the Great Cormorant, which was particularly emphasized by many authors studying this species (Ananin et al., 2018a; 2018b; Fefelov et al., 2018). However, in 2024, there were significantly fewer such birds in the colonies, but large feeding aggregations were observed in various parts of Lake Baikal, and a large pre-migration gathering of more than 73,000 birds was found in the Selenga Delta (Melnikov, Nikolaev, 2024). It should be noted that at the end of July near the city of Irkutsk (Irkutsk Reservoir), large migrating flocks of this species were observed—up to 300 individuals, flying towards Lake Baikal. Bird migration was also noted in the area of the Ushkany Islands (birds were flying from the valleys of the Upper Angara and Kichera rivers). This undoubtedly indicates that birds from a vast region adjacent to Lake Baikal gathered at the coast of the Selenga River delta.

In 2025, the water level at the mouth of the Selenga River was even higher. The western section of the kargi was completely submerged, while on the eastern section we recorded over 30,000 birds (only the highest part of the kargi ridge rose above the water). Counting was difficult due to the high density of birds, which were obscuring each other. At the same time, non-breeding birds were almost absent on the colonies, and their numbers at the nesting sites were noticeably lower. No flocks in transit were recorded during the survey, although they had been observed here multiple times before. Most likely, this aggregation was formed by local (Baikal) birds.

Conclusion. As a result of fieldwork in August 2025 using the research vessel "Professor A.A. Treskov," a count of the Great Cormorant population was conducted in the water area and coastal zone of Lake Baikal. Based on long-term observations, the majority of the birds remain along the shoreline (accounting strip about 3.0 km), and beyond it, they are very rarely encountered. As before, most

birds were recorded along the eastern coast. However, it should be borne in mind that weather factors – the direction and strength of the wind – contributed to the accumulation of birds of this species here, while its natural productivity was undoubtedly lower. A sharp decrease in birds was noted in the pre-flight gathering of the Great Cormorant along the edge of the Selenga River delta (karga). In early August 2025, 30.5 thousand individuals of the Great Cormorant were recorded here. This fact is related to the absence of birds arriving from the adjacent areas. The overall decline in the number of this species in the colonies, due to the absence of non-breeding birds that were common in previous survey periods, indicates that most likely all the Baikal birds preparing for departure had gathered in this congregation.

Their total number was 52,380 birds, i.e., it was at the level of previous years, and the increase in the species' abundance in 2024 was due to the formation of a large pre-departure aggregation consisting of birds from the surrounding areas. The great cormorant on Lake Baikal remains the dominant species, accounting for 36.4% to 77.0% of the total population of shorebirds and waterfowl present directly on the lake at this time.

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使用定制的 3D 打印股骨块和扩大的内侧脊治疗阿拉拜犬的医源性内侧髌骨脱位
TREATMENT OF IATROGENIC MEDIAL PATELLAR LUXATION IN AN ALABAI DOG USING CUSTOM 3D-PRINTED FEMORAL BLOCK WITH AN ENLARGED MEDIAL RIDGE

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注释：本文介绍了一例成功治疗医源性髌骨脱位的临床病例，该病例采用胫骨平台平整截骨术（TPLO）结合头外侧关节切开术进行胫骨矫正截骨术。治疗包括设计、制作和植入钛合金股骨滑车假体，该假体内侧脊增大，以防止髌骨内侧移位。

关键词：3D建模、髋关节置换、TPLO（胫骨平台平整截骨术）、前交叉韧带断裂、髌骨内侧脱位、3D打印、医源性髌骨脱位、膝关节置换、植入物打印。

Annotation. *A successful clinical case of iatrogenic patellar dislocation developed after corrective osteotomy of the tibia using the TPLO (Tibial Plateau Leveling Osteotomy) method with craniolateral arthrotomy is described. The treatment included the design, fabrication, and implantation of a titanium femoral trochlear prosthesis with an enlarged medial ridge to prevent medial patellar displacement.*

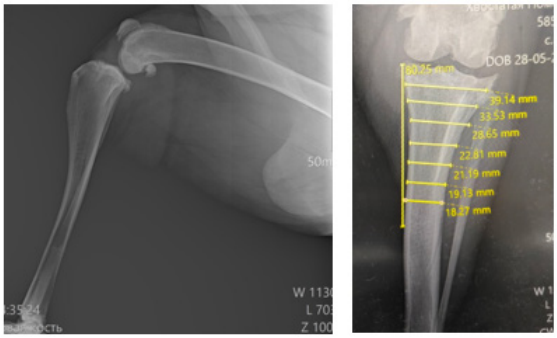
Keywords: *3D modeling, hip joint replacement, TPLO (Tibial Plateau Leveling Osteotomy), anterior cruciate ligament rupture, medial patellar dislocation, 3D printing, iatrogenic patellar dislocation, knee replacement, implant printing.*

1. Initial admission with anterior cruciate ligament rupture.

A 5-year-old male alabai named Bai, weighing 58 kg, was admitted to a third-party veterinary clinic complaining of lameness in his right hind limb for two months. A ruptured anterior cruciate ligament (ACL) and early stages of osteoarthritis of the right knee were diagnosed.

A corrective osteotomy using the TPLO (Tibial Plateau Leveling Osteotomy) method with a craniolateral arthrotomy was performed to revise the menisci. The revision revealed a tear in the caudal horn of the medial meniscus, and the damaged portion was removed. The joint capsule was sutured with Polyglycolide USP 2/0, and vertical duplication of the tensor fasciae latae was performed with Polydioxanone USP 1.

As a result of the surgery, the tibial plateau angle decreased from 24.4 to 6.7 degrees, which is a good result. However, due to errors in surgical technique, the cranial portion of the proximal tibia cut did not contact the tibial crest, causing caudal displacement of the proximal tibia cut and internal rotation of the proximal cut.



Photos 1 and 2. *X-rays before corrective osteotomy of the tibia. Unfortunately, no postoperative images remain.*

2. Complications after TPLO.

Within 10 days after the surgery, improvements in lameness were noted: the lameness grade decreased from 3 on the Osteosynthesis Association scale to 2. On the 11th day, Bai spontaneously lost weight on the operated limb. An orthopedic examination revealed a medial patellar dislocation, after which Bai was referred to our clinic for a second opinion.

Photo 3. *Support with the fingertips on the right pelvic limb for medial patellar dislocation*

3. Repeated duplication of the tensor fascia lata muscle.

Due to the minor rotational deformity of the tibia after the operation, we hypothesized that the myogenic component and/or failure of the internal sutures after the craniolateral approach to the knee joint are the cause of the medial patellar dislocation.

