



SCIENTIFIC RESEARCH OF THE SCO COUNTRIES: SYNERGY AND INTEGRATION

上合组织国家的科学研究：协同和一体化

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这些会议文结合了会议的材料 – 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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从院士 A.A. 的角度看马克扎克伯格的元宇宙。 乌赫托姆斯基的支配学说
**THE METAVERSE OF MARK ZUCKERBERG FROM THE
STANDPOINT OF THE ACADEMICIAN A.A. UKHTOMSKY'S
DOCTRINE OF THE DOMINANT**

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抽象的。在这部作品中，首次从学说的角度分析了 M. E. Zuckerberg 所谓的元宇宙的虚拟现实以及人类催眠睡眠状态下中枢神经系统的真实机制 院士 A.A. 的主导地位 乌赫托姆斯基。 我们已经证明，催眠是俄罗斯院士A.A. 提出的支配性工作机制之一。 乌赫托姆斯基。 在催眠状态下，一个人沉浸在虚拟现实中，在那里他可以睁着眼睛走路和说话，但看到的是催眠师给他的建议。 我们已经证明，由于大脑的独特工作，一个人长期使用虚拟现实机制，这证明了催眠状态的表现是占主导地位的。

关键词：虚拟现实，扎克伯格的元宇宙，催眠，主导 A.A. Ukhtomsky，机器人（计算机）的催眠。

Abstract. *In this work, for the first time, an analysis of the virtual reality of the alleged metauniverse of M. E. Zuckerberg and the real mechanisms of the central nervous system in a state of hypnotic sleep in humans is carried out from the point of view of the doctrine of the dominant of academician A.A. Ukhtomsky. We have proved that hypnosis is one of the mechanisms of the work of the dominant, proposed by the Russian academician A.A. Ukhtomsky. In a state of hypnosis, a*

person is immersed in virtual reality, where he can walk and talk with his eyes open, but sees what the hypnotist suggested to him. We have shown that a person has been using the mechanisms of virtual reality for a long time due to the unique work of the brain, which proves the manifestation of hypnotic states that are dominant.

Keywords: *virtual reality, Zuckerberg's metaverse, hypnosis, dominant A.A. Ukhtomsky, hypnosis of robots (computers).*

Relevance. The Metaverse represents the latest development in visual immersion technology. The metauniverse is understood as a constantly operating virtual space within which a person can interact with each other and with digital objects through their avatars using virtual reality technologies [3, 10, 11].

Interaction can be carried out using various technological devices, for example, using personal computers, as well as through virtual and augmented reality. The Metaverse is to create a virtual world that is both displayed and independent of the real world in cyberspace, using the improvement in the development of various digital technologies such as virtual reality and augmented reality. Its essence is a digital online space, parallel to the real world, which becomes a practical field for innovation and development of human society. [12, 13, 14] Interaction can be carried out using various technological devices, for example, using personal computers, as well as through virtual and augmented reality. The Metaverse is to create a virtual world that is both displayed and independent of the real world in cyberspace, using the improvement in the development of various digital technologies such as virtual reality and augmented reality. Its essence is a digital online space, parallel to the real world, which becomes a practical field for innovation and development of human society.

American internet entrepreneur and media mogul philanthropist, Mark Elliot Zuckerberg is best known as the co-founder of Meta (formerly Facebook) and the Breakthrough Starshot solar-powered spacecraft project.



He planned to create a superbrain, where instead of a single neuron, the brain of one person would be represented, which would be connected via a metauniverse computer network with hundreds of millions of brains of other people. Such a connection of millions of people into a supercomputer can, no doubt, bring enormous scientific progress, but, on the other hand, it can bring many, moreover, unexpected surprises. That is why the scientific study of the mechanisms and expected consequences of the introduction of the computer metaverse

system by Mark Zuckerberg is both a practical and a fundamental task of modern science.

Research methods. To study virtual reality in our studies, we used the voluntary immersion of students ($n = 19$) into a deep phase of medical hypnotic sleep [4], where they even saw the suggested virtual worlds with their eyes open, could walk, talk in this suggested environment (fig. 1).



Figure 1. Doctor of Medical Sciences Professor Ananiev V.N. doing hypnosis.

We analyzed the state and actions of students in hypnosis. It should be noted that after the hypnosis session, the majority (11 - 73.3%) of young people remembered everything that was suggested to them and shared their impressions about their color pictures during hypnotic journeys.

As for the analysis of hypnosis, we carried it out from the point of view of the theory of the dominant of academician A.A. Ukhtomsky [9]. We believe that hypnosis is the strongest dominant that suppresses all the others, and all information from receptors goes through this dominant, and information that is directed against this dominant is inhibited. Note that the dominant is introduced by the hypnotist and is absolute, therefore, it is performed by a person unquestioningly. In this case, the dominant sets a goal, and the person tries to achieve this goal.

When the computer is working, the goal (dominant) is set by the programmer, and the computer implicitly executes the program (dominant). A programmer for a computer, as well as for a person, is a hypnotist, while both create a dominant (ie a program of action) and the computer and the hypnotized person perform this

dominant. Based on these comparisons, the computer works according to the same algorithm as the human brain, using the dominant principle of Academician A.A. Ukhtomsky. This implies the generalization that computer hypnosis is the creation of a dominant (goal of activity) or writing a program for a computer. In this case, it should be recognized that we can hypnotize a computer quite easily, and as a more complex computer, we can hypnotize robots.

Results and its discussion. Prominent Russian physiologist Academician I.P. Pavlov [8] proved that the only physiological principle of brain activity that explains the holistic behavior of animals and humans is the principle of a conditioned reflex. Academician P.K. Anokhin proved [1] that the universal principle of all forms of life is the anticipatory reflection of the reality of the events of the external world.

The first computers on radio tubes worked in a binary information coding system, like the neurons of the brain, which is still happening in the work of modern computers. So far, scientists have not been able to fully study how information is processed in a neuron of the brain. Perhaps this phenomenon is one of the mysteries of the brain. Since the frequency of impulses in brain neurons is (mostly) only 100–200 Hz, while even a household computer has 4000000000 Hz (4 billion pulses per second), computers operate hundreds of millions of times faster than human brain neurons. But it is still not clear how the brain works much more efficiently than computers.

From this we can conclude that the human brain is better organized than computers, so the analysis of the mechanisms and principles of the brain can greatly improve the performance of computers. The work of the human brain is provided with the function, as we noted above, of approximately 86 billion neurons. Computers have long surpassed the human brain in terms of the number of initial elements that provide the “all or nothing” state; in computers, they are transistors. It is easy to calculate that only the second generation Epyc processors contain 39.54 billion transistors. In terms of computer systems that are made up of many integrated circuits, the supercomputer with the most transistors as of 2016 is the Chinese-developed Sunway TaihuLight, which has, for all processors/nodes in the aggregate, “about 400 trillion transistors in the computing hardware portion.” And DRAM in it includes about 12 quadrillion transistors.

Mark Zuckerberg decided to connect all the power of computers to connect human consciousness with the endless possibilities of the global computer world. At the end of June 2021, Facebook CEO Mark Zuckerberg told his employees about the new initiative. The company’s future will go far beyond its current project to build a set of connected social apps and some hardware to support them. Instead, he says, Facebook will aim to create a maximalist, interconnected set of experiences straight out of science fiction known as the metaverse. The company’s com-

munity, creator, commerce, and virtual reality businesses will increasingly work to realize this vision, he said in a remote employee address. "...I think the most interesting thing is how these themes come together in a larger idea," Zuckerberg said. "Our primary goal in all of these initiatives is to help bring the Metaverse to life."

As for the term metaverse, it first appeared in 1991 in the novel "Snow Crash" by American science fiction writer Neal Town Stephenson. The sharp plot of the novel was based on the idea of the Snow Crash virus, which can have a detrimental effect on people, both in digital reality and in biological forms. It was translated into Russian with the word "metaverse". The metaverse in Stevenson's book is the intertwined digital and physical worlds; when events in one world can affect life in another, and it is sometimes impossible to draw a line between worlds. How does M. Zuckerberg's statement stand out against this already fairly regular background of references to the metaverse? Firstly, of course, the scale of the resources that Facebook has and the influence of this company in general. Secondly, the complexity of the approach, which goes far beyond games and entertainment, although no one is going to neglect them.

The metaverse is what will be given to people in sensations, in what they will live. In our opinion, Zuckerberg is strongly obsessed with devices that will open up people to a richness of sensations and possibilities in the metaverse, and for him this device is clearly glasses or a helmet. His pathos is clear: the modern digital world is too diverse and powerful for the main interface to it to be a small parallelepiped with a screen in the palm of your hand. The smartphone has become a brake, although it once gave us freedom from wires and heavy computers. Mark Zuckerberg wants everyone in the world to connect to the global virtual reality network, communicate through it, live and even work in it. But, from our point of view, the one who sets the initial rules and parameters of this virtual network begins to own everyone who entered this network, begins to dictate his desires to them, can change the structure of the consciousness of the participants in the virtual network.

Our study showed that in the state of hypnosis, a superstrong dominant of what is suggested is formed, as a result, this strong dominant turns off the reverse afferentation and only the image of the goal of the action (dominant) remains in the acceptor of the results of the action and there is no comparison with the real reverse afferentation of what enters the brain from different receptors. A person begins to live in this super-strong dominant, which was inspired by the hypnotist, which will be virtual suggested reality. In the real life of a person, any super-strong goal can become a strong dominant that a person strives for.

It is known from human physiology that normally the dominant should disappear when it is satisfied, i.e. achieving the goal, while a person feels very strong

positive emotions (for example, happiness), which are provided by the production of hormones of happiness, beta-endorphins (opium-like substances) cause the strongest positive emotions. Hence the danger of using these substances in medicine. Paradoxically, it turns out that the purpose of life is to achieve the result of activity and produce milligrams of chemicals that cause joy and happiness. There is no such mechanism in the work of computers and robots yet. These substances, which are produced upon reaching the goal, cannot be taken without a medical prescription, since the body immediately stops its activity, since the ultimate goal has already been achieved. So, for example, rats, when stimulating the pleasure centers, pressed the stimulation lever continuously until they died of hunger.

We believe that virtual reality is already genetically incorporated into the functioning of the brain. For example, in a state of hypnosis, one can suggest that a person is in a forest, animals are walking nearby, and huge trees are growing around [3]. In hypnosis, a person can talk, walk, see what is suggested to him and act as if he is really in the forest, although he is sitting in front of the hypnotist. This property of the brain in hypnosis to see and be in suggested circumstances is virtual reality. It turns out that Mark Zuckerberg wants to immerse everyone in the world of illusions and fantasy as in a hypnotic dream. Since hypnosis is a real brain function that exists, Mark Zuckerberg's plans look more than realistic. Therefore, in our work, we analyzed the mechanisms of hypnosis and Zuckerberg's metaverse from the point of view of the doctrine of the dominant.

Conclusion. Our data that the state of hypnotic sleep is the dominant and normal physiological model of the virtual reality of the brain. We have proved that the Metaverse of Mark Zuckerberg can largely replace the natural function of the formation of a dominant in a person. The Metaverse of Mark Zuckerberg, in fact, is a system of mass hypnosis (the formation of a dominant) with a single control center. Most of the desires and fantasies of a person in Mark Zuckerberg's metaverse will be quickly satisfied virtually in computer fantasy, the functional system of the body will stop, there are no desires and goals, because everything is satisfied. And this is one of the main driving systems of the aspirations of the life of the organism, and stopping its work can lead to unpredictable results in society. This leads to the generalization that computer hypnosis is the creation of a dominant (goal of activity) or writing a program for a computer. In such a case, we must admit that we can hypnotize a computer quite easily and, as a more sophisticated computer, hypnotize robots.

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年轻人龋病的病因和患病率

ETIOLOGY AND PREVALENCE OF CARIES IN YOUNG PEOPLE

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抽象的。根据世界卫生组织, 龋齿被认为是最常见的疾病。所有年龄段的病变发生率数据都证实了这个问题的紧迫性。这种病理常常导致年轻人和成年人的牙齿脱落, 进而导致人群的一般工作能力暂时丧失。龋齿发生的强度是多种多样的, 并随年龄而变化。大多数情况下, 牙齿的龋齿过程发生在萌出后的头几个月, 在成年期和老年期较少观察到。众所周知, 这些过程与口腔和牙齿硬组织之间的代谢机制有关。

关键词: 龋齿预防, 牙釉质, 龋齿过程。

Abstract. *According to the World Health Organization, dental caries is considered the most common disease. The urgency of this problem is confirmed by data on the incidence of lesions in all age categories. This pathology often leads to the loss of teeth, both in young and mature people, which in turn causes a temporary loss of the general working capacity of the population. The intensity of the occurrence of dental caries is diverse and varies depending on age. Most often, the carious process of teeth develops in the first months after eruption, less often observed in adulthood and senile age. It is known that these processes are associated with the mechanisms of metabolism between the oral cavity and hard tissues of the teeth.*

Keywords: *caries prevention, enamel, carious process.*

Relevance

Different groups of teeth have a different predisposition to the development of a carious process. Most often, the first and second molars, especially their fissures,

are exposed to carious lesions, but with increasing age of patients, a change in localization occurs and caries is more often noted on the proximal surfaces. Then both premolars of the upper jaw, the second molar of the lower jaw, as well as incisors and canines of the upper jaw [3]. This information must be taken into account when developing preventive measures.

According to the literature, it was found that in terms of prevalence, dental caries ranks first among all types of dental diseases. So, in most countries of the world, from 85 to 98% of the population suffer from carious lesions. In our country, 85% of children need the help of a dentist by the age of one and a half, and 40% of children are analyzed for the presence of anomalies in the development of teeth and jaws. At the same time, periodontal disease occurs in 60% of adolescents, and in 80% of children aged 6-8 years, every third tooth is the source of odontogenic infection. Loss of teeth leads to disturbances in the work of the gastrointestinal tract and psycho-emotional disorders. Moreover, such an unfavorable condition of the oral cavity only worsens with age.

According to the World Health Organization, dental caries and periodontal tissue diseases occur in 82% - 100% of cases, and in recent years this incidence among children has been increasing, especially in economically underdeveloped countries. According to clinicians, a dental examination of patients conducted in 2020 made it possible to state that patients of the young age group from 25 to 39 years old most often seek dental care. At the same time, men seek dental care less often than women. Elderly patients aged 60 to 70 years and older seek consultations most rarely.

According to the literature, one of the most common reasons for visiting a dentist is the treatment of dental caries, in second place is the treatment of pulpitis, and in third place is the treatment of acute periapical periodontitis. Further, for the treatment of caries and its complications, a common disease for which patients seek treatment is acute periodontitis and stomatitis. The results of the study led to the conclusion that more often patients turn to the dentist with acute forms of diseases, and most of the population does not turn to doctors in a timely manner for dental care, as well as for the prevention of dental diseases.

Women most often seek dental care at the stage of the carious process, and men at the stage of complicated processes that are the result of neglected caries [6].

Scientists have found that the CFE index (caries, filling, extracted tooth) tends to increase with the age of patients, at the same time, the dynamics of the constituent values of the CFE index is ambiguous. The dynamics of the spread of the carious process in the age group of 15-49 years remains in the most equal values and tends to decrease at the age of 70 years and more. A large number of teeth affected by caries are observed in adolescence (15-19 years). There are data that indicate that the dynamics of the indicator - "filling" in adolescence gradually increases and at the age of 25 to 29 years becomes the most important. Also, with

increasing age, there is an increase in the indicator - “extracted tooth”, the maximum values of which were noted at the age of 70 years and older, since at this age there is a lack of more than half of the teeth in the oral cavity [2]. Based on the above information, it can be concluded that most of the population has dental caries and its complications.

Lack of treatment of caries and its complications, in most cases, leads to tooth loss, resulting in complex morphological and functional changes in the dental system, which leads to facial aesthetic disorders, difficulties in chewing food and speech disorders. The data of literary sources allow us to assert that the development of caries complications is confirmed by the following indicators: at the age of 35 to 44 years, the need for dental filling and orthopedic prosthetics is about 48%, and about 24% for tooth extraction. Untimely treatment of patients for the treatment of dental caries and removal as a result of its complications can lead to the appearance of secondary deformation of the dentition and the occurrence of pathology of the temporomandibular joint. The presence of a carious process in the oral cavity directly affects the health and quality of life of the patient, which leads to a violation of the chewing process up to the final loss of this body function, which affects the digestion process. Therefore, these data must be taken into account when developing preventive measures. In foreign and domestic literature sources, great importance is given to the study of the microstructure and physiology of hard tissues of the tooth. A large number of research works are devoted to the study of tooth enamel. First of all, this is due to the specifics of the tooth tissue and the need for a more detailed study of the pathogenesis of dental caries and other pathological processes that occur primarily in the enamel [4].

The hard tissues of the tooth are composed of organic, inorganic matter and water. The organic matter of enamel is represented by proteins, lipids and carbohydrates. The following fractions were identified in enamel proteins: soluble in acids - 0.17%, insoluble - 0.18%, peptides and free amino acids - 0.15%. Lipids were also found in the enamel - 0.6%, citrates - 0.1%. There is an opinion of scientists that caries resistance of enamel depends on the content of not only inorganic substances in it, but also protein. The total volume of water in the enamel is 3.8%. The inorganic basis of enamel is hydroxyapatite (75%), carbonate apatite (19%), chlorapatite (4.4%), fluorapatite (0.66%) and non-apatite forms (2%). The main structural unit of a prism is considered to be crystals of apatite-like origin, but the main one is hydroxyapatite. Each hydroxyapatite crystal is covered with a hydration shell about 1 nm thick, and the crystals themselves are located at a distance of 2.5 nm from each other and determine the strength of the enamel. The composition of ideal hydroxyapatite corresponds to the formula $\text{Ca}_{10}(\text{PO}_4)_6(\text{OH})_2$, where the Ca/P molar ratio is 1.67. But as a result of possible substitutions of Ca for other trace elements, the Ca/P ratio can vary from 1.33 to 2.0. So, when Ca is replaced by similar chemical elements, such as Ba, Cr or Mg, the Ca/P ratio can decrease

to 1.33, and the properties of apatite also change in the direction of reducing the resistance of enamel to adverse conditions [3].

As a result of the substitution of hydroxyl groups for fluorine, fluorapatite is formed from hydroxyapatite, which in its properties surpasses the “ideal” hydroxyapatite in strength, and the Ca/P ratio can increase to 2.0. Ca/P - coefficient is usually used as a criterion for caries resistance of hard tissues of teeth, since hydroxyapatite crystals are capable of physical and chemical exchange [5]. A comparative assessment of the composition of trace elements in intact enamel and enamel covered with plaque showed that plaque has a pronounced ability to demineralize enamel, which is reflected in a 44.23% decrease in inorganic matter and a 45.15% increase in organic matter, compared to intact enamel. The decrease in mineral substances occurred primarily due to calcium - 11.45% and phosphorus - 5.08% [1].

Thus, in the enamel affected by caries, there is an increase in the weight percentage of carbon, sulfur, chlorine and nitrogen, and the weight percentage of oxygen, sodium, phosphorus, calcium and zinc decreases.

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牙周炎患者牙痛伴牙龈退缩的治疗

**TREATMENT OF DENTAL HYPERESTHESIA ACCOMPANIED BY
GINGIVAL RECESSION IN PATIENTS WITH PERIODONTITIS**

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抽象的。对正在研究的主题的科学著作的分析结果表明,目前国内开发的脱敏卫生产品和再矿化制剂的使用水平是一种分阶段治疗牙齿敏感度增加并伴有牙龈退缩的患者的方法。牙周病的背景,不足。显然,这是由于基于证据的研究数量有限(包括一组对信息、实验室和临床指标的评估)。在现代条件下解决这些问题的权宜之计证明了这项研究与实际医疗保健的相关性。

关键词: 感觉过敏, 再矿化疗法, 牙龈萎缩。

Abstract. *The results of the analysis of scientific works on the subject under study indicate that at present the level of use of desensitizing hygiene products and remineralizing preparations of domestic development as a phased method of treating patients with increased sensitivity of the teeth, accompanied by gingival recession against the background of periodontal disease, is insufficient. Apparently, this is due to the limited number of evidence-based studies (including a set of assessments of informative, laboratory and clinical indicators). The expediency of solving these problems in modern conditions proves the relevance of this study for practical health care.*

Keywords: *hyperesthesia, remineralizing therapy, gum recession.*

Relevance.

In the structure of dental diseases, one of the leading places is occupied by inflammatory periodontal diseases. An analysis of the literature data of domestic and foreign authors indicates that the number of periodontal diseases is currently increasing. The results of numerous studies demonstrate that the intensity of these diseases among the Russian population is high [5]. In 68.5% of cases of the total number of periodontal tissue diseases, patients have periodontitis of moderate severity, in 22.5% of mild severity, which is accompanied by phenomena of increased sensitivity of hard dental tissues. Pathology of periodontal tissues can lead to gum recession as a result of atrophy, removal of inflammation and swelling, after professional oral hygiene, incorrect use of ultrasound equipment, resulting in mechanical damage to tooth structures. The appearance of a localized recession in individuals with periodontal tissue disease leads to increased complaints of increased sensitivity of hard dental tissues, discomfort in the oral cavity, and disruption of basic functions [2].

There are several groups of drugs that are used as a conservative treatment for increased tooth sensitivity. These are drugs that block the transmission of a nerve impulse; dentin adhesives; fluorine-containing varnishes; desensitizing toothpastes, rinses. In the complex treatment of hypersensitivity of hard tissues of the tooth during gum recession, the main aspect is the remineralization of hard tissues of the tooth. The main components of remineralizing preparations are calcium, phosphates, fluorides, macro- and microelements, which help to strengthen and restore the hard tissues of the tooth. Remineralizing solutions and suspensions do not have a prolonged effect on the hard tissues of the tooth, so the therapeutic effect is not long-lasting and relapses of the disease occur quite often [6]. Specialized fluorine-containing varnishes are kept on the tooth surface for a long time, forming a film adjacent to the tooth enamel. In recent years, desensitizing hygiene products (toothpastes, rinses, toothbrushes), as well as domestically developed remineralizing preparations (solutions, suspensions, gels, varnishes) have been developed and put into practice. However, there is no complexity in the treatment of hyperesthesia accompanied by gingival recession, which indicates the need to develop and use an experimental model and conduct additional studies (including a set of assessments of informative, laboratory and clinical indicators), improve the method of treating hyperesthesia of the teeth, accompanied by gingival recession [1].

Means that help patients control tooth sensitivity throughout almost their entire lives are special toothpastes. The use of these pastes is mainly a long-term indication for the continuation of the use of the paste are subjective sensations of the patient. Periodically it is recommended to replace the paste. Pastes contain biologically active components such as potassium salts (nitrate, chloride), fluo-

rides (sodium fluoride, aminofluoride, sodium monofluorophosphate), strontium salts (chloride), calcium compounds (calcium glycerophosphate, hydroxyapatite), citrates (zinc). The most common and effective pastes on the Russian market are: pastes of the Sensodine series - Sensodine C (contains active ingredients: 10% strontium chloride), Sensodine R (contains active ingredients: potassium chloride, zinc citrate and fluoride sodium). The desensitizing effect of these pastes appears quickly, after 2-3 days from the start of application. Oral-B series pastes Oral-B contains active ingredients: sodium fluoride and potassium nitrate. Dentin abrasiveness index (DAI) is 37. Improvement occurs after 3-5 days of use with 2 brushings. After 1 month, sensitivity disappears in 90% of patients. "Oral-B" contains an active ingredient - hydroxyapatite (17%), which fills the tubules, tightly clogging the inlets and restoring intratubular pressure. DAI is 30. Elimination of pain occurs on the 4th-9th day of use. Paste "President" contains active ingredients: potassium nitrate, sodium fluoride, in addition, linden and chamomile extracts. It is recommended to apply 2-3 times a day [3]. As desensitizing toothpastes of domestic production, we can recommend the following pastes: "Parodontol", containing hydroxyapatite. "Pardontol-sensitive" containing strontium chloride, zinc citrate, vitamin PP "Pearl" with 2.5% calcium glycerophosphate, "New Pearl" with calcium glycerophosphate, etc. Brushes for sensitive teeth should be soft or very soft depending on the severity of hypersensitivity manifestations, the tips of the bristles are rounded. The trimming shape of the brush field is preferably even. An example of such a brush can be a special toothbrush for sensitive teeth "Oral-B with super soft bristles" [2].

In order to prevent the occurrence and development of hypersensitivity of hard dental tissues, dentists should, when examining patients, pay attention to the initial signs of diseases leading to hypersensitivity: these are periodontal diseases, enamel erosion, enamel abrasion, wedge-shaped defects. Properly use tools for root treatment during tartar removal and polishing of the tooth surface, avoid excessive polishing of the exposed root during the removal of staining used to control the effectiveness of cleaning, isolate the gum during professional whitening, produce dentures and crowns with high quality and competently.

In order to prevent the occurrence and development of hypersensitivity of hard tissues of the teeth, patients should maintain oral hygiene, observing the correct brushing technique, use a small amount of toothpaste while brushing their teeth, brush their teeth without undue effort and no more than the recommended time, do not use brushes with a hard bristles, use brushes with rounded ends of the bristles, rinse your mouth with water immediately after eating acidified foods and carbonated drinks, brush your teeth no earlier than 30 minutes after eating acidified foods and drinks, avoid excessive or improper use of floss and other substances to clean contact surfaces teeth - when using toothpicks, do not damage the gums.

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固定条件下紧急医疗组织的现代方面
**MODERN ASPECTS OF THE ORGANIZATION OF EMERGENCY
MEDICAL CARE IN STATIONARY CONDITIONS**

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抽象的。 本文以科学出版物为基础，以医院中个别组织技术的例子为基础，论述了急救医疗组织的现代方面。 住院阶段为住院患者提供医疗服务的一个重要环节是救护车，其效率取决于根据科室不同区域的严重程度对患者进行正确分类以及紧急医疗服务启动的速度。

关键词: 医疗组织, 急救医疗, 住院条件

Abstract. *The article deals with modern aspects of the organization of emergency medical care on the examples of individual organizational technologies in hospitals based on scientific publications. An important link in the hospital stage of providing medical care in inpatient conditions is the ambulance unit, the efficiency of which is determined by the correct sorting of patients according to severity in different areas of the department and the speed of the start of emergency medical care.*

Keywords: *organization of medical care, emergency medical care, inpatient conditions*

The current stage of healthcare development is characterized by the standardization of processes for providing inpatient medical care and the gradual strengthening of its material and technical base. State guarantees for the provision of medical care are provided in hospitals around the clock in the following forms: emergency, urgent, planned.

In recent decades, there has been a steady increase in access to hospitals for emergency medical care, especially in urban areas, which is due to various factors:

changes in migration flows and patient routing, SARS and COVID-19 epidemics, growing urbanization, disruption of continuity in the work of polyclinics, emergency rooms and hospitals [1, 2, 3].

M.N. Sadykov and I.V. Klyushkin (2017) identified the main criteria for the quality of emergency medical care in a multidisciplinary hospital: arrival time; the correctness of medical care at the scene and during transportation; the presence of an anti-shock ward and an intensive care team in the admissions department; connection of the admission department with the ambulance team [4].

The main structural unit of a multidisciplinary hospital in the provision of emergency and urgent care is the admission and diagnostic department [5, 6]. E.I. Podgorbunskikh and E.V. Zimina (2014) studied the work of admission departments of 15 multidisciplinary hospitals in Moscow with more than 700 beds from the standpoint of a process approach. The authors identified eight sub-processes in the work of the admission department: organizational and coordinating; medical and diagnostic; expert; logistic; ethical-deontological; ensuring a sanitary and hygienic regime; preventing the spread of infectious diseases; work in emergency situations [7].

D.V. Belyshev et al (2015) also reviewed the work of the admissions department from a process approach. The authors compiled a passport for the process “Emergency Hospitalization of a Patient” and, using a medical information system, identified goals, limitations, a product of the process, a precedent, use case manager, role model, consumer, user, customer, process owner, performers, resource manager, resource owner, supplier process manager, and key metrics. The owner of the process “Emergency hospitalization of the patient” in the city clinical hospital № 1 named after N.I. Pirogov of Moscow is the head of the admissions department. The target indicators of the department’s work are the urgency of the reaction, the organization of diagnostics and the overall satisfaction of the patient. The “Emergency response” indicator is the time the patient spent in the emergency department from the moment of admission to the moment the diagnosis began. This indicator can be improved by reducing the average time for registering and identifying a patient by integrating with the automated information system of an ambulance station, by reducing the waiting time in the queue for seriously ill patients, by reducing the total time spent by the patient on the flow, by analyzing load peaks. The indicator “Organization of diagnostics” is the ratio of the time of carrying out diagnostic measures to the total time of the patient’s stay in the department. This indicator can be improved due to the rapid acquisition of data through the preparation of reports on time and by reducing the time for paperwork. To determine the indicator “Overall patient satisfaction”, it is necessary to conduct surveys and questionnaires [8].

I.M. Fazulzyanova and co-authors (2016) describe in their work several organizational approaches to improving the organization of the work of the admission

department: using the international principles of medical triage (APLS), identifying “weak points”, integrating various medical and diagnostic services within one admission department based on a process approach. On the basis of the Children’s Republican Clinical Hospital of the Republic of Tatarstan, after the implementation of the health care modernization program, the admission department was reformatted into a reception and diagnostic department, in which a round-the-clock post of an intensive care and advisory center was allocated. This center allows you to monitor the provision of emergency medical care in other medical institutions through the use of telemedicine technologies, as well as competently organize the routing of children in serious condition by communicating with resuscitation vehicles connected to the GLONASS system. The authors pay special attention to close interaction with the ambulance station and preliminary informing the staff of the admission department about the delivery of a patient in serious condition [9].

According to the experience of Novomoskovsk, Tula Oblast, the organization of a treatment and diagnostic department in a hospital reduces the number of repeated calls to the ambulance team, refusals to hospitalize, the risks of making an incorrect or inaccurate diagnosis by the ambulance team and hospitalization in a non-core department [10].

On the basis of CCH № 4 in Almaty, Kazakhstan, an innovative project for the provision of medical care was implemented using the methods of “multidisciplinary examination” and “team management of patients” in accordance with the world standards “Emergencyroom”. At the same time, all specialists who examine the patient and determine the tactics of treatment are in a single field. This approach to the organization of the admission department allowed: to reduce the number of medical errors and strengthen control over the examination of patients; reduce the time for transporting patients, reduce the waiting time for diagnostic procedures and reduce the time spent by medical personnel by automating the maintenance of medical records and increasing the efficiency of collecting anamnesis and making a preliminary diagnosis; reduce financial losses by optimizing the purchase of medicines and consumables, accounting for payment for all services, and eliminating the re-appointment of diagnostic tests [11].

According to G.K. Kausova and N.N. Musayeva (2017), the admission department of the hospital is the link between the pre-hospital and hospital stages of treatment, filtering patients who need and do not need hospitalization. The authors report an increasing role of emergency departments in the implementation of inpatient care systems, when physicians must more clearly differentiate between patients who need outpatient treatment and patients who need inpatient care [12].

At the same time, despite the success in providing emergency medical care, the problems of high mortality in patients with bleeding, peritonitis, concomitant injuries, and vascular diseases remain unresolved [13].

Non-observance of continuity in the activities of the outpatient healthcare system, ambulance and emergency medical teams, hospitals, as well as the mentality of doctors in the emergency department lead to an increase in the number of unreasonable hospitalizations. According to various literature sources, the number of hospitalized patients occupying an expensive inpatient bed without the necessary indications ranges from 15% to 40% [14, 15].

These factors make it necessary to carry out a scientific search for ways to solve problems. One of the solutions may be a new organizational technology for the Russian Federation based on international experience - the creation of emergency departments on the territory of large multidisciplinary hospitals [15, 16].

The inpatient emergency department is a modernized admissions department, the logistics center of the hospital, in which the entire primary laboratory and instrumental set of studies is performed and the profile of the patient is determined [17].

The work of Yu.P. Linets et al. (2017) is devoted to the first results of the work of the inpatient emergency department. In 2014, in the Alexander Hospital of St. Petersburg, an independent unit was organized in the reception and diagnostic unit - a 24-hour inpatient emergency department, consisting of seven short-stay beds and 13 dynamic observation beds, with a staff structure of 15.5 rates. The opening of such a department resulted in a reduction in the number of patients hospitalized in specialized beds by 11%, as a result of which a reserve of beds was created for planned hospitalization and an increase in the possibility of providing high-tech medical care. The authors note that the development of an emergency department in a hospital is possible only if the areas and staffing meet the standards of the order of the Ministry of Health of the Russian Federation dated June 20, 2013 № 388n "On approval of the procedure for providing emergency, including emergency specialized, medical care" [18].

Studies by R.R. Alimov and co-authors (2014) show that a large proportion of patients who seek emergency care in inpatient emergency departments are discharged after a few hours, and patients who are in serious condition or with impaired vital functions begin to receive assistance after a few minutes after admission [17].

V.M. Teplov et al. (2017) analyzed the generalized data on patients hospitalized in the intensive care units of the St. Petersburg SRC of emergency aid named after N.I. Dzhanelidze and the First St. Petersburg State Medical University. The analysis showed that in 10.4% of cases there were no indications for hospitalization in the intensive care unit. To optimize the work of intensive care units, it is advisable to create a three-level system of intensive care to provide basic (monitoring and minimal support for only one functional system), intermediate (monitoring and minimal support for at least two functional systems) and maximum

(presence or high risk of developing multiple organ failure or dysfunction) levels of intensive care [16].

Thus, in modern conditions, the inpatient emergency department is considered as the primary link of the hospital stage of medical care, the effectiveness of which is determined by the correct sorting of patients according to severity in different areas of the department and the speed of the start of medical care.

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秋明专门大学青年男性收缩血容量和分钟血容量
**SYSTOLIC AND MINUTE BLOOD VOLUME IN YOUNG MEN OF
SPECIALIZED UNIVERSITIES OF TYUMEN**

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摘要: 本文分析了秋明州四所专业大学的 136 名一年级青年男子的收缩压 (SBV, ml) 和分钟 (CO, ml) 血容量作为中心血流动力学重要指标的研究, 参与和不参与运动。 结果表明, 在年轻男性接受大学教育初期的中枢血流动力学评估中, CO 和 SBV 给出了其功能能力的客观概念。 经常锻炼有助于血液循环的经济化。

关键词: 青少年大学生, 中心血流动力学, 每搏和每分钟血容量, 运动。

Abstract: The article analyzes the study of systolic (SBV, ml) and minute (CO, ml) blood volume as important indicators of central hemodynamics in 136 first-year young men of four specialized universities in Tyumen, involved and not involved in sports. It is shown that in the assessment of central hemodynamics at the initial stage of obtaining university education by young men, CO and SBV give an objective idea of its functional capabilities. Regular exercise contributes to the economization of blood circulation.

Keywords: juvenile university students, central hemodynamics, stroke and minute blood volume, sports.

Introduction. Despite large-scale scientific and practical studies of central hemodynamics, the issue of its condition in adolescents living in Siberia, involved and not involved in sports, is not sufficiently covered [4, 5, 9, 15, 18].

Purpose: in adolescent students studying in the first year of specialized universities in Tyumen to consider the impact of sports on the indicators of systolic and minute blood volume.

Materials and methods. A survey of 136 youth students involved (53 - 39%) and not involved (83 - 61%) in sports, who started their studies in the first year at four specialized universities in the Siberian city of Tyumen, was conducted. Northern Trans-Ural State Agricultural University (NTUSAU) examined 42 students (25 and 17 boys respectively), 37 boys (22 and 15 respectively) were examined at the University of Tyumen (UOT), and Tyumen State Medical University (TymSMU) of the Ministry of Health of the Russian Federation examined 31 (respectively 19 and 12) students. The Industrial University of Tyumen (IUT) examined 26 (respectively 17 and 9) students. Sports: kettlebell lifting, cross-country skiing and biathlon, athletics, martial arts.

Heart rate (HR, beats/min) was determined by palpation by palpation of the radial artery in the wrist area. Measurement of systolic (SBP, mmHg) and diastolic (DBP, mmHg) blood pressure was carried out in a sitting position using the H.S. Korotkov's method. Pulse pressure (PBP, mmHg) was calculated from the difference between SBP and DBP values.

SBV was calculated according to the formula proposed in 1954 by I. Starr [25]:

$$SBV = 90.97 + (0.54 \times PBP) - (0.57 \times DBP) - (0.61 \times A),$$

where: SBV – systolic blood volume; PBP – pulse blood pressure; DBP – diastolic blood pressure; A – age, in years.

CO was calculated using the formula: $CO = SBV \times HR$.

During the study, physiological approaches to assessing the results obtained were followed [12, 16, 19].

The analysis of the material was carried out on the basis of mathematical calculations [8] with the calculation of the arithmetic mean (M), the arithmetic mean error (m). The significance of differences was assessed using Student's t-test. Results were considered statistically significant at $p < 0.05$. The examination was carried out in a state of physiological rest in the first half of the day in accordance with the sanitary and epidemiological rules on a voluntary basis with the informed consent of the students. The principles of voluntariness, the rights and freedoms of the individual, guaranteed by Articles 21 and 22 of the Constitution of the Russian Federation, as well as the Order of the Ministry of Health and Social Development of Russia №774n dated August 31, 2010 "On the Ethics Council" were observed.

Results and discussion. The calculation of SBV and CO using Starr's formula provides for HR, SBP, DBP, and PBP. We present the indicators of their values

among young men involved and not involved in sports at the initial stage of university education (tab. 1).