The first stage was a repeat arthrotomy with removal of previous sutures and application of a new vertical duplication with stronger threads (Polypropylene USP 2), medial release of soft tissues.

During the first seven days after the surgery, Bay's gait began to improve, but on the eighth day, his owners again complained of a spontaneous deterioration in his gait: his lameness had worsened. Examination revealed a recurrence of medial patellar dislocation.

4. Fabello-tibial suture and custom knee orthosis.

After a repeated recurrence of patellar dislocation, a decision was made to apply an antirotational suture (fabellotibial suture) using a modified technique: instead of fixation to the fabellofemoral ligament at the proximolateral point, the implant is secured between two cortical screws screwed into the lateral condyle of the femur.

To prevent recurrence, a custom-made knee brace was designed and manufactured by a third-party bioengineer specializing in veterinary braces. Wearing the brace for a month was intended to maintain the correct position of the pelvic limb muscles and the correct position of the patella within the femur.

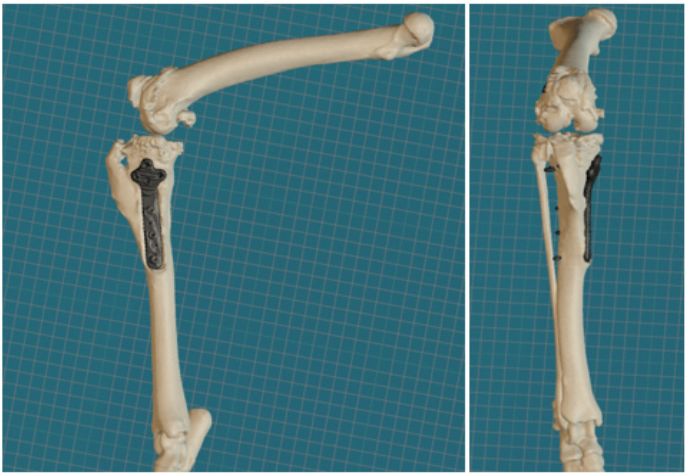
Photo 4,5. *Custom orthosis for fixing the patella in the correct position*

For a month after the surgery, Bai wore the brace constantly during the day, removing it at night. We achieved significant improvement in his lameness (the residual initial lameness was likely related to knee osteoarthritis). One and a half months after the surgery, Bai began limping again, and the owners returned for a follow-up appointment two weeks later.

A recurrence of medial patellar dislocation was detected.

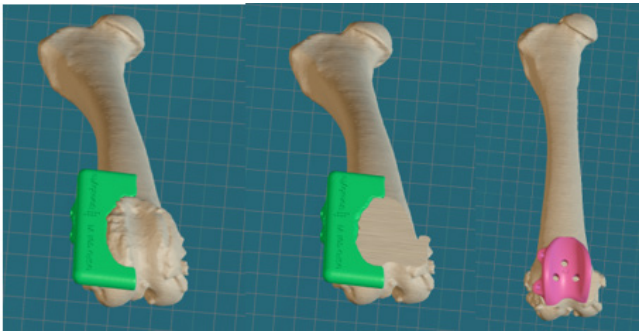
5. Custom 3D modeling of a femoral block prosthesis with an enlarged medial ridge for the treatment of medial patellar dislocation.

To plan further treatment, Bayu underwent a computed tomography (CT) scan of his pelvic limbs. The CT scan revealed no significant torsional or angular deformities, leading to the assumption of a myogenic patellar dislocation. The owners were offered a custom-molded femoral trochlea with an enlarged medial trochlea. This enlarged medial trochlea was intended to prevent medial displacement of the patella.

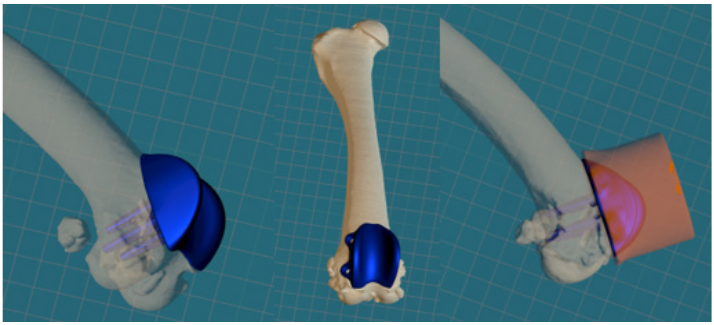


Photos 6,7. *results of computed tomography of the right pelvic limb*

A 3D model of the implants was created, including a guide for cutting the femoral block, a guide for fitting the block prosthesis and drilling holes for the prosthesis "legs" and fixing screws, the femoral block prosthesis itself (the part facing the bone has a porous structure for osseointegration, the part facing the patella is polished for better sliding) and an overlay for hammering the prosthesis into the bone.



Photos 8,9,10. *Guide for femoral block osteotomy and guide for fitting the femoral block prosthesis and drilling holes for screws and prosthesis "legs"*



Photos 11, 12, 13. *Femoral bone block prosthesis and an overlay for its hammering*

6. Protocol for the operation to install a femoral block prosthesis.

Three weeks after the design was developed, surgery was scheduled. The surgical procedures included a craniolateral approach to the knee joint, removal of the nylon implant (from the fabellotibial suture) and its fixing cortical screws. A femoral block sawing guide was then installed, and an osteotomy was performed. A drilling guide for the prosthesis stems and fixing screws were then placed on the resulting platform. After drilling the holes and trying in the implant, the prosthetic block itself was driven into the femur using a hammering pad and secured with screws through the lateral femoral condyle. The knee capsule was closed with Polydioxanone USP 0, the tensor fasciae lata was closed with Polypropylene 2, and then layered suturing was performed using the standard technique with Polypropylene USP 2/0.

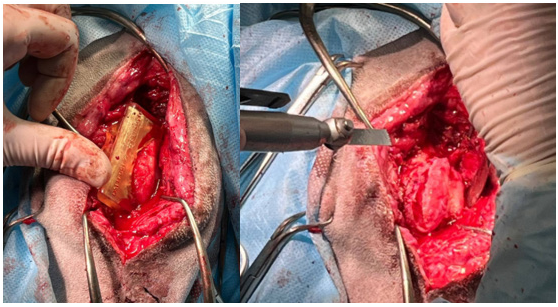


Photo 14, 15. *Positioning of the femoral trochlea osteotomy guide and femoral trochlea osteotomy*

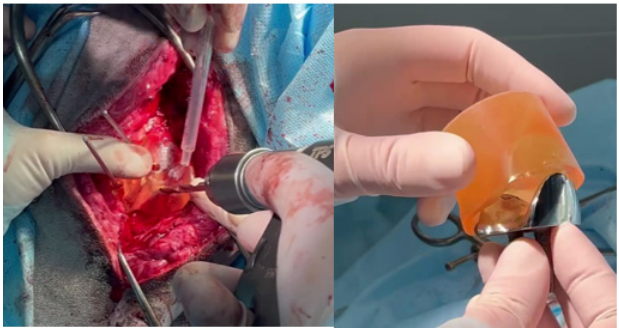


Photo 14. *Positioning the guide and drilling holes for the "prosthesis legs", the fixing pins also act as channels for the fixing cortical screws.*
Photo 15. *Overlay for the hip block prosthesis.*

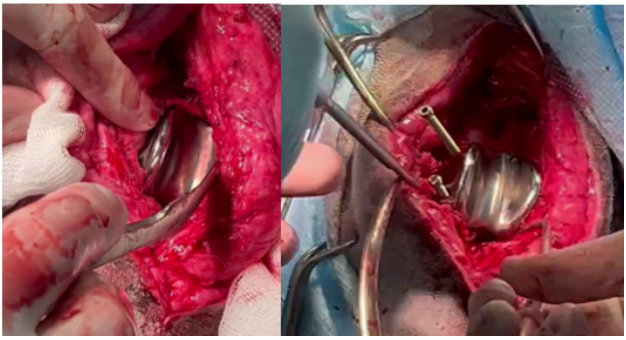


Photo 16,17. *The femoral block prosthesis driven into the wound, fixation of the block prosthesis with two screws.*

Photo 18. *Postoperative X-rays of the hip joint prosthesis*

7. Postoperative recovery.

For three weeks after surgery, Bai wore a knee brace. On the 20th day after surgery, his lameness remained only at the initial stage (for five minutes after sleep, after which it resolved). No deterioration in gait was noted after the brace was removed. Bai was referred for rehabilitation to strengthen the muscular corset of his right pelvic limb.

Three months after surgery, there were no more complaints of lameness, and there were no recurrences of patellar dislocation. The follow-up period after the last surgery was 12 months.

8. Conclusions.

The use of custom-designed 3D implants with an enlarged medial ridge can be used in complex cases of medial patellar dislocation. This technique prevents recurrence and eliminates the risk of delayed prosthetic failure due to the porous structure of the bone-facing portion of the implant, which allows for good osseo-integration of the prosthesis.

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选择杂粮面包成分中功能性成分比例的信息和分析依据

INFORMATION AND ANALYTICAL JUSTIFICATION FOR CHOOSING THE SHARE OF A FUNCTIONAL COMPONENT IN THE MULTIGRAIN BREAD COMPOSITION

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注释本文探讨了 IT 数据处理在评估多成分食品（杂粮面包）质量方面的潜力，该质量评估基于功能性成分（黑麦奶油）的比例，以实现均衡饮食。评估工具包括 Maple 应用程序和用于插值、线性规划和非线性回归的数学工具。虚拟平台由源数据、算法和数学模型组合而成，可用于食品系统分析。研究对象是生物能量特性，作为一整套共轭质量指标：面团中功能性成分的含量、考虑到工艺操作的完善程度的面包等级、蛋白质含量、碳水化合物、还原糖、脂肪、面包水分、专家感官评估、抗氧化活性、酸度、必需氨基酸的总量、必需氨基酸的效用以及面包的能量值。计算实验包括三个阶段，在此期间确定了广义生物能量技术指标和含有功能性成分（黑麦奶油）的杂粮面包的具体质量指标的模式。结果表明，广义生物能源技术指标函数在黑麦奶油含量为8.0%时达到最大值。

关键词：杂粮面包，黑麦奶油，功能成分，IT数据处理，Maple程序，生物能源技术指标。

Annotation. *This article examines the potential of IT data processing to assess the quality of a multi-component food product (multigrain bread) based on the proportion of a component with functional properties (rye cream) for a balanced diet. The assessment tools were a Maple application and mathematical tools for interpolation, linear programming, and nonlinear regression. The virtual platform consisted of a combination of source data, algorithms, and mathematical models enabling food system analysis. The object of the study was bioenergetic characteristics as a system of conjugated quality indicators: functional component*

content in the dough, bread grade, taking into account the perfection of the technological operation, protein content, carbohydrates, reducing sugars, fats, bread moisture, expert organoleptic assessment, antioxidant activity, acidity, the total amount of essential amino acids, the utility of essential amino acids, and the energy value of bread. The computational experiment included three stages, during which patterns in the generalized bioenergy-technological indicator and specific quality indicators of multigrain bread with a functional component (rye cream) were identified. It was shown that the generalized bioenergy-technological indicator function reaches its maximum value at a rye cream content of 8.0%.

Keywords: *multigrain bread, rye cream, functional component, IT data processing, program Maple, bioenergy technology indicator.*

Multigrain bread is a new type of food product. There are no separate regulations for this product. The draft standard for bakery products containing added grain and various grain-based products, developed jointly by specialists from Roskachestvo and the Scientific Research Institute of Bakery Products, has not received official status. This is due to the results of the draft's review by the Russian Guild of Bakers and Confectioners. According to experts, GOST 31807, GOST 25832, GOST R 58233, and the interstate standard GOST-2077-2023 provide a sufficient regulatory framework for the use of primary and secondary raw materials, as well as general technical conditions for the production of multigrain bread [1]. Indeed, at the technology application stage, excessive regulation hinders manufacturers from expanding their product range and leads to unnecessary costs. Therefore, the production of multigrain bread is currently highly variable. This not only allows for, but also stimulates the search for new technological solutions [2]. In particular, it is necessary to develop a methodology for selecting functional components and choosing their optimal combinations in the food matrix of multigrain bread.

Multigrain bread is a multicomponent food system combining diverse adaptogenic nutrients. An effective way to select optimal combinations of elements in this system is through IT data processing using the Maple application program. The virtual platform is a collection of source data, algorithms, and mathematical models that enable analysis of the food system [3].

The aim of the study was to identify patterns of change in the general bioenergetics indicator and specific quality indicators of multigrain bread with a functional component (rye cream) for a balanced diet. The object of the study was the bioenergetic characteristic as a system of associated quality indicators: functional component content in the dough, bread grade, taking into account the perfection of the technological operation, protein content, carbohydrates, reducing sugars, fats,

bread moisture, expert organoleptic assessment, antioxidant activity, acidity, total essential amino acids, essential amino acid utility, and bread energy value.