Table 1

Indicators of HR, SBP, DBP, PBP, SBV and CO among boys from universities in Tyumen in the first semester of university education (M±m)

| Index | University | | | |
|-------------------------------------|------------|-----------|-----------|-----------|
| | NTUSAU | UOT | TymSMU | IUT |
| Youth not involved in sports | | | | |
| HR | 76.6±1.8 | 75.2±1.7 | 79.2±1.9 | 75.6±1.6 |
| SBP | 121.4±2.4 | 120.8±2.2 | 124.5±2.3 | 120.5±2.3 |
| DBP | 71.3±1.4 | 68.5±1.2 | 74.1±1.5 | 71.7±1.5 |
| PBP | 50.1±1.4 | 52.3±1.4 | 50.4±1.3 | 49.1±1.1 |
| SBV | 66.71 | 69.18± | 64.96± | 66.16± |
| CO | 5109.98 | 5202.33 | 5144.83 | 5001.69 |
| Youths involved in sports | | | | |
| HR | 70.2±1.3 | 69.6±1.2 | 72.3±1.3 | 68.4±1.2 |
| SBP | 116.1±1.9 | 115.3±1.9 | 119.1±2.0 | 115.4±1.9 |
| DBP | 68.2±1.1 | 66.0±1.2 | 70.4±1.4 | 68.6±1.2 |
| PBP | 47.9±1.0 | 49.3±1.1 | 48.7±0.9 | 46.8±0.9 |
| SBV | 66.98 | 68.99 | 66.16 | 66.16 |
| CO | 4701.19 | 4801.70 | 4783.36 | 4525.34 |

Significant differences in HR were revealed among young men from various universities involved and not involved in sports ($p < 0.05$). Thus, the difference in HR between NTUSAU students and non-athletes in absolute terms was 6.0 beats/min, UOT students – 5.6 beats/min, TymSMU students – 6.9 beats/min, IUT students – 7.2 beats/min, which we regard as a manifestation of economization of blood circulation during regular sports (fig. 1).

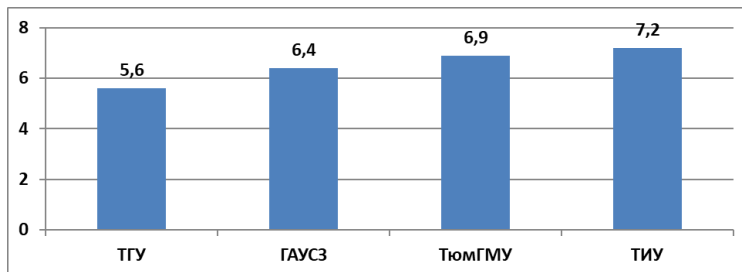


Figure 1. Differences in heart rate among young men from universities in Tyumen, involved and not involved in sports.

For many decades, SBP has always been in the field of view of specialists in various fields [3, 7, 11, 13, 17, 18, **22**, **23**], including physical education teachers working in universities and trainers of various specializations. SBP in the young men examined by us from various universities of the Siberian city was within the normative physiological values characteristic of adolescence. But, nevertheless, we should note that the SBP values in young men who regularly go in for sports are significantly ($p < 0.05$) lower than in non-athletes. Thus, the difference in SBP values between IUT students and non-athletes was 5.1 mmHg, NTUSAU students 5.3 mmHg, TymSMU students 5.4 mmHg, and UOT students 5.5 mmHg (fig. 2).

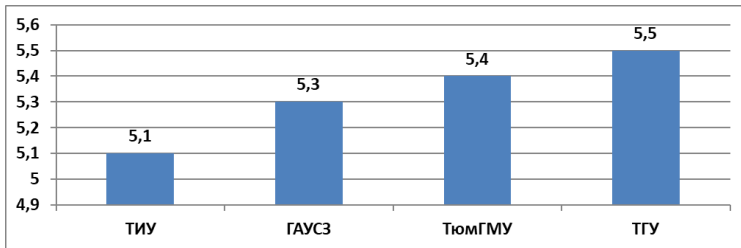


Figure 2. Differences in the value of systolic blood pressure among young men of universities in the city of Tyumen, involved and not involved in sports.

It is well known that the value of arterial pressure largely depends on both the stroke volume and the diameter of arterial vessels, which determine the peripheral resistance to blood flow [6, 10, 14, 20].

In the present study, SBV in young men involved in sports was in the extreme range from 66.16 ml to 69.18 ml, i.e. the difference was 3.02 ml. In young men not involved in sports, the spread of SBV values was noted in the range from 66.16 ml to 68.99 ml, i.e. the difference was 2.83 ml, which is therefore 0.19 ml less. For comparison, we note that [1, 2, 24], who studied hemodynamics in young men from the Tyumen Oblast, indicate SBV values of 60.1 ml for rural and 60.2 ml for urban boys.

In young men involved in sports, CO in absolute terms was less than that of their peers not involved in sports, which we attribute, first of all, to the economical work of the cardiovascular system (CVS) against the background of her constant training during sports. Thus, in NTUSAU students, the difference was 408.79 ml, in UOT students - 400.63 ml, in TymSMU students - 361.47 ml, and in IUT students - 476.35 ml (fig. 3).

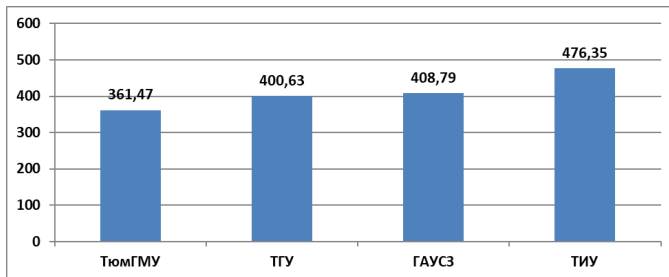


Figure 3. Differences in the value of minute blood volume among young men of universities in Tyumen, involved and not involved in sports in the first semester of study.

It should be borne in mind that the CO value depends not only on SBV and HR, but also on venous return, i.e. the amount of blood returned to the heart through the veins, because not all blood is ejected from the heart in one systole. Part of the blood always remains in the heart as a reserve (reserve volume), which is used, for example, during increasing physical exertion or emotional and mental stress [21, 26].

On the basis of the performed study, it can be concluded that at the initial stage of training young men in specialized universities in the city of Tyumen, the functional indicators of central hemodynamics are within the physiologically determined normative values. In assessing the CVS activity of young men, CO and SBV give an objective idea of its functional capabilities, and regular sports activities significantly contribute to the economization of blood circulation.

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牙周病二级预防的个性化方法

PERSONALIZED APPROACH TO SECONDARY PREVENTION OF PERIODONTAL DISEASES

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摘要。 俄罗斯人口中牙周病患病率高，生活质量与病理过程活动成正比，需要改进预防和预防性治疗措施。 在这种情况下，高科技设备方法变得越来越普遍——用于牙周袋卫生的“Vector”系统，同时用臭氧水进行防腐处理，专为牙周病学中的个性化预防和保守治疗而设计。

该研究的目的是在慢性牙周炎的二级预防和个性化治疗框架内研究改良载体治疗技术对牙齿组织及其代谢过程的影响。

关键词：牙周病，载体疗法，臭氧水，二级预防，个性化治疗。

Abstract. *High prevalence of periodontal diseases among Russian population, deterioration of life quality in proportion to the activity of pathological process require improvement of prophylactic and preventive treatment measures. In this situation high-tech apparatus methods are becoming more widespread - the system “Vector” for sanitation of periodontal pockets with simultaneous antiseptic treatment with ozonized water, designed for personalized prevention and conservative therapy in periodontology.*

The aim of the study was to study the impact of the modified vector-treatment technique within the framework of the secondary prevention and personalized therapy of chronic periodontitis on the tooth tissues and metabolic processes in them.

Keywords: *periodontal diseases, Vector therapy, ozonized water, secondary prevention, personalized therapy.*

Significance of a personalized approach to the prevention and treatment of inflammatory periodontal diseases.

Currently, 8 out of 10 people over 65 years of age globally have various forms of periodontal diseases. In most cases the process starts to develop in childhood and is often associated with orthodontic treatment [5]. In Russia, according to statistics, every 2 out of 3 patients do not take any action, giving up rather high medical costs as a reason. As reported by the recent study of the Russian Society of Periodontology conducted in 9 regions of the country, 65% of patients with a periodontal pathology of some sort are not adherent to treatment.

It should also be noted that in recent years inflammatory and inflammatory-destructive periodontal diseases are increasingly combined with comorbid pathologies, the fact aggravating patient's condition, contributing to the tooth loss, appearance of foci of chronic infection in the oral cavity, microbial sensitization and other disorders [1,2]. When performing periodontal checkups of the population, in addition to the microbial factor, it is necessary to monitor various significant aspects of pathology – hereditary background, socio-economic status, behavior, risk factors, ethnicity, etc.; all these allow planning proper prevention and treatment of periodontal diseases [6].

There are a great number of clinical and diagnostic approaches of different relevance in this very essential issue. However, the long-term ignorance of the etiopathogenetic relationship and interdependence of systemic diseases and periodontal pathology, disproportion between the level of professional knowledge and material support in a number of cases, underestimation of the motivational approach – all these create certain challenges for developing and introducing programs for the prevention and treatment of periodontal diseases. In addition, to develop a personalized program, it is necessary to identify features of each patient, and, accordingly, methods and means of prevention and treatment, based on the results of an individual set of diagnostic investigations [10]. Considering all the above, it becomes evident that new approaches to prevent the development of dental pathology and improve the effectiveness of other therapeutic manipulations are a must; these help highlight the priority areas of primary and secondary prevention of inflammatory periodontal diseases.

How significant is secondary prevention of periodontal diseases within specialized periodontal care?

Most experts consider primary and secondary prevention as two stages of a single process designed to ensure a high level of individual and public health, including its dental aspects. However, when solving the problem of preventing caries and inflammatory periodontal diseases, the main focus is not on primary prevention, but on the diagnosis and treatment of the incipient diseases and their complications, i.e. secondary and tertiary prevention.

Secondary prevention is aimed at early prevention of relapses and complications, as well as their progression. In case of periodontal pathology at this stage, dentists should strive (with the help of appropriate diagnostic investigations) to recognize the early signs of incipient pathology in order to prevent their degeneration into more severe conditions. In our opinion, secondary prevention should be aimed at identifying the risk of pathology in the periodontium.

As part of specific secondary prevention of periodontal pathology, medical and preventive options should be aimed at eliminating inflammation, preventing further destruction and, if possible, stimulating regeneration of the lost periodontal tissues and preventing relapses. To achieve these goals, it is necessary, first of all, to eliminate the microbial factor by thorough mechanical removal of supra- and subgingival dental plaque. In the treatment of initial forms of inflammatory periodontal diseases this can be achieved by scaling and root polishing, and by performing concomitant anti-inflammatory and, if indicated, antimicrobial therapy. [7,8,9].

Why should the ultrasound method using the Vector complex be preferred at the stage of individual secondary prevention of periodontal diseases and supporting therapy?

The minimally invasive hardware complex “VECTOR”, Durr Dental, Germany, has been a leader in the treatment and prevention of periodontal diseases for many years, as it is an almost painless treatment. It helps cope with such complex problems as elimination of the biofilm, granulation tissue, dental plaque, endotoxins; de-epithelializes the inner wall of the periodontal pocket; polishes tooth roots without excessive removal of cement, which is important for the tissue structure regeneration and rapid and effective elimination of bacteria. Remission of the disease becomes possible due to gentle exposure of the “VECTOR” complex. The treated surfaces of the root and surrounding soft tissues retain their condition unchanged for a long time after processing due to the unique work of the device and the use of a special suspension for polishing. In addition, it is possible to prevent the spread of infection in a medical facility, the fact being of special significance during current epidemiological situation. Absence of oscillatory movements of instruments does not result in any spray of infected aerosol from the oral cavity into the environment [3,4].

Why is it necessary to search for non-drug means for local treatment and individual prevention of periodontitis?

However, plaque control procedures are effective in combination with the conservative treatment, and an antibiotic therapy is a key part of this treatment due to the infectious etiology of the disease. The search for new antimicrobial agents is

an acute problem nowadays because of the increased resistance to antibiotics and antiseptics. Non-drug approaches are in the focus of attention nowadays. Having a pathogenetic effect, application of these techniques can replace or substantially limit the need for drugs. As reported, ozone therapy is a highly effective method of treating the diseases caused by the inflammation of the bacterial flora. Recently, local treatment of the periodontal pocket with ozonized physiological solution, ozonized water from a syringe, applications with ozonized olive oil has been given a priority before other therapeutic options. However, when applied locally, ozone has only a surface antibacterial effect and does not involve the entire trophism of the bone and periodontal tissues [8,9].

In this situation, high-tech hardware-based techniques are becoming more widespread, among them is the Vector system for sanitizing periodontal pockets with simultaneous antiseptic treatment with ozonized water intended for personalized prophylaxis and conservative therapy in periodontology.

Why is it necessary to study the effect of the modified vector therapy technique within the secondary prevention and personalized therapy of chronic periodontitis on the tooth tissues and metabolic processes in them?

When developing a personalized approach to treatment and medical and preventive procedures, we detected a direct dependence of the value of the caries intensity index on the severity of inflammatory periodontal events.

This implies that complex administration of methods and drugs aimed at the elimination of the cariogenic situation in the oral cavity combined with procedures to prevent the progression of periodontal pathology is the most important factor to increase the effectiveness of individual programs for the secondary prevention of periodontal diseases in the studied population. We performed laboratory studies of the enamel and cementum of the teeth removed for orthodontic treatment to evidence clinical effectiveness of these personalized measures.

How many patients were required to solve the main problem of the study?

The study included 71 patients of the dental clinic of Voronezh State Medical University with diagnosed chronic generalized periodontitis. As part of secondary prevention, all patients underwent professional teeth cleaning followed by instructions on individual oral hygiene. Patients of the experimental group (36 people-51%) were exposed to ultrasonic dental treatment using the “Vector” complex with ozonized water during the second visit to the dental office. Patients of the control group (35 people - 49%) were administered a course of conventional pharmacotherapy.

Clinical and laboratory investigations included: past medical history, dental examination, stomatoscopy, index assessment, X-ray examination, bacterioscopic

and cytological examination, scanning electron microscopy (SEM) and electron probe microanalysis (EMPA), which provide information about the events occurring at the micron and submicron levels.

What is the significance of the increased enamel resistance to pathological processes when performing medical procedures using the VECTOR complex with ozonized water?

The developed method of secondary prevention and personalized therapy of periodontitis resulted in a pronounced clinical effect. The index parameters were 2 times lower compared with those in patients of the control group; this evidenced elimination of inflammation in the periodontal structures, successful prevention of the process progression. These results were supported by the cyto-bacterioscopic examination and extended stomatoscopy findings throughout the year. Regeneration of the bone tissue up to 3 mm in 52.7% of cases in patients of the experimental group who received personalized treatment using ultrasound and ozonized water was supported radiographically.

What had to be done to confirm the results?

We performed laboratory studies of the hard tissues of 17 extracted teeth to confirm clinical effectiveness of the developed method for the prevention and treatment of chronic periodontitis. The combined automatic SEM of enamel, dentin and cementum at 50,000X magnification and EMPA provided us with an opportunity to determine their chemical composition, features of metabolic processes. In patients of the control group, where conventional methods of prophylaxis and treatment were applied, there was registered a decrease in the amount of Ca by 1.4%, Mg by 4.5% and Na - 38.3%. We can explain this fact as a decreased intake of these elements from the oral fluid due to an inflammatory and destructive process, and a violation of microcirculation in the periodontal structures surrounding the hard tissues of the tooth, which does not meet the goals of prevention. In patients of the experimental group there was registered an increase in the amount of “building” elements: Ca - by 35.2%, P - by 54.4%, Mg - by 76.2%, Na - by 32.5%. Our studies have demonstrated a great variability in the concentration of Mg, as the most active component in the metabolic processes of the enamel. The number of “destructive” elements accompanying pathological reactions in the hard tissues of the tooth and periodontium decreased: Cl by 43.5%, N by 9%, C by 22.3%. The parameters obtained with the help of EMPA allow us to conclude about the positive effect of preventive and personalized therapeutic measures using the Vector system with ozonized water on increased enamel caries resistance due to normal state of the periodontal tissue by reducing or eliminating the microbial factor that causes and aggravates damage to periodontal structures.

What is EPMA's support for preventive and therapeutic procedures for periodontal pathology?

As international experience demonstrates, under growing competitiveness, planning a high volume of preventive and therapeutic care, which is necessary for 100% of adults and children, is a kind of guaranteed stability. A key issue in this direction was the decision made at the 1st World Congress of the European Association for Preventive Personalized Preventive Medicine to create a dental department in Bonn, Germany, in September 2011. Since that the staff of the department have been actively involved in the prevention of periodontal disease and caries under the guidance of the above organization and annually present the results of their achievements at the European level.

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早产儿视网膜病变病程的特点

THE PECULIARITY OF THE COURSE OF RETINOPATHY OF PREMATURITY

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抽象的。本文介绍了 2017-2019 年 COVID-19 大流行期间以及 2021 年 COVID-19 大流行期间的躯体状态和动态早产儿视网膜病变病程特征的临床和统计分析结果。发病率从 3 年观察期间的 104 人增加到 1 年 (2021 年) 的 84 人。2021 年, 呼吸系统疾病 (83%) 在患者中占主导地位, 而不是 2017-2019 年盛行的神经病理学 (65.9%)。5% 的 RP 患儿感染了冠状病毒, 并伴有肺损伤。在大多数 RP 病例中, 疾病会自发消退。在发生频率方面, 2017-2019 年和 2021 年均以 I 期和 II 期疾病为主, 大多数患者在 3 区发展 (OD 为 54%, OS 为 62%)。

关键词: 早产儿视网膜病变, 躯体状态, 冠状病毒感染。

Abstract. *The article presents the results of a clinical and statistical analysis of the somatic status and characteristics of the course of retinopathy of prematurity in dynamics - for 2017-2019 and in more detail in 2021 during the COVID-19 pandemic. There was an increase in the incidence from 104 people during 3 years of observation to 84 people in 1 year (2021). In 2021, respiratory disorders (83%) are leading in patients, instead of neurological pathology (65.9%), which prevailed in 2017-2019. Coronavirus infection in children with RP was noted in 5% of cases and was accompanied by lung damage. In most cases of RP,*

spontaneous regression of the disease occurs. In terms of frequency of occurrence, both in 2017-2019 and in 2021, stages I and II of the disease prevail, developing in zone 3 in most patients (54% for OD and 62% for OS).

Keywords: *retinopathy of prematurity, somatic status, coronavirus infection.*

Relevance

Retinopathy of prematurity (RP) is a disease of the retina and choroid that is one of the leading causes of preventable blindness in children [1,2]. RP remains an urgent problem in pediatric ophthalmology, despite the development of modern methods of diagnosis and treatment [1]. One of the main factors in the occurrence of RP in children is early gestational age and low birth weight. Other specific factors of RP are comorbidities and related conditions: prolonged use of respiratory support, neonatal infections and sepsis, neurological dysfunctions, and others [3]. Kang E.Y., et. all. (2018) by conducting a study. found that in Taiwan over 10 years, the average prevalence of RP did not show any significant change, while the proportion of children requiring specialized ophthalmic treatment increased. Low birth weight, multiple pregnancies, being male rather than female, from their point of view, were independent risk factors for the development of RP [4]. In turn, a decrease in the risk of developing RP correlates with a decrease in the risk of comorbidities in preterm infants [3]. This determines the relevance of studying the somatic status of premature babies for the prevention and early diagnosis of RP. The ongoing search for risk factors and assessment of their impact on the incidence of RP will improve existing screening programs to determine the risk group. The interaction of ophthalmologists, neonatologists, anesthesiologists and pediatricians is important to carry out the necessary screening, treatment and follow-up of children with RP [3].

Purpose. Clinical and statistical analysis of the somatic status and characteristics of the course of retinopathy of prematurity in dynamics - for 2017-2019 and in more detail in 2021 during the COVID-19 pandemic.

Materials and methods. A retrospective analysis of the discharge from the perinatal center and outpatient records of 104 children with RP observed in 2017-2019 and 84 children with RP in 2021 was carried out in the consultative and diagnostic room on the basis of the ophthalmology department of the children's hospital SBHCI TO "OCH №2" in Tyumen. Statistical analysis of the results obtained was carried out using STATISTICA (version 10, license agreement № 4190051 of 03.05.2019).

Research results. The study showed that there was a trend towards an increase in the number of children with RP: for 1 year (in 2021) 84 people were identified, for 3 years (2017-2019) - 104 people. By gender, among children with RP in 2017-2019 and 2021, boys predominated - 60 and 44 patients, respectively (57.7% and

52%), girls accounted for 44 and 40 patients, respectively (42.3% and 48%).

It was found that the average gestational age of children with RP in 2021 was 28 weeks (24.5; 32.3) with an average birth weight of 1017 ± 286.0 19 children with RP (23%) were born from multiple pregnancies. In 2017-2019, concomitant somatic pathology of patients with RP was represented in 65.9% by neurological pathology, in 38.7% by surgical pathology, and in 24.9% by infectious pathology. In 2021, among the comorbidities of this group of patients, there is a predominance of respiratory disorders in 70 patients (83%), hematological pathology occupies the second place in terms of frequency of occurrence - in 61 patients (73%), the third place is given to neurological pathology - in 58 patients (69%) (tab.1).

Table 1
Structure of concomitant somatic pathology in children with RP in 2021

| Concomitant pathology | Number of patients | |
|---------------------------------|--------------------|----|
| | people (n) | % |
| Neurological | 58 | 69 |
| Respiratory disorders | 70 | 83 |
| Surgical | 31 | 37 |
| COVID-19 | 4 | 5 |
| Other infectious | 16 | 19 |
| Cardiovascular | 50 | 60 |
| Hematological | 61 | 73 |
| Pathology of the urinary system | 16 | 19 |
| Other | 54 | 64 |

Neurological pathology in most children with RP was represented by cerebral ischemia (64%, 54 patients), hematological - anemia of prematurity (71%, 60 patients). Among the surgical pathology, hemangiomas of various localization were in the lead (12%, 10 patients). Almost every second child had an atrial septal defect (54%, 45 patients) or bronchopulmonary dysplasia (BPD) (55%, 46 patients). 71 patients (85%) needed respiratory support in the neonatal period. Among the surgical pathology, hemangiomas of various localization were in the lead (12%, 10 patients). Almost every second child had an atrial septal defect (54%, 45 patients) or bronchopulmonary dysplasia (BPD) (55%, 46 patients). 71 patients (85%) needed respiratory support in the neonatal period.

In 2021, more frequent development of RP was found in the left eye (OS) - in 83 patients (99% of children with RP) than in the right eye (OD) - in 75 patients (89%), in both eyes (OU) RP occurred in 74 patients (88%). Among the stages of RP in 2021, as in 2017-2019, there is a predominance of stages I and II, while some children had intermediate options. In 1 patient (1%) in 2021, a posterior aggressive form of RP (PARP) was detected in both eyes (tab. 1).

Table 1

Distribution of children by RP stages in 2017-2019 and 2021

| RP Stages | Number of children with RP | | | | | |
|-----------|----------------------------|-------|------------------|--------|----|----|
| | 2017-2019 (104 people) | | 2021 (84 people) | | | |
| | people | % | OD | | OS | |
| people | | | % | people | % | |
| I | 60 | 57,69 | 36 | 43 | 44 | 52 |
| I-II | - | - | 8 | 10 | 7 | 8 |
| II | 20 | 19,23 | 15 | 18 | 18 | 21 |
| II-III | - | - | 3 | 4 | 4 | 5 |
| III | 23 | 22,12 | 10 | 12 | 9 | 11 |
| IVa | 1 | 0,96 | 1 | 1 | - | - |
| IVb | | | 1 | 1 | - | - |
| V | - | - | - | - | - | - |
| PARP | - | - | 1 | 1 | 1 | 1 |

It was found that in 2021 RP occurred mainly in zone 3 - in 45 people (54%) on OD and in 52 people (62%) on OS (tab. 2). “Plus” disease developed in 5 cases (6%) on OD and 4 cases (5%) on OS.

Table 2

Distribution of children depending on the area of localization of RP in 2021

| RP localization zone | Amount of children | | | |
|----------------------|--------------------|----|--------|----|
| | OD | | OS | |
| | people | % | people | % |
| 1 | 1 | 1 | 1 | 1 |
| 1-2 | 1 | 1 | 2 | 2 |
| 2 | 11 | 13 | 10 | 12 |
| 2-3 | 17 | 20 | 18 | 21 |
| 3 | 45 | 54 | 52 | 62 |

All 80 children with stage I-II RP in 2017-2019 had a spontaneous regression of the disease. In 82.6% of cases (19 patients) of stage III RP, laser coagulation of the retina (LCR) was required, after which induced regression was achieved in 18 patients (78.26%) from this group. In one patient, due to severe somatic pathology, LCS could not be performed. In 2021, self-regression of RP also occurred in the majority of patients - in 53 people (71%) on OD and in 62 people (75%) on OS. Induced regression after LKS was observed in 15 people (20%) on OD and in

13 people (16%) on OS. Two patients (3%) with stages IVa and IVb underwent vitreoshwartectomy.

Conclusions. The number of patients with diagnosed retinopathy of prematurity increased: 2017-2019 - 104 people, 2021 - 84 people. RP develops slightly more often in boys - 57.7% and 52% of patients in 2017-2019 and 2021, respectively. The peculiarities of the frequency of occurrence of somatic pathology in children with RP were revealed: in 2021, respiratory disorders are in the lead - in 83% of patients (of which BPD - 55%), instead of neurological pathology, which prevailed in 2017-2019 (65.9% of patients). In addition, hematological diseases (73% of patients), neurological pathology (69% of patients) prevail in the structure of comorbidities in 2021. Coronavirus infection in children with RP was noted in 5% of cases and was accompanied by lung damage. In 2021, in 88% of patients, RP occurred in both eyes, while it was more often observed in the left eye (99% of children with RP). In most cases of RP, spontaneous regression of the disease occurs (71% of patients on OD and 75% on OS). In terms of frequency of occurrence, both in 2017-2019 and in 2021, stages I and II of the disease prevail, developing in zone 3 in most patients (54% for OD and 62% for OS). "Plus" disease develops only in a small proportion of patients (6% for OD and 5% for OS).

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血脂异常引起的 Purcher 视网膜病变
PURCHER'S RETINOPATHY IN DYSLIPIDEMIA

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抽象的。本文介绍了对一名 71 岁 Purcher 型视网膜病变患者的临床、实验室和仪器研究方法的分析。去看医生的原因是结膜下出血。在代偿性动脉高血压 1 度和每年 2-3 次保守血管治疗疗程的背景下,显示胆固醇和甘油三酯升高。眼科表现是体内代谢过程失代偿的标志,也是对高胆固醇和甘油三酯进行血脂异常治疗的指征。

关键词: Purcher 视网膜病变、血脂异常、甘油三酯。

Abstract. *The article presents an analysis of clinical, laboratory and instrumental research methods in a 71-year-old patient with Purcher type retinopathy. The reason for going to the doctor was subconjunctival hemorrhage. Revealed an increase in cholesterol and triglycerides, against the background of compensated Arterial hypertension 1 degree, and courses of conservative vascular therapy 2-3 times a year. Ophthalmic manifestations are a marker of decompensation of metabolic processes in the body and an indication for prescribing dyslipidemic therapy for elevated cholesterol and triglycerides.*

Keywords: *Purcher's retinopathy, dyslipidemia, triglycerides.*

Modern scientific literature describes isolated rare clinical cases of Purcher's retinopathy (PR) against the background of acute pancreatitis (AP) and newly

diagnosed type 2 diabetes mellitus (DM) [2]. In 1910, O. Purtscher first described changes in the fundus of the eye in compression trauma of the skull, which, from his point of view, were caused by lymphorrhagia [7]. As etiological factors of changes in the retina, 2 groups of causes are distinguished. The first group is associated with acute compression injuries of the skull, trunk, chest, abdomen, fractures of tubular bones, orthopedic interventions, fat embolism, liposuction, barotrauma, shaken baby syndrome. The second group of causes, leading to similar changes in the retina, is not associated with trauma, and is commonly called Purcher's type retinopathy (PR). Her reasons: AP, pancreatic adenocarcinoma, chronic renal failure, hemolytic uremic syndrome, systemic connective tissue diseases, preeclampsia and difficult labor, postpartum period, lymphoproliferative diseases, including multiple myeloma, lymphomas, bone marrow transplantation, thrombotic thrombocytopenic purpura, cryoglobulinemia, intraorbital steroid injections, retrobulbar anesthesia and other conditions. Eye involvement can be unilateral or bilateral. In 60% of cases with AP, a bilateral lesion is typical [2,4]. Diagnostic criteria for PR have been developed: extensive cotton-wool lesions in the macular area and around the optic nerve disc (OND) (in 93% of cases), retinal hemorrhages in 65% of cases [4]. White spots are pathognomonic for PR. They are multiple white retinal lesions with a clear demarcation line (within 50 μm) between the affected retina and adjacent normal retinal vessels. Due to the fusion of "cotton" spots in the macula and OND, a picture of a pseudo-cherry spot may occur, which must be distinguished from the "true" cherry-red spot in central retinal artery occlusion [2,3,4].

Modern theories explain the development of retinopathy by the formation of microemboli. Their source can be air emboli during traumatic chest compression, fat embolism is formed in the case of fractures of tubular bones or enzymatic digestion of omental fat in pancreatitis, amniotic fluid embolism can develop during childbirth and the postpartum period, as well as the accumulation of granulocytes as a result of complement activation. In general, arterial occlusion causes the formation of an infarction of the microvascular bed against the background of angiospasm [2,3].

Dyslipidemia is the most important factor in the formation and progression of atherosclerosis, as well as related cardiovascular diseases (CVD), including infarcts of the heart and brain vessels. Significant progress has been made in the diagnosis and treatment of atherosclerosis. However, the prevalence of CVD risk factors such as diabetes mellitus and arterial hypertension is on the rise. At the same time, there is a high frequency of comorbid pathology, which has a progressive course, leading to disability and early mortality [5,6]. Currently, within the framework of comorbid pathology, mainly in the elderly, there is a high frequency of vascular lesions of the structures of the eyeball and adnexa of the eye. We have

described various variants of ophthalmopathy, including ischemic neuropathy, which are the most important medical and social problem leading to blindness and low vision [1,5,6].

The purpose of the study is to present an analysis of the clinical observation of a patient with Purcher's retinopathy against the background of dyslipidemia.

Materials and methods. In October 2022, 3 patients with eye fundus changes characteristic of Purcher's retinopathy, two of them men aged 71 and 74 years, and 1 woman aged 72 years, applied to the multidisciplinary clinic of the university. The analysis of clinical and laboratory parameters revealed lipid profile disorders with an increase in cholesterol and triglycerides (TG). According to the biochemical study, no damage to the pancreas was detected, the indicators of sugar in capillary blood were within the age norm. Standard ophthalmological examination included: visometry, tonometry, perimetry, biomicroscopy of the anterior segment of the eye and vitreous body, as well as ophthalmoscopy of the fundus. Visometry - determination of visual acuity without correction and maximally corrected visual acuity was carried out according to the standard method. Tonometry - measurement of intraocular pressure was carried out using a non-contact automatic pneumotonometer from Reichert. Perimetry - the study of the peripheral boundaries of the field of view, the identification of central and paracentral scotomas was carried out on the perimeter of PNR-2-01 (Russia). Biomicroscopy of the anterior segment of the eye and the vitreous body was carried out using a SL-140 slit lamp manufactured by Carl Zeiss Meditec AG (Germany). Fundus ophthalmoscopy was performed behind a slit lamp under conditions of mydriasis using an Ocular MaxField 78D non-contact lens. In-depth special research methods included: OCT, ultrasound of the eyeball. Ultrasound of the eyeball (Ocuscan R×P from Alcon (USA)). Optical coherence tomography on the device RTVue-2000 OST (Optovue, Inc., Fremont), autofluorescence of retinal vessels.

Results and discussion. Patient P., aged 71, complained of a hemorrhage in the projection of the palpebral fissure of the right eye, against the background of complete health for a day. History Arterial hypertension of the 1st degree, compensated by the constant intake of antihypertensive drugs systemically. Independently undergoes courses of vascular therapy in a day hospital 2-3 times a year, after which he notes an improvement in well-being, a decrease in the dose of antihypertensive drugs. It is not observed by an ophthalmologist, it is used only for the selection of spectacle correction for presbyopia.

On examination revealed. Visual acuity OD 0.5 with +1.5 correction D = 1.0 / OS 0.5 with +1.5 correction D = 1.0. IOP 14/13 mmHg OS - subconjunctival hemorrhage in the projection of the palpebral fissure from the limbus from 13.00 to 15.30, extending up to 1.0 cm. OU - phacosclerosis, a slightly pronounced asteroid in the vitreous body. The fundus of the eye: OND is pale pink, borders are

thin, E/D 0.3 arteries are narrowed, veins are moderately dilated, slightly uneven in caliber, extensive cotton-wool foci along the upper and lower vascular bundles. They are multiple white retinal lesions with a clear demarcation line between the affected retina and adjacent normal retinal vessels.

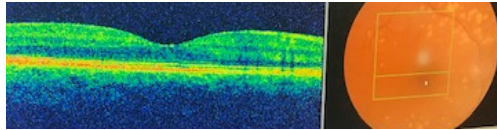


Figure 1. OCT linear section of the macular area of the retina, retinogram of the right eye of patient P., 71 g

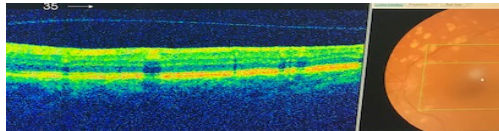


Figure 2. OCT linear section of the macular area of the retina, retinogram of the left eye of patient P., 71 g

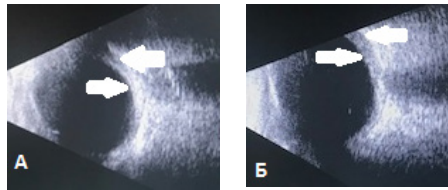


Figure 3. Ultrasonograms of the right (A) and left eye (B) eyeball of patient P., 71 g (white arrows indicate the thickened choroid of the posterior pole of the eye)

According to the blood lipid spectrum, an increase in cholesterol 5.98 mmol / l (reference value < 5.1 mmol / l), triglycerides 2.8 mmol / l (reference value 0-2.3), while low density lipoproteins 2.92 mmol/l (reference value 2.5-5.3), high-density lipoprotein 1.14 mmol/l (reference value 0.85-2.38); blood glucose 5.1 mmol/l, ALT and AST normal.

Conclusions.

With dyslipidemia, accompanied by an increase in cholesterol and triglycerides, against the background of compensated Arterial hypertension of the 1st degree, regular courses of vascular therapy 2-3 times a year in a day hospital, Purcher's retinopathy does not cause vision loss. However, the emerging subconjunctival hemorrhage and the presence of retinopathy serve as a marker of decom-

pensation of metabolic processes in the body and require a review of systemic therapy with the appointment of lipid-lowering agents as a method of treating clinical manifestations of eye damage in dyslipidemia.

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UDC 611.2-613.9

索引 D.I. Bogomazova 在评估秋明市大学生的心肺系统功能状态
**INDEX D.I. BOGOMAZOVA IN ASSESSING THE FUNCTIONAL
STATE OF THE CARDIORESPIRATORY SYSTEM OF YOUTH
STUDENTS OF UNIVERSITIES IN THE CITY OF TYUMEN**

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抽象的。目标：根据D.I.评估心肺系统的功能状态。博戈马佐夫。

材料与方法。对居住在城市并就读于秋明州三所专业大学的 125 名青年学生（18-22 岁）进行了检查。秋明州农学院（TyuSAA）检查了41名学生，秋明大学（UoT）检查了46名青年，俄罗斯联邦卫生部秋明国立医科大学检查了38名青年（TyuSMU）。在 Stange 和 Gench 测试的帮助下，研究了外部呼吸功能的指标，并在此基础上计算了 Bogomazov 指数（BI, c.u.）。

结果。根据在各专业大学学习的年轻人的 Stange 和 Gench 测试结果，确定了在吸气时自愿屏气的总持续时间没有超过青春期的正常生理值特征。就绝对值而言，在 20 岁时以及所有年轻男性中，无论训练情况如何，吸气和呼气时任意屏气持续时间的最大值均被记录下来。BI 证明了心肺系统活动的良好协调和年轻机体的高水平非特异性适应能力。当我们接近第一个成熟年龄段时，BI 值会降低。

结论。需要注意的是，从 21 岁开始，随着护照年龄的增加，吸气和呼气时任意屏气的时间以及 BI 都会减少。

关键词：男学生，大学，呼吸功能，Bogomazov 指数。

Abstract. Target: to assess the functional state of the cardiorespiratory system according to the D.I. Bogomazov.

Material and methods. 125 students of youthful age (18-22 years old) who lived in cities and enrolled in three specialized universities in Tyumen were examined. 41 students were examined at the Tyumen State Agricultural Academy (TyuSAA), 46 young men were examined at the University of Tyumen (UoT), and 38 young men were examined at the Tyumen State Medical University of the Ministry of Health of the Russian Federation (TyuSMU). With the help of Stange and Gench tests, indicators of the function of external respiration were studied and, on their basis, the calculation of the Bogomazov index (BI, c.u.) was carried out.

Results. It was established that the total duration of voluntary breath holding on inspiration, according to the results of the Stange and Gench tests in young men studying in various specialized universities, did not go beyond the normative physiological values characteristic of the period of adolescence. In absolute terms, the maximum values of the duration of arbitrary breath holding on inhalation and exhalation were noted at the age of 20 years, and in all young men, regardless of the training profile. BI testified to good coordination in the activity of the cardiorespiratory system and a high level of nonspecific adaptive capabilities of the youthful organism. As we approach the period of the first mature age, the BI values decrease.

Conclusions. It should be taken into account that starting from the age of 21, as the passport age increases, the duration of arbitrary breath holding on inhalation and exhalation, as well as BI, decrease.

Keywords: male students, universities, respiratory function, Bogomazov index.