The computational experiment was carried out on a computer using the Maple program to combine the results of instrumental laboratory measurements, expert assessments of the influence of the functional component (rye cream), ranking indicators of technological excellence in the area of efficiency of the generalized bioenergy-technological indicator, i.e., for a compromise solution to the problems of optimizing the food matrix and bioenergetic characteristics bread.

The computational experiment consisted of three stages. In the first stage, changes in acidity, moisture, and reducing sugars were determined across experimental variants as the proportions of each of the three components of the food matrix varied to establish an effective ingredient ratio (Fig. 1).

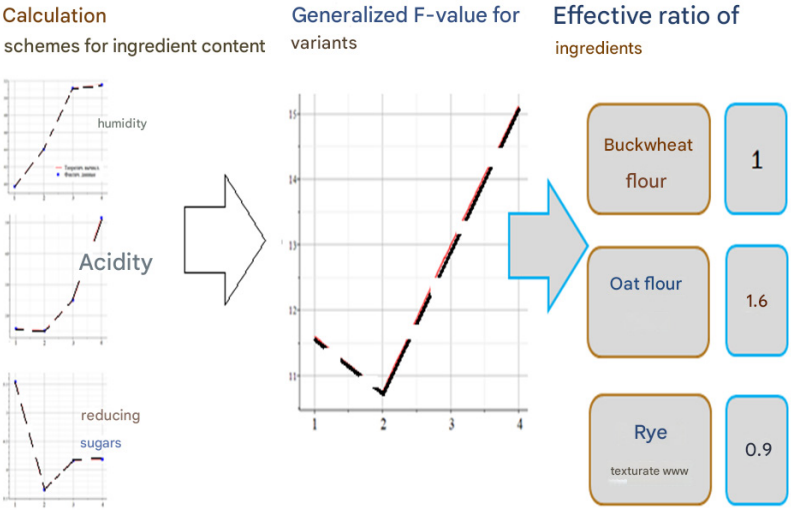

Figure 1. *Determining the effective ratio of ingredients by the method of mathematical modeling*

In the second stage, the results were adjusted for the functional component – rye cream (RC). For this, the antioxidant activity, ORAC (*oxygen radical absorbance capacity,* oxygen radical absorbance capacity) according to the experimental variants with a change in the mass fraction of RS 4%; 8%; 16; 32% (Fig. 2).

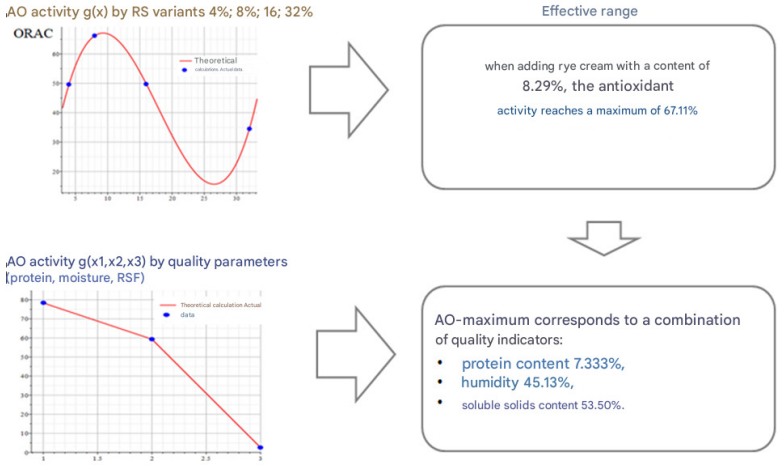

Figure 2. *Identifying the effective range of values proportions of added rye cream*

At the third stage, 3D functions (f) were analyzed with arguments x1 – "rank of expert assessment", x2 – "proportion of rye cream" (Fig. 3).

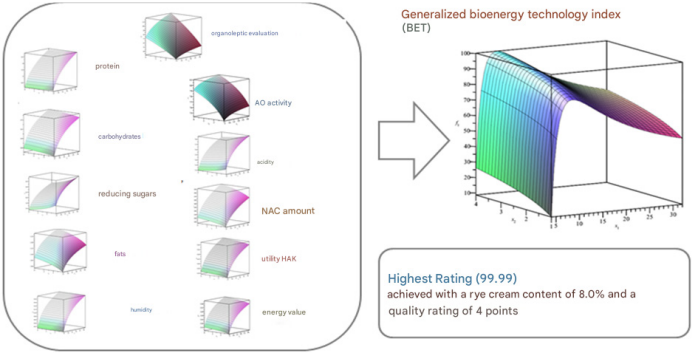

Figure 3. *Expert-analytical model of bioenergetics characteristics of multigrain bread with added rye cream*

The graph obtained for the generalized bioenergy-technological indicator (BET) shows that the function's maximum is achieved at a rye cream content of 8.0%. The computational experiment utilized mathematical tools such as interpolation, linear programming, and nonlinear regression.

Thus, modeling and forecasting the bioenergetic characteristics of multigrain bread with a functional component made it possible to substantiate the food matrix and technology for producing an innovative product.

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添加功能成分“黑麦奶油”的新型杂粮面包的工艺及安全指标
TECHNOLOGY AND SAFETY INDICATORS OF A NEW MULTIGRAIN BREAD WITH THE FUNCTIONAL COMPONENT “RYE CREAM”

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注释。本文探讨了一种新型烘焙产品的安全性能，该产品通过在黑麦面包食品基质中使用麦芽黑麦乳剂（黑麦奶油）来实现其功能特性。与同类产品不同，这种杂粮面包不含小麦粉，麸质含量低。一种专门开发的技术可将黑麦发芽速度提高两倍，同时确保食品体系的杀菌性能。这一成果是通过使用天然自由基调节剂实现的。安全性能采用经过验证的方法进行评估。目标产品不仅符合质量和安全标准，还具备功能特性。根据化学发光分析，杂粮面包的抗氧化活性高于原型产品——博罗丁斯基黑麦小麦面包。使用功能性成分（黑麦奶油）可以开发出一种均衡的食品体系，其中的氧化剂可以抑制病原体的生长，而抗氧化剂则可以增强人体的非特异性抵抗力。