Relevance. For many decades, one of the most studied problems of modern age-related physiology, clinical and sports medicine is the function of external respiration of people living in different regions of our country [6, 7, 8, 12]. In scientific and practical terms, studies showing the mechanisms of external respiration in connection with living in conditions of low atmospheric air temperature [3, 13], especially when playing outdoor sports [27], are important, which is especially relevant for residents of the Tyumen Oblast.

In clinical and sports practice, the function of external respiration is widely studied using Stange and Gench tests [5, 9, 17] to assess the resistance of the human body to hypoxia [19, 21, 24], including when playing sports [15, 28, 29, 32].

We cannot agree with the point of view [25] that the test with arbitrary breath holding on inspiration proposed in 1914 by the Russian doctor Vladimir Adolfovich Shtange and the test with arbitrary breath holding on exhalation proposed in 1926 by the Hungarian doctor Gönczy are currently routine. The tests mentioned above that we used showed their high efficiency in assessing the function of external respiration of various contingents of the population [16, 22, 31].

It should be noted that in our country, for many years, unique in nature and large-scale scientific research has been carried out, concerning the study of the

influence of the harsh climate of a number of regions of the Russian Federation on human health and vital activity [1, 2, 10, 18, 26, 30], in including respiratory function. As for the study of the function of external respiration and the resistance of the organism of male youth studying in various universities of the Tyumen Oblast to hypoxia, there are few such works in the literature available to us, which was the motivation for the study. There can be no doubt about the fact that in order to assess and control the function of external respiration of students, a physical education teacher of any university should have not only the easiest to use, but also the most safe methods for humans, allowing in a matter of seconds to assess the capabilities of the respiratory system of any student. In our opinion, the method of assessing the functional state of the cardiorespiratory system according to the D.I. index is simple and valid. Bogomazov [4, 14].

Target: to assess the functional state of the cardiorespiratory system according to the D.I. Bogomazov.

Material and methods. 125 students of youthful age enrolled in three specialized universities in Tyumen were examined. Of these, at the Tyumen State Agrarian University of the Northern Trans-Urals (TyuSAA) - 41 (32.8%) students; at Tyumen State University (UoT) - 46 (36.8%); at the Tyumen State Medical University of the Ministry of Health of the Russian Federation (TyuSMU) - 38 (30.4%) boys (fig. 1).

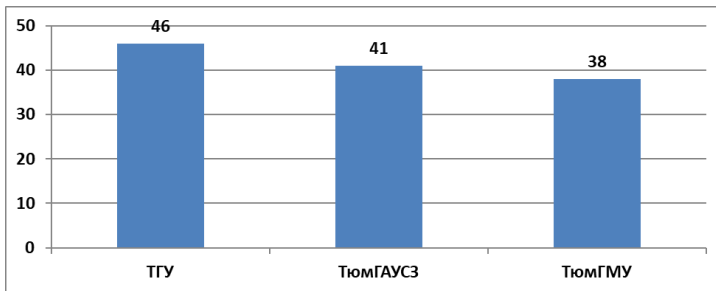


Figure 1. The number of surveyed male students studying in specialized universities in the city of Tyumen.

When identifying age groups, we used the “Scheme of age periodization of human ontogenesis”, adopted at the VII All-Union Conference on the problems of age morphology, physiology and biochemistry of the Academy of Sciences of the USSR (Moscow, 1965).

The assessment of the functional state of the cardiorespiratory system was carried out according to the formula of D.I. Bogomazov [14, 23]:

$$BI = (\text{Stange test (s)} + \text{Gench test (s)} / 90) \times 100.$$

To study the function of external respiration in students, we used the Stange test, which consists in an arbitrary stop of external respiration on inspiration. This sample was chosen by us due to the fact that it allows us to determine the general functional state of the cardiorespiratory system, the body's resistance to hypoxia and hypercapnia. What impresses in this test is that it is easy to use, accessible to every student and teacher. In addition, the performance of the test does not require special equipment, which is important in the conditions of mass examinations. The correctness of the test was controlled by us by palpation determining the beginning of reflex contractions of the diaphragm before the end of arbitrary apnea. The Stange test was evaluated according to the following criteria: less than 39 s - unsatisfactory, from 40 to 49 s - satisfactory, more than 50 s - good.

The Gench test was performed according to the classical method and was evaluated by us as follows: less than 34 s - unsatisfactory, from 35 to 39 s - satisfactory, more than 40 s - good [20]. The time interval between two samples was at least three minutes.

The results of the study were processed on a personal computer using modern electronic programs (STATISTIKA). The analysis of the material was carried out on the basis of mathematical calculations with the calculation of the arithmetic mean, arithmetic mean error, standard deviation. The significance of differences was assessed using Student's t-test [11].

The study complied with the Order of the Ministry of Health of the Russian Federation №226 dated June 19, 2003 "On Approval of the Rules of Clinical Practice in the Russian Federation". The principles of voluntariness, the rights and freedoms of the individual, guaranteed by Articles 21 and 22 of the Constitution of the Russian Federation, as well as the Order of the Ministry of Health and Social Development of Russia № 774n dated August 31, 2010 "On the Ethics Council" were observed. The study was conducted in compliance with the ethical standards set forth in the Declaration of Helsinki and the Directives of the European Community (8/609EC) and approved by the local UoT Ethics Committee.

Results and its discussion. Analyzing the duration of voluntary breath holding on inspiration when using the Stange test in young men studying in various specialized universities in Tyumen, we can conclude that, firstly, it has no statistically significant differences ($p > 0.05$). Secondly, in absolute terms, the maximum duration of breath holding on inhalation was noted at the age of 20 years, and in all young men, regardless of the training profile. Thirdly, starting from the age of 20 years, there is a slight, but a decrease in the time of arbitrary breath holding on inspiration (tab. 1).

Table 1

Age-related dynamics of the duration of voluntary breath holding on inhalation (Stange's test) and exhalation (Gencha's test) for adolescent students of various universities in the city of Tyumen ($M \pm m$)

| University | Age | | | | |
|--------------------|--------------------|--------------------|--------------------|--------------------|--------------------|
| | 18 years n = 27 | 19 years n = 26 | 20 years n = 26 | 21 years n = 23 | 22 years n = 23 |
| Stange test | | | | | |
| TyuSAA | 51,2±2,2 | 52,3±2,3 | 53,5±2,4 | 52,9±2,2 | 52,3±2,3 |
| UoT | 51,6±2,4 | 51,7±2,4 | 53,3±2,3 | 52,9±2,2 | 52,4±2,2 |
| TyuSMU | 49,7±1,8 | 50,5±1,9 | 51,3±2,2 | 50,7±1,9 | 50,5±1,9 |
| Gencha test | | | | | |
| TyuSAA | 34,6±1,1 | 35,2±1,3 | 35,3±1,2 | 34,9±1,1 | 34,4±1,1 |
| UoT | 35,0±1,3 | 35,1±1,2 | 35,2±1,2 | 35,0±1,2 | 34,8±1,2 |
| TyuSMU | 34,4±1,1 | 34,7±1,2 | 34,8±1,1 | 33,6±1,0 | 34,8±1,2 |

Thus, in particular, the duration of voluntary breath holding on inspiration in young men aged 20 years studying at TyuSAA is 2.3 s longer in absolute terms than at the age of 18 years. For UoT boys this difference was 1.7 s, for TyuSMU boys it was 1.6 s (fig. 2).

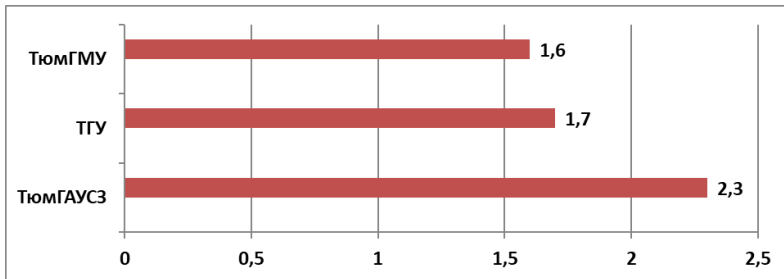


Figure 2. Differences in voluntary breath holding on inspiration among university students in Tyumen.

The study of the age values of the test with arbitrary breath holding on exhalation in boys aged 20 showed that in absolute terms it is longer (fig. 3) than in boys aged 18, although there are no statistically significant differences ($p > 0.05$).

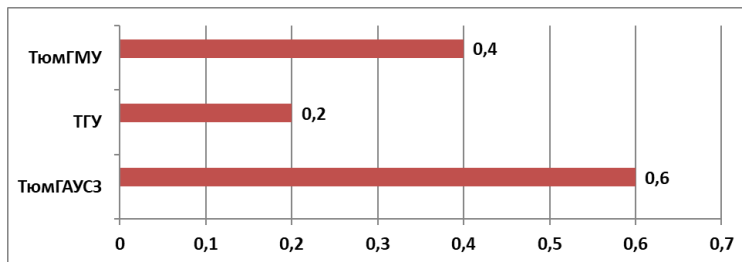


Figure 3. Differences in voluntary breath holding on exhalation among university students in Tyumen.

The analysis of BI values testified to a good coordination in the activity of the respiratory and cardiovascular systems, as well as a high level of non-specific adaptive capabilities of the youthful organism, regardless of the training profile. It is noteworthy that as we approach the period of the first mature age, i.e., starting from the age of 21, the BI values decrease (tab. 2).

Table 2
Indicators of the Bogomazov index among youth students of specialized universities in the city of Tyumen

| University | Age | | | | |
|------------|----------|----------|----------|----------|----------|
| | 18 years | 19 years | 20 years | 21 years | 22 years |
| TyuSAA | 95,33 | 97,22 | 98,67 | 97,56 | 96,33 |
| UoT | 98,44 | 96,33 | 98,33 | 97,67 | 96,89 |
| TyuSMU | 93,44 | 94,67 | 95,67 | 93,67 | 94,78 |

It was found that in all young men, regardless of the training profile, BI was stably kept within the range from 93.44 to 98.67 c.u., which we regard as a good functional state of the cardiorespiratory system.

Based on the study carried out, the following conclusions can be drawn:

1. Functional tests of Stange and Gench, having ease of implementation, validity and high information content, allow you to quickly assess the resistance of the human body to hypoxia, which is important in the conditions of mass examinations.

2. The duration of arbitrary breath holding on inhalation and exhalation, as well as the values of the Bogomazov index in adolescent students of specialized universities in Tyumen, are at the level of physiological normative values characteristic of this age period, indicating a good level of nonspecific adaptive capabilities of their body. At the same time, it should be noted that starting from the age of 21, the functionality of the cardiorespiratory system of young men decreases.

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Research transparency. The study was not sponsored. The authors are solely responsible for providing the final version of the manuscript for publication.

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耳源性鼻窦血栓形成：我们提供医疗服务的经验
**OTOGENIC SINUS THROMBOSIS: OUR EXPERIENCE IN
PROVIDING MEDICAL CARE**

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抽象的。由于脑窦血栓形成 (CST) 的诊断不及时和医疗策略不当, 死亡率可达 10%。根据病因, 这种病理学具有多种微生物特征, 在选择全身抗生素治疗时必须考虑到这一点。

对 21 名患者病历的回顾性分析显示, 儿童耳源性病因的 CST 的所有耳源性并发症占 12.2% (根据儿科耳鼻喉科)。根据实验室研究, 所有儿童在入院时都表现出高凝状态的倾向。在分离的微生物群中, 对万古霉素具有 100% 敏感性的葡萄球菌占优势, 在每三分之一的病例中, 微生物更具胃肠道特征, 肠球菌属。和大肠杆菌。在抗菌药物中, 更经常使用 III-IV 代头孢菌素 (在脓肿形成的情况下 - 与甲硝唑联合使用), 碳青霉烯类, 美罗培南。在没有积极动态的情况下或根据微生物学研究的结果, 在 48-72 小时后进行抗生素治疗的校正。在所有病例中, 均规定了在 APTT 控制下使用 UFH 进行抗凝治疗, 然后改用华法林。平均而言, 在第 24 ± 2.26 天, 患者康复出院, 无神经功能障碍。结论。及时诊断和专业护理可以避免严重的并发症, 并实现循环系统血栓形成的完全康复。

关键词: 中耳炎, 脑窦, 血栓形成, 抗生素, 抗凝剂, 儿童。

Abstract. *With untimely diagnosis and inadequate tactics of providing medical care for cerebral sinus thrombosis (CST), mortality can reach 10%. According to the etiological factor, this pathology has a polymicrobial character, which must be taken into account when choosing systemic antibiotic therapy.*

A retrospective analysis of medical records of 21 patients revealed 12.2% of all otogenic complications with CST of otogenic etiology in children (according

to the pediatric ENT department). According to laboratory studies, all children showed a tendency to hypercoagulability at admission. Of the isolated microflora, staphylococci with a sensitivity of 100% to vancomycin prevailed, in every third case, microorganisms more characteristic of the gastrointestinal tract, *Enterococcus spp.* and *Escherichia coli*. Of the antibacterial drugs, cephalosporins of III-IV generations were more often used (in the case of abscess formation - in combination with metronidazole), of carbapenems, meropenem was prescribed. Correction of antibiotic therapy was carried out after 48-72 hours in the absence of positive dynamics or according to the results of a microbiological study. In all cases, anticoagulant therapy with UFH under the control of APTT was prescribed, followed by a switch to warfarin. On average, on day 24±2.26, patients were discharged from the hospital with recovery without neurological deficit. Conclusion. Timely diagnosis and specialized care allows avoiding severe complications and achieving complete recovery from thrombosis of the circulatory system.

Keywords: otitis media, cerebral sinuses, thrombosis, antibiotics, anticoagulants, children.

Introduction

Acute cerebrovascular accidents, in particular cerebral sinus thrombosis (CST), are currently one of the most urgent problems for pediatric patients [1]. Despite the fact that CST is a rare intracranial complication of acute or chronic otitis media, mastoiditis, it ranks 3rd-4th in frequency among all otogenic intracranial complications in children [2]. According to the literature, its prevalence is up to 2.7% [3]. At the same time, CST is a serious complication of an infectious pathology of the middle ear in children, because untimely diagnosis and treatment of this condition is associated with high rates of deaths, reaching up to 5-10% [3]. Otogenic CSTs have a polymicrobial etiology, which must be taken into account when choosing systemic antibiotic therapy. According to a number of authors, *Streptococcus spp.*, *Pseudomonas aeruginosa*, *Proteus mirabilis*, *Staphylococcus aureus*, *Fusobacterium necrophorum*, *Haemophilus influenzae*, etc. are sown in this pathology [3]. At the same time, infection with *Fusobacterium necrophorum* was associated with a more severe and protracted course of the disease with the development of osteomyelitis [2, 3].

Purpose of the study: to study the prevalence of CST of otogenic etiology, age and gender characteristics, the microbial landscape in CST and the tactics of drug therapy for this pathology in children according to the pediatric otorhinolaryngology department of SBHCl TO«OCH № 2» of the city of Tyumen.

Materials and methods

A retrospective analysis of the medical records of 21 patients who were hospitalized in the ENT department from 2009 to 2021 was carried out. Upon admis-

sion, in order to verify otogenic CST, computed tomography (CT) of the head with intravenous contrast, magnetic resonance imaging (MRI) was performed. The age and gender characteristics of children with CST of otogenic etiology, the results of microbiological examination, and the nature of drug therapy were studied. The biomaterial was taken according to the guidelines of MU 4.2.2039-05 "Technique for collecting and transporting biomaterials to microbiological laboratories". The main stages of microbiological studies were carried out in accordance with the order of the Ministry of Health of the Russian Federation № 535 "On the unification of microbiological (bacteriological) research methods used in clinical diagnostic laboratories of medical institutions" dated April 22, 1985. Identification of microorganisms was carried out according to the 11th edition of Bergey's Bacteria Guide by the classical routine method, non-fermenting gram-negative bacteria (GNB) using the NEFERMtest 24 microlatest Erba Lachema kit [4]. Sensitivity to antibacterial drugs was studied using disk-diffusion method on the Mueller-Hinton 2 medium (manufacturer Conda, Spain) according to EUCAST criteria using disks with antibacterial drugs manufactured by Biorad (USA). Monitoring of antibiotic resistance of isolated pathogens was performed using the WHONET 5.6 computer program. [5]. The results obtained were processed using the Microsoft Office Excel 2007 computer program. Descriptive statistics methods were used.

Research results

CST (sigmoid, transverse, bulb of the jugular vein) were detected in 21 children, which accounted for 0.2% of the total number of children with ear pathology during the study period and 12.2% of all otogenic complications. The mean age of the patients was 7.25 ± 1.11 years. When studying gender differences, it was revealed that male patients predominated (72.7%). When analyzing clinical and laboratory parameters, it was found that upon admission, the average body temperature was $36.96 \pm 0.42^\circ\text{C}$, which did not indicate the presence of a pronounced inflammatory process in children. In the general blood test at admission, the average leukocyte counts were at the level of $14.8 \pm 4.1 \times 10^9/\text{l}$ with fluctuations from hyperleukocytosis ($61.6 \times 10^9/\text{l}$) to leukopenia ($1.61 \times 10^9/\text{l}$). The level of platelets at admission was $367.8 \pm 61.3 \times 10_9/\text{l}$ with maximum values of $738.0 \times 10_9/\text{l}$, which in some situations indicated a state of hypercoagulability. Mean fibrinogen levels were higher than normal (5.24 ± 0.92 g/l), which indicated both the presence of an inflammatory process and the state of hypercoagulability. The values of activated partial thromboplastin time (APTT) before the administration of unfractionated heparin (UFH) were at the lower limit of normal with a tendency to hypercoagulability - $23.37 \pm 7.19''$. Analysis of all the results of microbiological examination of the material from the wound revealed that positive results amounted to 54.3%. The spectrum of the isolated microflora in CST is shown in figure 1.

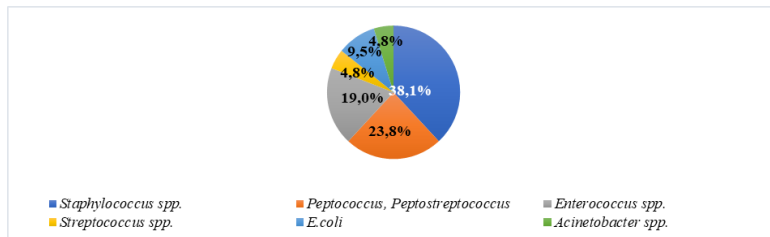


Figure 1. Microbial landscape in purulent ROO.

Among the representatives of *Staphylococcus spp.* *S. haemolyticus* occupied the leading positions. The anaerobic microflora was represented by positive *Peptococcus spp.* and *Peptostreptococcus spp.* The third position was occupied by *Enterococcus spp.*, which belongs to the opportunistic microflora of the large intestine. In fourth place in the structure of the isolated microflora is *Escherichia coli*, which is a representative of the order *Enterobacteriales* and belongs to the normal intestinal microflora. In isolated cases, *Acinetobacter baumannii*, *Streptococcus spp.* (*S.pneumoniae*).

Analysis of local antibiotic resistance of microorganisms isolated in this pathology revealed that *S. haemolyticus* strains related to coagulase-negative staphylococci were sensitive in 100% of cases only to the reserve antibiotic - vancomycin, to other anti-staphylococcal antibiotics (oxacillin, gentamicin, lincomycin, ciprofloxacin) sensitivity fluctuated from 63.3% to 87.9%. All strains of *E. coli* did not produce extended-spectrum β -lactamases (ESBL) and were characterized by good sensitivity to carbapenems, amikacin, and ciprofloxacin. With respect to isolated strains of *A. baumannii*, only protected cephalosporins (cefoperazone/sulbactam) and carbapenems showed maximum activity. Strains of *Enterococcus spp.* only in one case were resistant to ampicillin, in other cases 100% sensitivity to titratable antibiotics was noted. When providing assistance in this pathology, the method of early surgical intervention was used: extended antromastoidotomy, myringotomy or shunting, in 23.8% of cases an autopsy was performed, drainage of the sigmoid, transverse sinus until partial blood flow was obtained with the removal of a septic thrombus and subsequent plasty of the sinus wall with a tachocomb; in 4.8% - removal of a septic thrombus from the sigmoid sinus and bulb of the jugular vein. Since otogenic CST is a complication of a purulent process (otitis/mastoiditis), all children on admission, taking into account the expected microflora, were prescribed antibiotic therapy with drugs that penetrate the blood-brain barrier well, in septic dosages. The most commonly used cephalosporins of III-IV generations, cefotaxime, ceftriaxone, cefepime (in the case of abscessing process - in combination with metronidazole), meropenem was prescribed from carbapenems. Correction of antibiotic therapy was carried out after 48-72 hours

in the absence of positive dynamics or according to the results of a microbiological study. When seeding methicillin-resistant strains of staphylococci (MRSA) or ampicillin/gentamicin-resistant strains of enterococci (ARE), vancomycin was added to therapy.

The average duration of antibiotic therapy was 20.3 ± 1.6 days with a maximum of 30 days in the presence of CST in a child in combination with a brain abscess, which is consistent with the literature data [6]. In all cases, anticoagulant therapy with UFH was prescribed, the control of the correct dose selection of which was carried out by monitoring APTT, bringing the dose of UFH to the state of hypocoagulation (60-85 seconds). The average daily doses of prescribed NF were 187.9 ± 19.6 U/kg (with a maximum of 294.1 U/kg per day). On average, at 7.6 ± 0.3 days, an oral anticoagulant, warfarin, approved in pediatric practice, was added to UFH therapy at a starting dose of 0.1–0.2 mg/kg per day, followed by dose adjustment to achieve the target level of the international normalized ratio (INR) from 2.0 to 3.0. After reaching the target level of INR, UFH was canceled and further children received warfarin in a hospital setting. Warfarin therapy continued in the hospital for 17.8 ± 2.8 days, followed by a CT scan. On average, on day 24 ± 2.26 , patients were discharged from the hospital with recovery without neurological deficit. According to the results of the control CT scan, complete recanalization of the cerebral sinuses occurred after an average of 3-6 months in all patients.

Discussion

As a rule, when verifying the diagnosis of otogenic CST, empirical antimicrobial therapy is prescribed, taking into account the alleged pathogen. Pathogens such as *Staphylococcus aureus*, *Streptococcus pyogenes*, *Pseudomonas aeruginosa*, *Escherichia coli*, *Klebsiella pneumoniae*, *Haemophilus influenzae* increase the likelihood of thrombotic complications. *This is due to the systemic inflammatory response caused by these microorganisms and the release of cytokines IL-6, IL-8 and tumor necrosis factor alpha (TNF- α), which leads to endothelial damage, platelet activation and aggregation, an increase in procoagulant proteins such as tissue factor, and decreased activity of anticoagulant mechanisms such as fibrinolysis [7]. At the same time, pathogens themselves are often able to modulate the blood coagulation system by producing procoagulant proteins [7].* When choosing antibiotic therapy for otogenic intracranial complications in children, it is necessary to take into account the permeability of drugs through the blood-brain barrier (BBB). According to the level of penetration of antimicrobial agents through the BBB, they can be divided into three groups: the first group is drugs characterized by good penetration, it includes fluoroquinolones, linezolid, chloramphenicol, metronidazole (these antibacterial agents can be used in standard dosages). The second group includes antibiotics with moderate penetration,

however, the permeability of BBB for drugs increases with the use of maximum dosages without pronounced risks of developing adverse drug reactions, this group includes β -lactam antibiotics (penicillins, cephalosporins, carbapenems), fosfomycin, sulfamethazole/trimethoprim. The third group is represented by antimicrobial agents with poor penetration through the BBB, and with increasing doses, the likelihood of side effects increases (aminoglycosides, vancomycin, polymyxins, daptomycin, tigecycline) [8]. To reduce the likelihood of thrombosis progression, an obligatory component of CST therapy is the appointment of anticoagulant therapy, the timely use of which, as is known, can reduce the risk of fatal outcomes and severe disability [10]. When analyzing the main recommendations for antithrombotic therapy in adult patients and taking into account age-related characteristics in pediatrics, antithrombotic therapy is started with intravenous administration of UFH. The dose of heparin is adjusted to achieve an APTT interval of 60–85 s (which corresponds to a level of anti-Xa activity of 0.35–0.7) [9]. An alternative to UFH is the subcutaneous administration of low molecular weight heparins (LMWH) - sodium dalteparin, enoxaparin [3, 9]. Despite the advantages of LMWH in children with severe CST ([2, 3] we did not use this group of drugs. In pediatric practice, warfarin is allowed among oral anticoagulants [11]. In a study by Coutinho G., et al. [10] demonstrated the effectiveness of long-term therapy (average 9 months) with warfarin for cerebral thrombosis in pediatric practice [10]. When using warfarin in the treatment of venous thrombosis, it is necessary to achieve a state of hypocoagulation (INR range - 2.0-3.0), since it has been demonstrated that with $INR < 2.0$, the risk of thrombotic complications increases, and with $INR > 3.0$ - risk of bleeding [12]. However, in pediatric practice, there are certain difficulties in the selection of doses of warfarin. This is also due to the genetic characteristics of the metabolism of the drug, the nutritional characteristics of children in different age periods (unstable concentration of vitamin K in breast milk, eating food rich in vitamin K: fresh herbs, green vegetables, significantly reduces the effectiveness of this anticoagulant) [11]. It is also necessary to be aware of all possible interactions of warfarin with other drugs. These interactions may be accompanied by either a decrease in the anticoagulant efficacy of the drug (metamizol sodium, haloperidol, phenobarbital, systemic glucocorticosteroids, high doses of ascorbic acid, vitamin K and some others) or an increase in the action of the anticoagulant with an increased risk of developing hemorrhagic complications (practically all cephalosporins, antibiotics from the group macrolides - azithromycin, clarithromycin, erythromycin; some representatives of penicillins - ticarcillin, piperacillin; hyposecretory agents - omeprazole, esomeprazole, etc.; non-steroidal anti-inflammatory drugs - diclofenac, ibuprofen; tocopherol, phenobarbital, etc.) [11]. Thus, CST therapy is a difficult task not only in surgical intervention, but also in the selection of the optimal amount of drug therapy.

Conclusion

Timely diagnosis and specialized care allows avoiding severe complications and achieving complete recovery from thrombosis of the circulatory system.

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实验性甲状腺毒症肝脏免疫组织化学检查指标

INDICATORS OF IMMUNOHISTOCHEMICAL EXAMINATION OF THE LIVER IN EXPERIMENTAL THYROTOXICOSIS

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摘要: 甲状腺毒症 - 是一种综合征, 其存在与血液中甲状腺激素含量增加有关, 发生在各种疾病或外源性过量摄入甲状腺激素中。目前, 免疫组织化学研究方法被积极用于其诊断。特别是, 在它的帮助下, 可以检测和研究肝细胞的特征性变化。在这项工作中, 研究了实验性甲状腺毒症中肝脏的变化。

关键词: 甲状腺毒症, 免疫组织化学研究, 肝脏变化。

Abstract: *thyrotoxicosis - is a syndrome, the presence of which is associated with an increased content of thyroid hormones in the blood, which occurs in various diseases or exogenous excess intake of thyroid hormones. Currently, the method of immunohistochemical research is actively used for its diagnosis. In particular, with its help, characteristic changes in liver cells are detected and studied. In the work, changes in the liver were studied in experimental thyrotoxicosis.*

Keywords: *thyrotoxicosis, immunohistochemical study, liver changes.*

Introduction

Immunohistochemistry (IHC) is a technique for pinpointing the exact location of specific antigens in tissues based on the recognition of an antigen by the corresponding antibody and the results of this binding. Visualization of the results of the antigen-antibody reaction in biopsied tissue sections is carried out using a microscope.

The fundamental difference between immunohistochemical analysis and other methods of immunological diagnostics, which use the antigen-antibody binding reaction, is the structural specificity of the study. That is, in the reaction, both the presence of a signal (there is staining or not) and its strength (staining intensity),

as well as the spatial distribution of the signal in the tissue (staining of cell membranes, cytoplasm, nucleus and other structures) are noted.

Relevance

IHC, among other things, is used in the diagnosis of thyroid pathology. According to WHO, this disease covers 7% of the world's population, which is associated with the rapid growth of industry and environmental pollution with industrial and radioactive waste, changes in the microelement composition of the soil, hereditary predisposition¹.

Immunohistochemical study is based on the identification of proteins specific to a particular type of cell. For this purpose, the Ki-67 marker is used, a non-histone protein involved in the cell cycle. It is involved in ribosome biogenesis, heterochromatin organization, and mitotic chromosome separation, but its full range of functions is still unclear. The reliability of the method approaches 100%, so this method is used to diagnose thyrotoxicosis.

The pathogenesis of thyrotoxicosis

Thyroid pathology is accompanied by impaired production of thyroid hormones with the development of hypothyroidism or thyrotoxicosis. Thyrotoxicosis is a syndrome, the presence of which is associated with an increased content of thyroid hormones in the blood, which occurs in various diseases or exogenous excess intake of thyroid hormones. Thyrotoxicosis includes such conditions in which there are clinical and biochemical manifestations of an excess content of thyroid hormones in the blood, without taking into account the genesis of their increase in level.²

Thyrotoxicosis is accompanied by numerous disorders in all organs and systems, which is due to the diverse effects of thyroid hormones. First of all, the cardiovascular system, the digestive system (thyrotoxic hepatitis), the central nervous system, the organ of vision, the reproductive system and other organs are affected.³

In the liver with thyrotoxicosis, pronounced functional and structural changes develop. The liver metabolizes thyroxine by oxidative deamination, deiodination, conjugation, and excretion into the bile. According to different authors, with thyrotoxicosis, fatty degeneration, cirrhosis, and hepatic coma develop in the liver.⁴

In the course of studying liver lesions in thyrotoxicosis, the main focus is on clinical manifestations. At the same time, due to the paucity and fragmentation of information, structural changes that develop in the liver in this pathology, their morphogenesis and outcomes remain insufficiently studied.

Sexually mature white male Wistar rats weighing from 250 to 300 grams were selected for the study. Animals were kept under optimal conditions; rations for laboratory animals were used for feeding in accordance with GOST R 50258-92.

By daily administration of L-thyroxine at a dose of 1.6 mg per 1 kg of body weight, an experimental model of thyrotoxicosis was obtained on male white rats.

For immunohistochemical studies, liver pieces were fixed in a 10% buffered formalin solution, after which paraffin blocks were prepared and serial sections were made from each block with a thickness of 5 μm . The study was carried out by an indirect immunoperoxidase method with the restoration of antigenic specificity. Tissues fixed in formalin and embedded in paraffin were exposed to microwaves. Serial sections were deposited according to the standard scheme, treated for 5 min in 3% H_2O_2 solution to block endogenous peroxidase, and washed in distilled water for 5 min. For the next 2 hours, the sections were processed in a microwave oven at 750 W, after which they were washed in phosphate buffer (pH-7.6) for 5 minutes and incubated with primary monoclonal antibodies for 18 hours at a temperature of +4 degrees C. Further, after repeated washing in phosphate buffer, sections were incubated with secondary antibodies labeled with biotin for 20 minutes at room temperature. This was followed by staining with diaminobenzidine and embedding in epoxy resin. Liver tissue without application of primary antibodies was used as a control material.

Liver sections were used as materials for morphological studies. The analysis was carried out according to the principles of a systematic approach in the study of the quantitative-spatial organization of morphological structures in normal and pathological conditions using the methods of Grigory Gerasimovich Avtandilov.

Statistical processing of the study results was carried out using the Statistic 6.0 for Windows software package, the Biostat statistical analysis program (1998), and the Excel module of the Microsoft Office 2007 Enterprise package in the Windows Vista Home Premium environment. Data processing was carried out using descriptive statistics methods to obtain the mean value (M) followed by multiple pairwise comparison using the Newman-Keuls test at a 5% significance level of differences.

Indicators of immunohistochemical study of the liver in experimental thyrotoxicosis.

The method of immunohistochemical study using monoclonal antibodies Ki-67 was used to evaluate the proliferative activity of hepatocytes at different times of the experiment. Ki-67 is a marker of cell proliferation at any stage of mitosis and stains dividing cells. In the control group, the proliferation index was 2-2.5% in the field of view, while the nuclei were stained dark brown. A positive reaction to Ki-67 in the control group was detected mainly in zone I (periportal zones).

On the 7th day of the experiment, the proliferation index was 2-3%, Ki-67 expression was found in zone I, and the nuclei also stained brown.

On the 14th day of the experiment, Ki-67 expression was 3%, hepatocyte nuclei were also stained brown. In the indicated terms of the experiment, there is a slight increase in the proliferation index from 2-2.5% (control) to 3% (day 14). However, this difference is statistically insignificant.

On the 21st day, the Ki-67 index was 4-5%. In this case, the nuclei of hepatocytes are stained brown. Positive expression of Ki-67 was found not only in zone I, but also in zone II.

On the 21st day, a statistically significant increase in the expression of Ki-67 was revealed compared with the control. The proliferation index on the 21st day is 2 times higher (4-5%) compared to the control (2-2.5%). In the indicated terms, increased expression of Ki-67 is observed not only in zone I, but also in zone II. Proliferating hepatocytes move from zone I to zone II.

On the 28th day, there is a statistically significant increase in the hepatocyte proliferation index: Ki-67 is 5-7%. At the specified time, proliferating hepatocytes were found in zones I and II, where they are located diffusely. Single proliferating hepatocytes are found in zone III, which indicates their movement from zone I.

On the 45th day, the expression of Ki-67 reaches the highest values and is 9-10%. The proliferation index increases almost 4 times compared to the control (2-2.5%). Proliferating hepatocytes are located in all zones, the nuclei of hepatocytes are stained brown. The described immunohistochemical picture of the liver corresponds to the highest degree of damage to hepatocytes, which stimulates reparative processes.

On the 60th and 90th day, Ki-67 expression decreases, the proliferation index is 0.5-1%. Single proliferating hepatocytes with a low level of Ki-67 expression are scattered throughout the liver section. The decrease in Ki-67 expression by the end of the experiment was due to the development of severe dystrophic and destructive processes in the liver.

Conclusions

Based on the data obtained, it can be concluded that experimental thyrotoxicosis revealed an increase in the expression of the Ki-67 protein on the 21st day up to 4-5% (control - 2-2.5), which reaches a maximum level by the 45th day - 9-10%, and by the end of the experiment it drops below the control figures, to 0.5-1.0%.

Conclusion

As a result of the work done, the proliferative activity of hepatocytes was recorded in dynamics, which made it possible to assess the immunohistological changes in the liver in experimental thyrotoxicosis.

As a result of the experiment, it was concluded that the cells were most active in the middle of the observed period. This indicates the highest degree of destructive processes in the liver cells, which stimulates reparative processes.

The obtained data of immunohistochemical studies can be used as diagnostic criteria for determining thyrotoxic liver damage.

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磷酸锌水门汀结构特性的研究与比较

**STUDY AND COMPARATIVE CHARACTERISTICS OF THE
STRUCTURAL CHARACTERISTICS OF ZINC-PHOSPHATE
CEMENTS**

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抽象的。今天，在矫形牙科中，许多不同的材料被用来固定固定假体以替代牙列中的缺陷，包括属于矿物组的磷酸锌粘固剂。它们的组成成分各不相同，因此具有不同的特征。然而，由于此类水泥的物理和机械性能较低，因此开始使用频率大大降低。值得考虑的是，今天类似物之间的选择相当大。本文专门对同组部分竞争水泥的物理力学性能强度特性进行比较。

关键词：固定结构，义齿，磷酸锌水门汀，物理和机械性能，固定结构的固定，人工牙冠。

Abstract. *Today, in orthopedic dentistry, many different materials are used to fix fixed prostheses that replace defects in the dentition, including zinc-phosphate cements, which belong to the mineral group. All of them are different in their constituent components and, accordingly, characteristics. However, this class of cements began to be used much less frequently, referring to their low physical and mechanical properties. It is worth considering that the choice between analogues, today, is quite large. This article is devoted to a comparison of the strength characteristics of the physical and mechanical properties of some competing cements of the same group.*

Keywords: *fixed structures, dentures, zinc phosphate cements, physical and mechanical properties, fixation of fixed structures, artificial crowns.*

Relevance

According to studies reflected in the literature, it can be seen that in the first 3 years of using fixed prostheses, in particular artificial crowns, the percentage of

patients who applied for complications is quite large and amounts to about 25%. The most common complication is early failure of fixation. Due to the development of new technologies, higher requirements are set for cements, and it is becoming more and more difficult for the group of zinc-phosphate cements to fight for a priority place in the market, despite its centuries-old history and the presence of positive qualities. They should have the same volume throughout the entire period of use, high compatibility with the tissues of the tooth and various materials for the construction of dentures, the absence of an irritating effect on the pulp and tissues surrounding the tooth, and low solubility in the oral cavity. Unfortunately, this group of cements has rather low performance in terms of the above parameters, so manufacturers pay great attention to refining the formulation in order to increase the parameters that are key in the treatment of fixed dentures.

The dentist must choose a fixing material based on a set of properties that satisfy it. Zinc-phosphate cements are quite promising and, with various modifications, it is possible to obtain a high-tech, suitable for all requirements and relatively inexpensive material.

Purpose of the study

To study and compare the strength characteristics of zinc-phosphate cements.

Materials and methods

To carry out a comparative characterization of the strength characteristics of zinc-phosphate cements, samples were taken: “NeoDent” (Celite LLC), “WIS-CIN” (Raduga R LLC), Adhesor (SpofaDental, Czech Republic). As a means of research, the main method was taken, which determines the primary property of fixing materials - compressive strength.

This method allows you to determine the strength of the material under study. According to the method specified in GOST 31578-2012, cement samples were made in the form of cylinders 6 mm high and 4 mm in diameter, for which special metal molds with clamps were used, which were previously kept in a thermostat at a temperature of $(23 \pm 1)^\circ\text{C}$. To eliminate possible errors during the testing process, 10 samples of each representative of zinc-phosphate cement were prepared. After the final crystallization process, for 24 hours in a thermostatic condition, an experiment was carried out using an IR5040 tensile testing machine, using a compression rate of 1 mm/min. The end of the test was the manifestation of the destruction of the sample and the value of the maximum applied force was recorded.