关键词：杂粮面包、黑麦奶油、功能性成分、食品体系、黑麦麦芽、自由基过程、面包安全指标。

Annotation. *This article examines the safety performance of a new type of bakery product with functional properties achieved through the use of malted rye grain emulsion (rye cream) in the rye bread food matrix. Unlike similar products, this multigrain bread does not contain wheat flour and is low in gluten. A specially developed technology features twice the acceleration of rye grain germination while simultaneously ensuring microbicidal properties in the food system. This result was achieved through the use of natural free-radical regulators. Safety performance was assessed using validated methods. The target product not only met quality and safety standards but also possessed functional properties. According to chemiluminescence analysis, the multigrain bread had higher antioxidant activity than the prototype, Borodinsky rye-wheat bread. The use of a functional ingredient (rye cream) allowed for the development of a food system*

balanced in oxidants that inhibit the development of pathogens, and antioxidants, factors of non-specific resistance of the body

Keywords: *multigrain bread, rye cream, functional component, food system, rye malt, free radical processes, bread safety indicators.*

Rye bread is one of the food items that has both economic and cultural significance for national identity. Rye grain surpasses wheat in many respects of its chemical composition and agronomic properties, and is a source of adaptogens, such as biosorbents, essential amino acids, antioxidants, and others. However, the existing range of rye products is inferior to their wheat counterparts. Nutritional dysfunctions are on the rise, necessitating the development of new technologies for the production of rye bakery products for everyday consumption with functional properties to enhance the body's nonspecific resistance. Fermented rye malt is traditionally used to improve the taste and quality of bread [1]. Currently, freshly prepared raw malt is not used in bakery production. This is due, in particular, to the duration of the malting stage, which takes from 24 to 72 hours [2]. To overcome this barrier, a biotechnological approach was applied, which utilized free-radical chain processes at the stage of grain bioactivation.

The aim of this work was to develop a technology for a new type of bread based on accelerated malted rye grain, followed by an assessment of the safety indicators of the resulting new product.

Figure 1 shows a flow chart of the main stages of multigrain bread production.

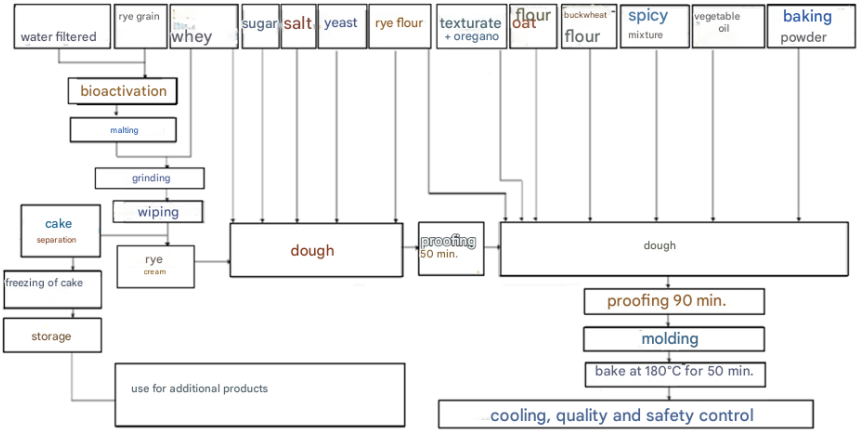

Figure 1. *Steps in the process of making multigrain bread on rye cream*

The product composition in accordance with GOST 32677 included: In addition to rye flour, the following grains and their derivatives are included: oat flour, buckwheat flour, textured rye grain soaked in oregano extract, as well as the main functional component – "rye cream." The authors use this term to describe the processed product of bioactivated grain. The main difference from traditional technology is the use of a filtered emulsion obtained after grinding sprouts in the food matrix of the new type of rye bread, rather than fermented malt.

The malting stages included germination of the grain in a mixture of phytoextract (thyme, a fragrant, spicy wild plant with strong antioxidant properties) with the addition of hydrogen peroxide and iron (II) sulfate. This redox system was used to initiate a free-radical process. The reactive oxygen species formed during the breakdown of hydrogen peroxide (superoxide anion radical, hydroxyl radical, and singlet oxygen) stimulated the destruction of membranes and the cellular matrix, which facilitated accelerated hydration and swelling of the grain. As a result, malt formation was reduced to 10-12 hours while simultaneously ensuring the microbicidal properties of the food system.

The hydrogen peroxide concentration was significantly lower than the microbicidal concentration of the grain treatment product and the minimum concentration of this product for thermal antiseptics. The resulting hydrogen peroxide consumption was several times lower than that achieved with alpha-hydroxy acids with a detergent effect.

Fig. 2 shows semi-finished products and the final product.

Figure 2. *Appearance of semi-finished products and the product*

Based on research using physicochemical methods, it was established that the new multigrain bread complies with current regulations for total acidity and moisture. The increased protein content (11.2±0.7% versus 4.5–8% in traditional breads [3]) slows down the staling of the bread, and the combination of biologically active compounds ensures high antioxidant activity. A safety assessment was conducted at BioKhimAnalit Research Institute (Krasnoyarsk). The results indicate that the safety parameters complied with established regulations (Fig. 3).

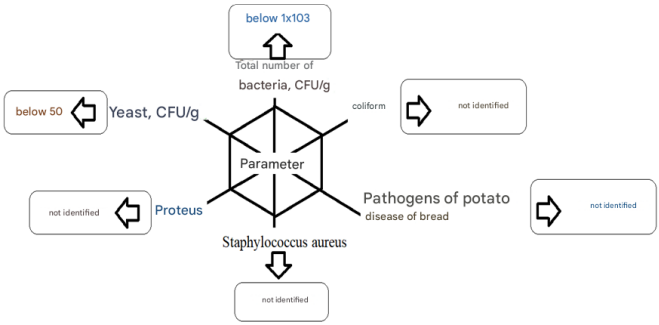

Figure 3. *Safety indicators of rye cream bread*

Thus, the multigrain bread with rye cream meets quality and safety requirements. The product was shown to possess functional properties, as chemiluminescence analysis showed higher antioxidant activity compared to the Borodinsky rye-wheat bread (prototype). The use of a functional ingredient (rye cream) allowed the formation of a food system balanced in oxidants that inhibit the development of pathogens, and antioxidants, factors of non-specific resistance of the body.