Results and its discussion

When measuring the compressive strength of 10 samples of each studied zinc-phosphate cement for fixing fixed denture structures in a comparative aspect,

the results were obtained, which were subjected to statistical processing and are shown in Table 1.

Table 1
Results of tests of compressive strength, MPa.

| Study No. | «NeoDent» | «WISCIN» | «Adhesor» |
|-------------|------------------|---------------|----------------|
| 1 | 126 | 92 | 99 |
| 2 | 98 | 85 | 91 |
| 3 | 102 | 96 | 96 |
| 4 | 97 | 81 | 101 |
| 5 | 106 | 90 | 88 |
| 6 | 89 | 86 | 79 |
| 7 | 113 | 101 | 112 |
| 8 | 84 | 86 | 115 |
| 9 | 102 | 84 | 108 |
| 10 | 119 | 75 | 95 |
| Me [lq; uq] | 101, 5 [97; 113] | 87,5 [84; 92] | 98,3 [91; 108] |

Application: *Me* – median; *nq* – lower quartile, *vq* – upper quartile.

For the “NeoDent” zinc-phosphate cement, the average force required to destroy the samples, in accordance with the median obtained, was 101.5 MPa, for the “VISCIN” zinc-phosphate cement - 87.5 MPa, for the “Adhesor” zinc-phosphate cement - 98.3 MPa. In accordance with the requirements, the minimum allowable indicator for zinc-phosphate cements, according to this criterion, is a value equal to 70 MPa.

Conclusions

Due to the fact that more and more requirements are being imposed on materials for fixing fixed structures of dentures, it is necessary to refine the formulation of zinc-phosphate cements to meet the needs of an orthopedic dentist. After the study, analyzing the data recorded by the tensile testing machine, it was found that all representatives reflected in this article comply with the standards reflected in GOST.

Concluding, it can be noted that of the selected samples of zinc-phosphate cements used for fixing fixed structures of dentures, “NeoDent”, manufactured by “Celite” LLC, had the highest strength characteristics, while the subject “WISCIN” from “Raduga-R” LLC indicator of this criterion is almost at the border of the minimum value of the norm, and the foreign analogue of “Adhesor”, produced by the company “Sporadental”, took the second place according to the test results. Moreover, having studied the price policy of the materials included in the compar-

ison list, it can be determined that “NeoDent” zinc-phosphate cement is the most affordable, making it more competitive when choosing a practitioner.

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中性粒细胞淋巴细胞指数在运动性毒血症患者死亡过程中的变化特点
**FEATURES OF CHANGES IN THE NEUTROPHIL-LYMPHOCYTE
INDEX IN THANATOGENESIS OF PATIENTS WITH AMBUSTIAL
TOXEMIA**

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抽象的。通过研究中性粒细胞-淋巴细胞指数(NLI),对40例RRCEM中因伏击伤死亡的患者的临床和实验室参数进行回顾性分析,发现该指标的变化与白细胞数量、中等分子量肽(MMWP)和白细胞中毒指数(LII)。预期寿命的增加与心率的增加以及淀粉酶水平的增加之间存在直接关系,严重燃烧性毒血症中的MMWP可能表明严重烧伤后具有相对较大的适应能力。在老年人中,更严重的烧伤并没有伴随心率增加,这是应激反应的特征。但是,相反,显示出心动过缓的趋势,这表明60岁以上的人缺乏适应性储备。可以说,NLI评估技术作为一种评估中性粒细胞功能活动的实验室方法很有前途,可以在烧伤毒血症患者的并发症的预后、发展和严重程度方面提供有价值的信息,并用作指标的治疗效果。

关键词:中性粒细胞-淋巴细胞指数,烧伤毒血症,致死率,致死。

Abstract. *Based on a retrospective analysis of the clinical and laboratory parameters of 40 patients who died in the RRCEM due to ambustial injury by studying the neutrophil-lymphocyte index (NLI), it was found that the change in this indicator was most consistent with deviations in the number of leukocytes, medium molecular weight peptides (MMWP) and leukocyte intoxication index (LII). A direct relationship between an increase in life expectancy and an increase in heart rate, as well as an increase in the level of diastase, MMWP in severe ambustial toxemia may indicate a relatively large adaptive capacity after a severe burn injury. In older people, a more severe burn injury was not accompanied by an increase in heart rate, characteristic of a stress reaction. But, on the contrary, a tendency to bradycardia was revealed, which indicated the absence of adaptive reserves in people over 60 years of age. It can be argued that the NLI assessment technique is promising as a laboratory method for assessing the functional activity of neutrophils and can provide valuable information in terms of prognosis, development and severity of complications in a patient with burn toxemia, and be used as an indicator of treatment effectiveness.*

Keywords: *neutrophil-lymphocyte index, burn toxemia, lethality, thanatogenesis.*

Relevance. The problem of treatment of burn disease and its complications does not lose its relevance to the present day. In the structure of mortality of severely burned patients, the leading place is occupied by an infection leading to the development of pneumonia and sepsis. The development and generalization of infection in severely burned patients is realized due to the influence of thermal injury on the immune system, in particular, the phagocytic link of immunity suffers. Dysfunction of phagocytes is manifested in a violation of the destruction of bacteria, changes in the level of secretion of interleukins and cytokines by macrophages, activation and degranulation of neutrophils with the development of oxidative stress. The described mechanisms cause systemic tissue damage, leading to the development of multiple organ failure and death of the patient. Therefore, the assessment of the function of the phagocytic link of immunity is appropriate at all stages of burn disease. In this case, a special role is played by the determination of the activity of neutrophils as key effector cells responsible for the development of inflammation and purulent-septic complications in burn disease. Identification of neutrophilic dysfunction will allow timely prediction of the course of burn disease and the development of purulent-septic complications.

There are a number of methods for assessing the bactericidal activity of neutrophils. Leukocyte intoxication index (LII) is an indicator showing the severity of inflammation, endogenous or exogenous intoxication. It makes it possible to have an idea of the severity of the process and the effectiveness of the therapy. With bacteremia and sepsis, the value of the leukocyte index will be from 4 to 9. A high level of leukocytes in the blood, along with an intoxication index value of ≥ 10 , is a sign of infectious-toxic shock. A white blood cell count ≤ 4.0 G/L is a poor prognostic sign. The result of the parameter within 1 ± 0.6 is considered the norm. The value increases as the patient's condition worsens. With sepsis, the indicator is high, over 25. According to this formula, doctors evaluate the possibility of suppuration after the operation. Medium molecules (MM) are endogenous components, the molecular weight of which is 500-5000 daltons. The name "medium molecules" is based on the commonality of a group feature - the magnitude of the molecular weight. They occupy an intermediate (average) position in their molecular weight between simple substances in the blood serum (urea, creatinine, bilirubin, etc.) and proteins. The chemical composition of the MM group is very heterogeneous. A significant part of MM is formed in the process of protein catabolism in the body. An essential feature of MM is their high biological activity. Medium molecules have neurotoxic activity, inhibit the processes of protein biosynthesis, are able to suppress the activity of a number of enzymes, uncouple the processes

of oxidation and phosphorylation, cause secondary immunosuppression, and have a toxic effect on erythropoiesis. Having a relatively small molecular weight, MM is normally removed from the body by the kidneys by glomerular filtration. A decrease in the functional ability of the kidneys to remove MM leads to the fact that with renal failure, hypergastrinemia, an excess of parathyroid hormone in the blood, may occur, and due to a slowdown in the inactivation of insulin in the kidneys, the need for insulin may decrease in diabetic patients. That is why the accumulation of MM in the body in renal failure largely determines the variety of clinical manifestations of endotoxemia (somnia, "uncontrolled" hypertension, anemia, pseudodiabetes, vomiting, diarrhea, uremic osteopathy, etc.). In recent years, the importance of MM in the pathogenesis of a number of diseases has been shown: uremic intoxication, hepatic coma, acute ambulatory toxemia, peritonitis, acute pancreatitis, myocardial infarction, exacerbation of tuberculosis, rheumatism, and oncological diseases. An increase in the level of MM in the blood serum depends on the condition of the patients. Extremely high values of the level of MM (0.8-0.9 units and above) are observed in persons with acute and chronic renal failure. Average values (0.4-0.8 units) - in patients with hepatic coma, diffuse purulent peritonitis, acute pancreatitis, thromboembolic complications, sepsis, burn toxemia. Low (0.3-0.4 units) - in patients after surgical interventions (appendectomy, cholecystectomy), in patients with traumatic brain injury, with local peritonitis, oncological diseases, in patients with cerebrovascular accidents. In malnourished patients, even in the presence of diffuse purulent peritonitis, no increase in the level of MM in the blood is detected. With endogenous intoxication, there is a direct relationship between an increase in the level of MM and a deterioration in the patient's condition. Inclusion in our study, in addition to indicators of blood leukocytes and LII, hemoglobin and blood lymphocytes is due to the fact that with endogenous intoxications (purulent, etc.), the red blood germ is suppressed with the development of anemia and lymphocytopenia, which is an indicator of immunodeficiency.

The neutrophil-lymphocyte index (NLI) is a simple marker of the systemic inflammatory response, which, according to studies, can serve as an independent prognostic factor in some solid malignant tumors, including prostate cancer (PC), the diagnosis of which is an actual problem of modern urology. The authors note that the assessment of NLI, as an indicator of immunity stress, will make it possible to predict the occurrence of acute infectious diseases [1-7]. In order to study the features of the period of toxemia depending on the severity of the systemic inflammatory reaction upon admission, we studied and assessed changes in the homeostasis systems of burned patients, taking into account the severity of the body's immune response, and also tried to identify the relationship with the severity, area of the burn, age, and data from physical examinations of patients with lethal outcome.

Objective. To study the features of changes in the neutrophilic-lymphocytic index in the thanatogenesis of ambustial toxemia.

Material and research methods. The division into groups was based on the neutrophil-lymphocyte index (NLI) (the norm is 2.3 units). Monitoring of the dynamics of the state was carried out in groups: group 1 - NLI 2.4-10 units; 2 group 11-30 units; group 3 - 31-59 units; 4 - <2.3 units. In the studied cohort of patients, the number with a moderate inflammatory reaction according to the NLI significantly prevailed (indicators of 31 patients - inflammatory reaction of the 1st degree). Of these, the cause of the severity of the condition was a combined injury: 7 patients with carbon monoxide poisoning, 1 - STBI, 2 - amputation of one / both limbs, the condition was complicated by the addition of pneumonia -14, acute renal failure -4, liver failure due to cirrhosis of the liver 8 and toxic/viral 19/4 hepatitis, MODS in 31 patients. According to the degree of severity of NLI deviations, these patients were studied by combining into group 1 patients with an inflammatory reaction of the 1st degree (NLI - 2.3-10 units), in group 2 they combined the data of patients with NLI 11-30 units (severe inflammatory reaction of 2 degrees, in Group 3 NLI indicators 31-51 or more units (excessive inflammatory response - 3 degrees), group 4 3 patients with NLI less than 2.3 units (no inflammatory response) (Table 1).

Table 1.
Characteristics of patients according to the level of NLI (un)

| | Moderate inflammatory reaction (1 degree) | Pronounced inflammatory reaction (2 degree) | Excessive inflammatory response (3 degree) | Lack of reactive reaction (0 degree) |
|-------------------|--|--|---|---|
| Groups | 1 | 2 | 3 | 4 |
| degrees | 2,3- 10 un | 11-30 un | 31-59 un | <2,3 un |
| NLI (40 patients) | 77% (31) | 7,7% (3) | 7,5% (3) | 7,7% (36) |

Considering the high lethality of 77% of patients with NLI, corresponding to a systemic inflammatory reaction of the 1st degree (NLI-2.3-10 units), we made an attempt to study and find out the reasons for the identified discrepancy.

Table 2.
Assessment of the area and depth of the burn by age with a moderate inflammatory response according to NLI (in group 1).

| | kol bh | Age, years | 2-3AB,% | 3B,% | IF, units |
|-----------------|---------------|-------------------|----------------|-------------|------------------|
| <18 years old | 9,6% (3) | 11,5±2,5 | 83,6±7,1 | 50±10 | 212±18 |
| 19-40 years old | 32% (10) | 31,6±4,9* | 79,4±13,7 | 42±16 | 181±46 |

| | | | | | |
|-------------------|-----------|-----------|-----------|-----------|--------|
| 41-50 years old | 12,9% (4) | 45,7±1,7* | 58,7±16,2 | 26,7±9,8 | 139±42 |
| 51-60 years old | 32% (10) | 55,6±2,3* | 79,9±13,9 | 40,5±15,7 | 183±42 |
| 61-70 years old | 6,4% (2) | 69±0,1* | 32,5±2,5* | 17,5±7,5* | 67±17* |
| Over 71 years old | 6,4% (2) | 83,5±1,5* | 32,5±2,6* | 20±5* | 80±20* |
| Total | 100% (31) | | | | |

* - Significantly significant relative to the indicator of pediatric patients

In children aged 11.5±2.5 years, mortality was due to burns 2-3A degree 83.6±7%, 3B degree 50±10%, IF 212±18 units. It was found that with a significantly smaller by 59% area of a thermal burn of 2-3A degree, which amounted to 32.5±2.5%, 3B - 17.5±7.5%, the index of IF - 50-100 units in persons aged older than 61 years did not improve the severe outcome of burn disease (Table 2).

An analysis was made of patients who died with moderate growth (Group 1) NLI (at admission (31) (Table 3, Fig. 1). 77% of the deceased were at the age of 45.1 ± 15.2 years, the area of the burn surface of varying severity 71.3±20.3%, EIA 163.7±52.2 units.

Table 3

Evaluation of the severity of burns that caused an inflammatory reaction of the 1st degree (NLI-2.3-10 units)

| Number of patients | Age | 2-3AB | 3B | 4 deg | EIA | TIT | ind Baux |
|--------------------|-----------|-----------|-----------|----------|------------|---------|-----------|
| 31 | 45,1±15,2 | 71,3±20,3 | 38,3±16,5 | 4,0±0,01 | 163,7±52,2 | 1,4±0,5 | 112,0±5,3 |

Table 3. Correlations with age in group 2 (31 patients)

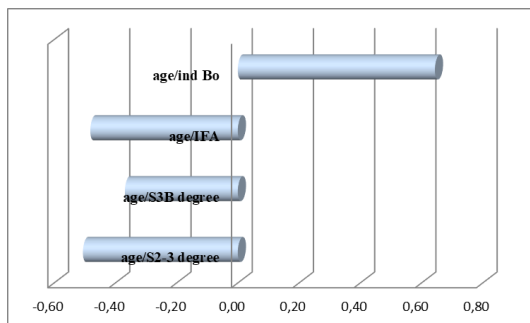


Figure 1. Correlations of age with a moderate inflammatory response (in group 1)

The tendency of the inverse dependence of the indicators of the area and depth of the burn surface, the EIA index on age was revealed, that is, the older the age, the smaller the area and depth of damage to the skin surface by a thermal burn caused a deterioration in the condition of patients in group 1 (Fig. 1). There is a direct upward trend in the Baux index at an older age.

Table 4
Changes at admission depending on the severity of the inflammatory response (according to NLI)

| Number of patients in groups | Age | b/d | Glasgow Scale | RR | SBP | DBP | HR |
|------------------------------|----------------|---------------|---------------|--------------|-----------------|---------------|----------------|
| 1 rp (31) | 45,0± 15,1 | 26,9± 17,4 | 14,2± 0,9 | 21,7± 1,6 | 122,1± 12,2 | 74,3± 10,3 | 104,1± 8,6 |
| 2 -3 gr (6) | 23,5± 9,0 | 24,8± 19,8 | 12,0± 2,7 | 24,8± 5,8 | 102,8± 13,8 | 61,2± 7,8 | 124,7± 13,1 |
| 4 gr (3) | 60,0± 20,7* | 48,0± 36,0 | 12,7± 0,9 | 20,3± 1,1 | 125,0± 13,3* | 76,7± 11,1 | 98,3± 15,8 |

*-significantly relative to the indicator in groups 2-3

Revealed a significant difference in some indicators between groups 2-3 with an excessive inflammatory response and group 4 with no signs of an inflammatory response according to NLI. Thus, the age of patients in group 4 turned out to be 150% (by 36.5 years) more than in groups 2-3 ($p < 0.05$), the SBP level was higher by 21% (23.8 mmHg) ($p < 0.05$) (Table 4).

Table 5
Indicators of analyzes with varying degrees of inflammatory response (according to NLI)

| | ALT | AST | Diastase | hemogl | Leuko- cytes | SMP | LII | ISN | eryth- rocytes | biliru- bin total |
|------------|-----------------|-----------------|---------------|----------------|-----------------------------|----------------------------|---------------|-------------|-------------------|----------------------|
| 1 gr (31) | 150,3± 107,7 | 195,9± 140,0 | 35,7± 17,7 | 148,2± 14,2 | 12,3± 3,1 | 2,5± 1,7 | 4,8± 1,4 | 0,0± 0,0 | 4,9± 0,5 | 20,9± 8,9 |
| 2-3 gr (6) | 116,4± 99,7 | 143,8± 103,7 | 27,5± 3,2 | 145,8± 22,9 | 22,7± 5,8 ^{'''} | 0,5± ^{'''} 0,1 | 27,6± 14,6 | 0,1± 0,1 | 4,8± 0,7 | 20,6± 3,4 |
| 4 gr (3) | 303,0± 143,3 | 310,3± 137,8 | 31,3± 4,4 | 137,0± 2,7 | 7,5± 1,1 [□] | 0,3± 0,1 | 1,8± 0,3 | 0,0± 0,0 | 4,5± 0,1 | 29,5± 11,0 |

^{'''}-difference is significant relative to the indicator in group 1

[□]-significantly relative to the indicator in groups 2-3

A significantly significant increase in the number of leukocytes was revealed with a pronounced and excessive inflammatory reaction (groups 2-3) relative to

group 1 by 84% ($p < 0.05$). The number of leukocytes in group 4 was significantly less than in group 1 by 39% ($p < 0.05$), than in groups 2-3 by 66% ($p < 0.05$, respectively) (Table 5).

The SMP index turned out to be the highest in group 1, exceeding the result in groups 2-3 by 5 times ($p < 0.05$), in group 4 by almost 8 times ($p < 0.05$). Also, significantly significant differences were found in the LII indicator, when the highest indicator was in groups 2-3 (27.6 ± 14.6), 185% and 73% less ($p < 0.05$) than in group 1. That is, the indicators of the number of leukocytes and LII were most consistent with the severity of the inflammatory reaction (Table 5). Significant differences in the groups of indicators of ISN, erythrocytes, hemoglobin, bilirubin, ALT, AST, diastase could not be identified.