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创建和应用干邑蒸馏液和干邑白兰地的非挥发性化合物和颜色特征综合数据库
CREATION AND APPLICATION OF A COMPREHENSIVE DATABASE OF NON-VOLATILE COMPOUNDS AND COLOR CHARACTERISTICS OF COGNAC DISTILLATES AND COGNACS

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注释。本文介绍了一个综合数据库的开发和实际应用成果，该数据库积累了关键非挥发性化合物（酚醛、呋喃醛和酸、单宁）的质量浓度以及干邑蒸馏液和成品干邑的颜色特征信息。该数据库的相关性源于需要深入研究工艺参数（尤其是橡木桶的准备）对饮料感官特征形成和稳定性的影响。该数据库包含在受控条件下获得的未陈酿和陈酿蒸馏液的研究结果，以及各种不同陈酿时间的商业干邑样品。结果表明，该数据库是建立工艺条件和化学成分之间相关性、预测质量、识别假冒产品以及优化干邑和白兰地生产工艺的有效工具。使用该数据库可以将高品质酒精饮料生产各个阶段的控制从经验管理转变为科学控制。

关键词：数据库、干邑蒸馏液、干邑、非挥发性化合物、酚类化合物、颜色特征、橡木桶、陈酿、干燥、烘焙、质量控制。

Annotation. *This paper presents the results of the development and practical application of a comprehensive database accumulating information on the mass concentrations of key non-volatile compounds (phenolic and furan aldehydes and acids, tannins) and the color characteristics of cognac distillates and finished cognacs. The relevance of the database stems from the need for an in-depth study of the influence of process parameters, in particular, oak barrel preparation, on the formation of the organoleptic profile and stability of beverages. The database includes the results of studies of young and aged distillates obtained under controlled conditions, as well as a wide range of commercial cognac samples of varying aging. It is demonstrated that the database serves as an effective tool for establishing correlations between process conditions and chemical composition,*

predicting quality, identifying counterfeits, and optimizing cognac and brandy production processes. Using the database allows for a transition from empirical management to scientifically based control at all stages of the creation of high-quality alcoholic beverages.

Keywords: *Database, cognac distillates, cognacs, non-volatile compounds, phenolic compounds, color characteristics, oak barrel, aging, drying, roasting, quality control.*

Introduction. Cognacs and brandies, produced from aged wine distillates, occupy a stable niche in the spirits market, characterized by high added value and export potential [1]. The quality of these beverages is largely determined by the aging process in oak barrels, during which a wide range of non-volatile compounds from the wood are extracted and subsequently transformed. These compounds, including phenolic aldehydes (vanillin, sinapic, syringic, coniferyl aldehydes, 4-hydroxybenzaldehyde), phenolic acids (gallic, ellagic, vanillic, syringic, sinapic), furan aldehydes (furfural, 5-hydroxymethylfurfural, 5-methylfurfural), and tannins, directly determine key consumer properties such as taste, aroma, and color [2, 3].

The key technological parameters of wood preparation for aging, influencing the chemical composition of the aged distillate and its color characteristics, are the duration of natural (atmospheric) drying of oak staves and the intensity of their subsequent thermal roasting [4, 5]. Long-term drying promotes the hydrolysis of hemicelluloses and tannins, improving the extraction potential of wood, while roasting induces the thermal decomposition of lignin and cellulose, leading to the formation of aromatic aldehydes and furan compounds [2, 4]. Despite a general understanding of these processes, the quantitative patterns of the influence of various drying-roasting combinations on the final chemical composition remain poorly understood, which complicates precise technology control.

Therefore, the goal of this work is to create a comprehensive database that combines detailed information on the non-volatile components and objective color characteristics of distillates and cognacs, a pressing scientific and practical challenge. Such a database can serve not only as an information archive but also as a powerful analytical tool for solving problems of standardization, identification, and process optimization.

Objects and methods of research. The database was populated through both targeted experiments and analysis of commercial samples. In a controlled experiment, young wine distillates were aged for six months in oak barrels made from staves of sessile oak with variable parameters: air-drying period (6 months, 3 years, 8 years) and degree of toasting (light, medium, heavy). This allowed for strictly comparable data on the impact of each factor. Furthermore, the database

includes data on numerous samples of cognac distillates aged from 1 to 45 years and finished cognacs from various producers in Russia and the CIS, ensuring representativeness and breadth of coverage.

The mass concentration of phenolic and furan compounds was determined using the Agilent 1220 Infinity II high-performance liquid chromatography system (Agilent technology, USA) according to GOST 33407-2015 Cognacs, distillates, cognac, brandy. The mass concentration of tannins was determined by the titrimetric method (Certificate of Attestation of Measurement Methodology No. 124-01.00218-2011; Registration number - FR.1.31.2011.11237). Mass concentrations of alkali and alkaline earth metal cations (NH4+, K+, Na+, Mg2+, Ca2+) were determined using the method developed at the Winemaking Research Center and the Center for Shared Use of High-Tech Equipment of the Federal State Budgetary Scientific Institution North Caucasus Federal Scientific Center of Winemaking (certification certificate No. 61-10 dated October 20, 2010) using a Kapel-105M high-performance capillary electrophoresis system (Lumex, Russia). Chromatic characteristics were obtained by measuring the optical density/transmittance coefficients on a UNICO 1201 spectrophotometer (USA). Calculated color indices (intensity, hue, yellowness, and color coordinates in the CIELab system) were determined using Excel. Analyses were performed under repeatability conditions.

Discussion of results. The database being developed is a Microsoft Excel spreadsheet, the structure of which reflects a multiparameter approach to characterizing distillates and cognacs. The main data blocks include:

1. General information about the sample: name, manufacturer, country of origin, sample code, age (excerpt).
2. Mass concentrations of non-volatile compounds: Phenolic aldehydes: vanillin, sinapic aldehyde, coniferyl aldehyde, syringaldehyde, 4-hydroxybenzaldehyde; Phenolic acids: syringic acid, vanillic acid, p-coumaric acid, sinapic acid, gallic acid, ellagic acid; Furan aldehydes: furfural, 5-hydroxymethylfurfural, 5-methylfurfural; tannins (in total).
3. Mineral composition: concentrations of ammonium (NH_4^+), potassium (K^+), sodium (Na^+), magnesium (Mg^{2+}), calcium (Ca^{2+}), and iron (Fe) cations.
4. Color characteristics: optical densities at wavelengths of 420, 520, 620 nm (A420, A520, A620), light transmittance at 440, 520, 570, 630 nm (T450, T520, T570, T630), color coordinates in the CIE Lab (L, a, b) and XYZ systems, as well as calculated indicators such as color intensity and hue.

The database will serve as a basis for statistical analysis and the identification of stable relationships between technological parameters and chemical composition. Systematization of the data will allow for a quantitative assessment of the impact of wood processing on mineral composition, which is important for preventing defects such as crystalline opacities associated with excess calcium salts [6, 7].

Integrating chemical composition and color data opens up opportunities for predicting organoleptic profiles and identifying correlations between the levels of specific compounds and tasting scores. Samples with an optimal balance of phenolic aldehydes, moderate furan content, and tannins [2] consistently receive top scores for a complex aroma with cognac-like tones and a harmonious flavor.

Color parameters (L, a, b), such as brightness (L) and the a+ (red) and b+ (yellow) values, objectively confirm the intensity and shade of the color acquired as a result of oak aging and the extraction of caramelisation and lignin degradation products.

The database can be used as a reference for establishing the authenticity of cognacs. Comparative analysis of the declared age and region of origin with the actual chemical profile (ratios of various aldehydes and acids, specific mineral composition) allows for the identification of deviations characteristic of counterfeit products. For example, abnormally low vanillin and ellagic acid contents despite the claimed long aging period may indicate the use of alternative wood extracts or unaged spirits.

Having a comprehensive database of distillates of varying ages and chemical compositions will allow technologists to virtually model future blends, selecting components to achieve a specific sensory profile and color characteristics of the final product, reducing the time and resources spent on experimentation.

Conclusion. The comprehensive database of non-volatile compounds and color characteristics of cognac distillates and brandies under development represents a valuable scientific and practical tool. Its creation will systematize the accumulated knowledge about the chemical processes occurring during aging and elevate beverage quality management to a whole new level.

The quantitative patterns of influence of oak wood preparation (drying and firing) on the formation of a complex of non-volatile compounds, established using the database, will provide manufacturers with clear recommendations for technology optimization.

The practical application of the database covers such areas as scientifically based management of technological aging processes, objective quality control and authenticity of finished products, forecasting organoleptic properties based on chemical composition, and optimization of blending recipes.

Further development of the database is expected through the addition of new samples, the inclusion of data on volatile aroma-forming compounds, and the use of machine learning methods for a more in-depth analysis of multivariate dependencies.

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农业措施对淋溶黑钙土中铵态氮含量影响的因子分析
FACTOR ANALYSIS OF THE INFLUENCE OF AGRICULTURAL PRACTICES ON AMMONIUM NITROGEN CONTENT IN LEACHED CHERNOZEM

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摘要：在农学发展的现阶段，研究农作物氮素营养的形成具有重要的科学和实际意义。由于耕作深度对肥力参数的影响，长期田间试验中耕作土层的分化尤为重要。本研究通过因子分析，评估了长期（在阿尔泰鄂毕河地区森林草原区进行了25年田间试验）耕地利用条件下，主要作物生产管理措施对耕作土层铵态氮含量的影响。研究表明，在所有耕作土层样品中，施肥仍然是决定铵态氮含量的主要因素。作物轮作有利于有机质沿剖面分布更均匀，并优化微生物活性。耕作制度对表层（0–10 cm）和深层（20–30 cm）的影响最大。农药施用的影响不太明显，并通过与其他因素的组合相互作用表现出来。

关键词：可持续农业、长期实地经验、铵态氮、淋溶黑钙土、数据挖掘。

Abstract. *At the current stage of agronomic science development, research on the formation of nitrogen nutrition in agricultural crops holds high scientific and practical significance. The differentiation of the arable soil layer in long-term field experiments is of particular interest due to the influence of tillage depth on fertility parameters. This study presents the results of factor analysis evaluating the influence of main agricultural practices for managing crop productivity on ammonium nitrogen content in the arable soil layer under long-term (25-year field experiment in the forest-steppe of the Altai Ob region) arable land use. The research established that in all samples of the arable soil layer, fertilizer application remained the leading factor determining ammonium nitrogen content. Crop rotation compliance contributed to more uniform distribution of organic matter along the profile and optimization of microbiological activity. The influence of the tillage system was maximal in the surface (0-10 cm) and deeper (20-30 cm) layers. The effect of pesticide application proved less evident and manifested through combinatorial interactions with other factors.*

Keywords: *sustainable agriculture, long-term field experience, ammonium nitrogen, leached chernozem, data mining.*

Field experiments constitute the primary tool in conducting agronomic research, while long-term multifactorial experiments serve as the foundation for knowledge formation in agricultural science and practice. The implementation of long-term experiments and observations enables data acquisition on the effectiveness of agrochemical agent application [1,2], soil fertility [3], establishment of relationships between crop yield and yield-forming factors [4,5], among others.

Research on the formation of nitrogen nutrition in agricultural crops is highly relevant, and the differentiation of the arable soil layer in long-term field experiments is of particular interest due to the influence of tillage depth on fertility parameters [6,7].

Statistical analysis was performed using data from a long-term field experiment at the Federal Altai Scientific Centre of Agro-BioTechnologies, operating since 2001 in the forest-steppe of the Altai Ob region [8]. The experimental site soil is leached chernozem, medium-depth, low-humus, medium-loamy on a south-east-facing slope with a gradient of 1-2°. The humus content in the arable soil layer was 3.8%.

The dataset consisted of 72 records containing information on soil ammonium nitrogen content and factors affecting it (5 features in total, including soil sampling depth). Features included categorical variables: wheat cultivation variants (continuous monoculture and in crop rotation); primary tillage systems (no-till, deep subsurface tillage at 25-27 cm, shallow subsurface tillage at 14-16 cm); fertilizers (no fertilizers, $N_{46}P_{25}$); plant protection products (no protection; herbicides, insec-

ticide, fungicide). Soil samples were collected in May from depths of 0-10 cm, 10-20 cm, and 20-30 cm.

Statistical calculations and graphical constructions were performed using the Python programming language in Jupyter interactive notebooks. The proprietary program Crop Yield Analysis & Forecast (CYAF) [9] was also used for analyzing agronomic data.

The working hypothesis of the research was that with long-term (25 years) application of main agricultural practices for managing crop productivity, effects should accumulate in the arable soil layer, particularly in ammonium nitrogen content, which can be represented as certain patterns using various statistical methods.

Considering the pronounced stratification of ammonium nitrogen (NH_4^+) content along the soil profile depth, factor analysis was conducted for each soil sampling depth. This approach allows assessment of the relative contribution of agricultural factors (pesticides, tillage, fertilizers) while eliminating the depth effect and revealing the specificity of their influence in different soil layers. For each crop cultivation variant and depth, 12 observations were analyzed in a complete factorial experiment 2×3×2. Analysis of NH_4^+ vertical distribution confirmed a regular increase in its concentration with depth for both crop cultivation variants (Figure).

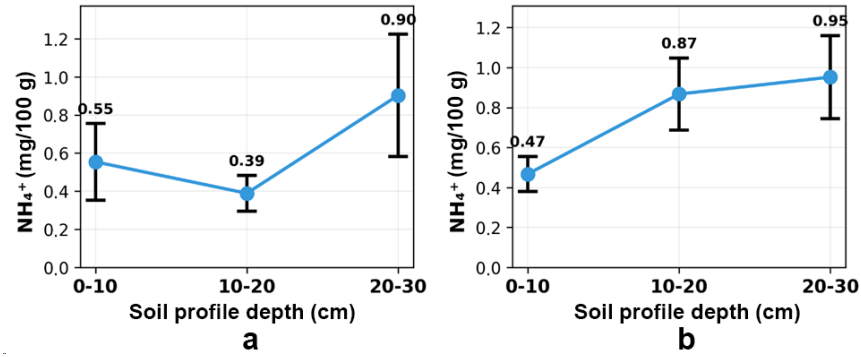

Figure. *Dynamics of average ammonium nitrogen content along the soil profile depth: a) continuous wheat monoculture, b) wheat in crop rotation*

In the arable soil layer under continuous wheat cultivation, the average ammonium nitrogen content increased from 0.53 mg/100 g in the 0-10 cm layer to 0.89 mg/100 g in the 20-30 cm layer (+68%); under wheat cultivation in crop rotation – from 0.47 to 0.88 mg/100 g (+87%). Standard deviations also increased with depth, reaching a maximum in the 20-30 cm layer (0.30-0.33 mg/100 g), indicating increasing influence of agricultural factors.

Application of mineral fertilizers resulted in the most stable and pronounced effect in all layers of the arable horizon for both crop cultivation variants. In the 0-10 cm layer, fertilizer application increased NH_4^+ content from 0.49 to 0.57 mg/100 g (+16.3%, t=1.42, p=0.186). In the 10-20 cm layer, the effect intensified: from 0.34 to 0.45 mg/100 g (+32.4%, t=2.08, p=0.065). The maximum effect was observed in the 20-30 cm layer: from 0.72 to 1.05 mg/100 g (+45.8%, t=3.15, p=0.011**), reaching statistical significance. This dynamic possibly reflects processes of vertical migration of mineral nitrogen with its subsequent reduction to ammonium form under anaerobic conditions in lower horizons.

The fertilizer effect under wheat cultivation in crop rotation proved more homogeneous along the profile: +19.1% (0-10 cm, t=2.45, p=0.035*), +31.4% (10-20 cm, t=3.78, p=0.004**), +20.7% (20-30 cm, t=2.31, p=0.045*). Statistical significance was achieved in all analyzed soil layers, indicating a more stable nitrogen regime. Crop rotation apparently contributed to more uniform distribution of organic matter along the profile and optimization of microbiological activity.

The influence of pesticides was characterized by considerable variability depending on wheat cultivation variants and soil sampling depth. For continuous wheat, pesticide application generally did not exert a statistically significant effect in any layer ($p>0.05$), with slight variation of means from -3.5% to +1.7%. This result is consistent with correlation analysis, which showed a weak relationship between pesticide application and NH_4^+ content (r=0.071).

Under wheat cultivation in crop rotation, an opposite tendency was observed in the surface horizon: pesticide application reduced NH_4^+ content from 0.49 to 0.44 mg/100 g (-10.2%, t=-1.89, p=0.088) in the 0-10 cm layer. In deeper layers, the effect changed to positive: +3.7% (10-20 cm) and +4.4% (20-30 cm), though statistically insignificant.

The tillage system effect manifested nonlinearly and depended on the crop cultivation variant. Under continuous wheat cultivation in the 0-10 cm layer, shallow subsurface tillage promoted a 21.0% increase in NH_4^+ content relative to the no-till control (F=2.87, p=0.105), while deep subsurface tillage reduced it by 14.3%. In the 10-20 cm layer, all three systems yielded similar results (variation <10%). In the 20-30 cm layer, an opposite tendency was observed: maximum under no-till (1.05 mg/100 g), minimum under shallow subsurface tillage (0.82 mg/100 g, -22.4%).

Under wheat cultivation in crop rotation, patterns differed: in the 0-10 cm layer, maximum content was observed with shallow subsurface tillage (0.53 mg/100 g, +16.5% relative to control). In the 10-20 cm layer, deep subsurface tillage showed an advantage (+14.8%). In the 20-30 cm layer, the tillage system effect was leveled.

Analysis of the complete factorial experiment revealed substantial interactions between features. Maximum NH_4^+ content under continuous wheat cultivation was observed with the following combinations:

- 0-10 cm layer: shallow subsurface tillage without fertilizers and without pesticides (0.91 mg/100 g);
- 10-20 cm layer: no-till with fertilizers and without pesticides (0.56 mg/100 g);
- 20-30 cm layer: shallow subsurface tillage with fertilizers and pesticides (1.47 mg/100 g).

Maximum NH_4^+ content under wheat cultivation in crop rotation was observed with the following combinations:

- 0-10 cm layer: shallow subsurface tillage with fertilizers without pesticides (0.62 mg/100 g);
- 10-20 cm layer: shallow subsurface tillage with fertilizers and pesticides (1.18 mg/100 g);
- 20-30 cm layer: shallow subsurface tillage with fertilizers and pesticides (1.35 mg/100 g) or deep subsurface tillage with fertilizers and without pesticides (1.30 mg/100 g).

Analysis of the two-factor interaction “fertilizers × pesticides” showed a synergistic effect under wheat cultivation in crop rotation, which manifested in deeper layers: with combined application of both factors, the increase in NH_4^+ content exceeded the sum of their individual effects. Under continuous wheat cultivation, the interaction was less pronounced, with predominance of the fertilizer effect regardless of pesticide application.

The relative importance of agricultural factors varied by depth:

- 0-10 cm layer: fertilizers >> tillage > pesticides;
- 10-20 cm layer: fertilizers >>> pesticides ≈ tillage;
- 20-30 cm layer: fertilizers >> tillage > pesticides.

In all samples of the arable soil layer, fertilizer application remained the leading factor determining ammonium nitrogen content. The influence of the tillage system was maximal in the surface (0-10 cm) and deeper (20-30 cm) layers. The pesticide effect proved least predictable and manifested predominantly through interactions with other factors.

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