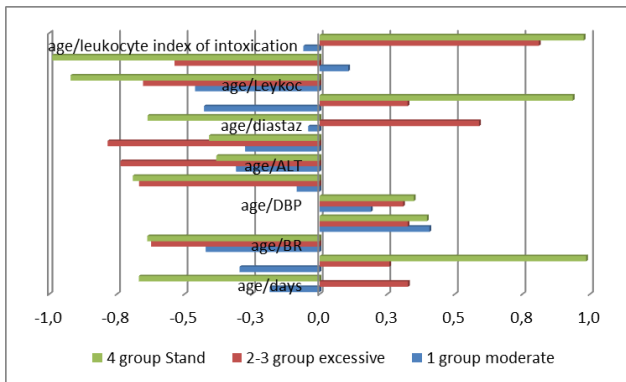


Figure 2. Correlations of age depending on the degree of increase in NLI.

A direct strong relationship was found in the 4th group of age and the level of total bilirubin (0.9), age and number of erythrocytes (0.9), which was most likely associated with dehydration, age and ISN (0.9), age and LII (0.9), age and hemoglobin (0.9), age and level of consciousness according to the Glasgow scale (0.9), it is possible that the identified features of the inflammatory reaction of older age are associated with due to the smaller area and depth of the burn surface, which was 2-3A degree $32.5 \pm 2.5\%$, 3B degree $17.5 \pm 7.5\%$, IF 67 ± 17 units. At the same time, an inverse relationship was observed between age and SMP (-0.9), that is, the older the patient, the lower the level of SMP, which can be associated, given the lower trauma of the burn with background immunodeficiency. Of interest is the compensatory reaction of the CVS in groups 2-3 and 4, which It was manifested by a decrease in heart rate in elderly and senile patients (-0.7), i.e., a more severe burn injury was not accompanied by an increase in heart rate characteristic of a stress reaction, but, on the contrary, a tendency to bradycardia was revealed,

of age. Thus, it can be argued that the NLI assessment technique is promising as a laboratory method for assessing the functional activity of neutrophils and can provide valuable information in terms of predicting the development and severity of complications in a patient with burn toxemia, and be used as an indicator of treatment effectiveness.

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接受皮质类固醇治疗的青少年哮喘患者的混合唾液
**MIXED SALIVA IN ADOLESCENTS WITH ASTHMA WITH
CORTICOSTEROID THERAPY**

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概括。对支气管哮喘患者的混合唾液 IgA、IgG、IgM、IL-1 β 、IL-6、ASAT、ALAT、ALP 和 LDH 活性的研究表明，所有研究参数均显著高于健康参与者的值。这就需要一套针对抗菌消炎治疗的措施。

关键词：支气管哮喘，唾液，酶，白细胞介素，免疫球蛋白。

Summary. *A study in mixed saliva of patients with bronchial asthma IgA, IgG, IgM, IL- 1 β , IL-6, ASAT, ALAT, ALP and LDH activity showed that all studied parameters are significantly higher than the values obtained in healthy participants. This requires a set of measures aimed at antibacterial and anti-inflammatory therapy.*

Keywords: *bronchial asthma, saliva, enzymes, interleukins, immunoglobulins.*

Bronchial asthma is a chronic inflammatory disease of the respiratory tract characterized by bronchopulmonary spasm causing shortness of breath, cough, heaviness in the chest and rapid breathing. According to WHO recommendations, bronchial asthma is one of the main conditions requiring prescription in the form of inhalations of corticosteroid hormones and beta-2-agonists to stop spasms [5]. The worldwide prevalence of bronchial asthma disease is currently 300 million, and this figure is projected to increase by another 100 million people by 2025 [4].

Some studies were devoted to determining the effect of bronchial asthma on the condition of oral tissues, and showed a correlation between saliva characteristics and manifestations in the oral cavity [1, 2, 4]. It was found that bronchial asthma, as well as its pharmacotherapy (including inhaled corticosteroids) can

lead to a decrease in salivation rate, changes in saliva composition, including pH, and plaque formation [6, 8]. Also, frequent cough leads to the appearance in saliva of various proteins that are not characteristic of the norm. In particular, one work showed the presence of pepsin in the saliva of patients with bronchial asthma, which the authors associate with severe reflux of the respiratory tract and ingestion of contents from the stomach [7]. A number of circulating proteins of blood plasma, of tissue origin, in bronchial asthma found in saliva, for example, amphiregulin, can reflect their increased regulation in serum/plasma [3].

Understanding the impact of bronchial asthma on oral tissue health will enable the development of early diagnosis methods and a comprehensive dental treatment algorithm.

The purpose of the study: to study the mixed saliva parameters in adolescents with bronchial asthma with glucocorticosteroid therapy.

Materials and methods. The present study was conducted at the Department of Orthodontics and was approved by the Ethics Committee of the Moscow State Medical and Dental University, Moscow, Russia. The study included 40 patients with mild to moderate bronchial asthma and 18 patients without somatic status of both sexes aged 13 to 17 years (mean-14 years). The diagnosis of bronchial asthma was made by an allergist in accordance with the international GINA criteria.

Inclusion criteria for participants with bronchial asthma were the use of inhaled corticosteroids for at least three months and beta-2 agonists to relieve spasms at least once a week. Exclusion criteria were subjects who, in addition to corticosteroids, used other inhaled drugs, with diagnosed oral candidiasis, and systemic diseases, including allergic rhinitis. All adolescents suffering from bronchial asthma used steroids in the form of dry powder inhalers. As a comparison group, healthy participants who did not have bronchial asthma, of similar age and sex, and denied the use of drugs were selected.

To obtain samples of unstimulated saliva, adolescents were seated in an upright position, with the head inclined forward, as motionless as possible, while passively flowing from the open mouth into a disposable plastic cup for 10 minutes. Saliva samples were centrifuged at 3000 rpm. within 15 minutes. The supernatant was then separated and stored at -22 ° C until examined. In the saliva supernatant, the amount in pg/ml immunoglobulins (Ig) A, G, M, interleukins (IL) - 1 β and IL-6; spectrophotometric method enzyme activity in international units (IU/L) - aspartate aminotransferase (ASAT), alanine transaminase (ALAT), alkaline phosphatase (ALP), lactate dehydrogenase (LDH). Semi-automatic analyzers BioChem SA ("High Technology Inc.," USA) and Stat Fax 1904 Plus ("Awareness Technology, Inc.," USA) were used to determine saliva parameters. Protein values in saliva samples were determined according to the instructions developed for these test systems by the manufacturer "Vector-BEST" (Russia).

Descriptive statistics were used to display frequency of occurrence, mean quadratic deviation, and variance. Comparative analysis was performed using a non-parametric Mann-Whitney test and chi-square test, which were considered significant at $p < 0.05$.

Results of a research. The research of amount of A, G, M immunoglobulins showed that at teenagers against the background of bronchial asthma in saliva authentically ($p < 0.001$) the number of IGA, IgG and IgM is increased. It demonstrates to change of the immune status, owing to violation of a homeostasis in a mouth. Even more reflect these shifts of change in amount of the cytokines and enzymes reflecting inflammatory processes and a condition of hygiene of a mouth. At teenagers with asthma the quantity of IL-1 β and IL-6 is reliable ($p < 0.001$; $p < 0.05$) is higher in comparison with the data obtained at somatic healthy teenagers (table 1).

Table 1
Amount of immunoglobulins and interleukins in saliva of teenagers with bronchial asthma (M \pm m)

| proteins | Ig A pg/ml | Ig G pg/ml | Ig M pg/ml | IL-1 pg/ml | IL-6 pg/ml |
|------------------|----------------|-----------------|----------------|------------------|-----------------|
| Asthma (n=40) | 857 \pm 13,5 | 186 \pm 22,4 | 217 \pm 14,3 | 0,66 \pm 0,03 | 5,17 \pm 0,21 |
| p | <0,001 | <0,001 | <0,05 | <0,05 | <0,05 |
| Normal (n=10) | 290 \pm 23,8 | 0,26 \pm 0,04 | 129 \pm 11,2 | 0,05 \pm 0,002 | 1,81 \pm 0,03 |

Studying activity of LDH in the mixed saliva of teenagers with asthma revealed that was available authentically ($p < 0.05$) the increased result (table 2). The activity of this oxidation-reduction enzyme mainly reflects the anaerobic processes connected in a mouth with pathogenic microorganisms. It is known that LDH catalyzes the last reaction of glycolysis in which pyruvic acid turns into a lactate. The quantity of this metabolite is distinguished from a cage in матрикс a dental plaque and collects there. It promotes acidulation of the environment around enamel and activation of processes of demineralization, not carious and carious cavities on solid tissues of teeth thereby can be formed. Products of metabolism of anaerobic bacteria can settle on soft fabrics of the oral and cause inflammatory processes in them.

Table 2

Activity of enzymes in saliva of teenagers with bronchial asthma (M±m)

| enzyme | LDH IU/L | ASAT IU/L | ALAT IU/L | ALP IU/L |
|------------------|-------------|--------------|--------------|-------------|
| Asthma (n=40) | 206±18,9 | 76,8±2,44 | 39,1±4,55 | 120±8,79 |
| p | <0,05 | <0,05 | <0,05 | <0,001 |
| Normal (n=10) | 95,0±10,2 | 19,9±1,67 | 11,6±0,13 | 18,1±1,33 |

Bacteria of a dental plaque have proteolytic activity that leads to disintegration of proteinaceous molecules both saliva, and oral tissue. It is followed by release of the amino-acid remains which, in turn, are exposed to rotting with formation of toxic volatile compounds (oil, acetic acids, etc.). In reactions of transamination α -ketonic acids which bacteria can turn into glucose are formed. Glucose is power material for cages and also a source for synthesis of sticky polysaccharides. Sticky polysaccharides are levan and dextrans, in turn, provide the adhesive environment for components of a dental plaque. Enzymes of ASAT and ALAT as a result of which they are released the 2-oxoglutarate and oxaloacetic acid, turning in reactions of gluconeogenesis into glucose participate in reactions of transamination. These ketonic acids can also connect calcium ions that provides formation of a scale. In the mixed saliva of teenagers with asthma, the activity of ASAT was almost twice higher, and the activity of ALAT significantly didn't change. The received data indirectly confirm at teenagers with bronchial asthma an active proteoliz in a mouth.

The ALP enzyme containing an ion of zinc in the active center and which is localized mainly in cell membranes reflects rather fully destructive cellular processes. At teenagers with bronchial asthma activity of this enzyme in saliva it is reliable ($p<0.05$) higher in comparison with control group. This hydrolase can come to saliva both from microorganisms, and from the changed oral cages.

Conclusion. Study in saliva of teenagers with bronchial asthma of activity of enzymes, participants of metabolic processes, showed activation of pathogenic microflora along with inflammatory processes in oral tissue. It is confirmed by increase in level IL-1 β and -6 in saliva, responsible for development of inflammatory process. Components of inflammatory reaction and an invasion of pathogens is followed by increase in amount of immunoglobulins. The received results demand purpose of local treatment of tissues of mouth anti-inflammatory and antibacterial means. Especially it is important concerning the patients with asthma who are on glucocorticoid therapy.

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激光治疗代谢紊乱背景下 2 型糖尿病患者的疗效

**THE EFFECTIVENESS OF LASER TREATMENT IN PATIENTS
SUFFERING FROM TYPE 2 DIABETES MELLITUS ON THE
BACKGROUND OF METABOLIC DISORDERS**

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抽象的。在 100 名患有不同严重程度的慢性肾病 (CKD) 的 2 型糖尿病患者中研究了激光治疗 (全视网膜激光凝固) 的有效性。根据糖尿病肾病的严重程度,分为 3 组。第 1 组 (n=31) 包括 1 期慢性肾病患者,第 2 组 (n=45) 包括 2 期 CKD 患者,第 3 组 (n=24) 包括 3 期 CKD 患者。揭示了性别特征——女性患者在所有三组中占主导地位。CKD 的严重程度与 2 型糖尿病的年龄和持续时间相关。缺血性心脏病以及病态肥胖在第 3 组患者中更为常见 (p=0.0002)。肾损伤的严重程度影响黄斑水肿的严重程度。

关键词: 肾脏全视网膜激光凝固术, 慢性肾脏病, 黄斑水肿。

Abstract. *The effectiveness of laser treatment (panretinal laser coagulation) was studied in 100 patients with type 2 diabetes mellitus with chronic kidney disease (CKD) of varying severity. Depending on the severity of diabetic nephropathy, 3 groups were distinguished. Group 1 (n=31) included patients with stage 1 chronic kidney disease, group 2 (n=45) included patients with stage 2 CKD, group 3 (n=24) included patients with stage 3 CKD. Gender features were revealed - the predominance of female patients in all three groups. The severity of CKD correlates with age and duration of type 2 diabetes mellitus. Ischemic heart*

disease is significantly ($p=0.0002$) more common in patients of group 3, as well as morbid obesity. The severity of kidney damage affects the severity of macular edema.

Keywords: *panretinal laser coagulation of the kidneys, chronic kidney disease, macular edema.*

Introduction

Diabetes mellitus (DM) belongs to the group of metabolic (metabolic) diseases, in which both macro- and microangiopathies develop [1,2]. Macroangiopathies in most cases are accompanied by the development of cardiovascular diseases [3,4]. Microangiopathies are characterized by damage to the vessels of the eyeball and kidneys, they have similar physiological changes, which are based, among other things, on impaired glucose metabolism, inflammation and other processes. In addition, there is almost the same frequency of damage to the retina and kidneys (34.6% and 33.2%, respectively) [5,6]. Chronic kidney disease (CKD) is a supra-nosological concept, which defines a violation of the structure or function of the kidneys that persists for more than 3 months [1]. Depending on the severity of the pathological process, there are 5 stages of CKD. Diabetic retinopathy (DR) is a specific late neuromicrovascular complication of DM and one of the manifestations of generalized microangiopathy [7]. The “gold standard” for the treatment of proliferative DR is panretinal laser coagulation [8], which is effective from 60 to 99% [9] and depends on many factors: clinical features, laboratory parameters, psychosomatic status [1].

Purpose of the study. To study the effect of metabolic disorders in chronic kidney disease on the effectiveness of laser treatment of retinopathy in patients with type 2 diabetes mellitus.

Materials and methods

The study was conducted at FSBEI HE Tyumen State Medical University of the Ministry of Health of Russia, Tyumen on the basis of SBHCI TO “Multifunctional Clinical and Diagnostic Center” Tyumen. The object of the study were 100 patients with type 2 DM and the presence of diabetic retinopathy in various forms of its manifestation, for which all patients underwent panretinal laser coagulation of the retina. The median age was 64 years, the interquartile range (Q_1 ; Q_3) was 58-68 years, the proportion of women was 65% (65/100), men 35% (35/100). Group 1 ($n=31$) included patients with microvascular changes in the form of diabetic nephropathy in the CKD stage 1 - 31% of patients (31/100), group 2 ($n=45$) included patients with diabetic nephropathy in the CKD stage 2 - 45 % of patients (45/100), group 3 ($n=31$) included patients with diabetic nephropathy in the stages of CKD 3A and 3B - 24% (24/100). A standard ophthalmological examination was performed: visometry, tonometry (non-contact automatic pneumotonometer

by Reichert), perimetry (PNR-2-01), biomicroscopy of the anterior segment of the eye and vitreous body (SL-140 slit lamp by Carl Zeiss Meditec AG), fundus ophthalmoscopy (using a non-contact lens Ocular MaxField 78D), the thickness of the central retinal region was assessed using optical coherence tomography before and after panretinal laser coagulation using RTVue-100 (OptoVue, USA). To determine the severity and presence of chronic kidney disease (CKD), indicators of glomerular filtration rate (GFR) were estimated, calculated on the basis of creatinine concentration. GFR was calculated using a calculator (<https://nefrosovnet.ru/main/948/scf-calc.html>) and included the use of the Cockcroft-Gault formula, the MDRD formula and the CKD-EPI equation, in accordance with clinical guidelines [13]. In the study, CKD staging [3, 9, 13] was based on this formula, due to the fact that the vast majority of patients in the study groups had pronounced decreases in GFR. Determination of laboratory indicators of high and low density lipoproteins, HbA1c in peripheral blood was carried out by standard methods. The study protocol was approved by the ethical committee FSBEI HE Tyumen SMU, all participants signed an informed consent. Statistical analysis of the results obtained was carried out using the statistical packages SPSS for Windows (version 12.0) and STATISTICA (version 10, license agreement №4190051 of 03.05.2019).

Results and discussion

A comparative analysis of the studied groups of the presented groups did not show significant differences in age ($p=0.37$). The structure of gender characteristics is presented as follows: in group 1, the proportion of women is 64.52% (20/31), men - 35.48% (11/31), in group 2, women 66.66% (30/45), men 33, 34% (15/45), in group 3 women 62.5% (15/24), men 37.5% (9/24). Note the predominance of women in all three groups. A tendency towards an increase in the body mass index in the second and third groups and the incidence of arterial hypertension was revealed. The exception was the presence of such concomitant pathology as coronary heart disease (CHD) and the presence of morbid obesity. In group 1, the proportion of CHD was -35.48% (11), in group 2 - 33.33% (15), while in group 3, the proportion of CHD was 83.33% (20), which is statistically significantly higher ($p=0.0002$). When analyzing the structure of obesity, it was found that the proportion of morbid obesity correlates with the stage of diabetic kidney damage, so in the 1st group of patients, the proportion of morbid obesity was 19.3%, in the 2nd group 24.5%, and in the 3rd group 37.5%, respectively, which is a statistically significant indicator ($p=0.001$).

Comparative analysis of laboratory data of the studied groups did not show statistically significant differences in a number of indicators. These include the severity of lipid profile disorders (cholesterol, low-density lipoprotein, high-density lipoprotein - $p=0.26$, $p=0.31$, $p=0.34$, respectively), fasting blood glucose

concentration ($p=0.11$) and a postprandial period ($p=0.17$); glycated hemoglobin ($p=0.09$); liver parameters (ALT and AST -- $p=0.24$, $p=0.13$, respectively). The exception was the level of creatinine ($p=0.0003$) and glomerular filtration rate ($p=0.0005$).

In accordance with the goal, we analyzed the morphometric parameters of the thickness of the central region of the retina in the study groups before and after panretinal laser coagulation of the retina. Table 1 shows retinal thickness data by groups.

Table 1
Morphometric indices of retinal thickness before and after panretinal laser coagulation.

| Indicator | Group 1 (n=31) | Group 2 (n=45) | Group 3 (n=24) |
|---|-------------------|-------------------|-------------------|
| Retinal thickness in the fovea in nm. to PRC | 212,71± 38,75 | 219,33± 56,32 | 246,54± 72,31 |
| Retinal thickness in the fovea in nm. after PRC | 206,61± 27,17 | 208,81± 47,21 | 244,91± 59,12 |

Note: PRC – panretinal laser coagulation of the retina.

Based on the data presented in Table 1, there is a tendency to increase the thickness of the central region of the retina in group 3 patients both before and after PRC. When analyzing the presence and severity of diabetic macular edema of the retina by groups, 22.6% (7 cases) of macular edema were detected in group 1, 35.55% (16 cases) in group 2, and 66.67% (16 cases) in group 3.) macular edema. In addition, there was no pronounced reduction in retinal thickness after PRC in the third group. In patients with a history of morbid obesity and coronary heart disease, negative dynamics were recorded after PRC in the form of further progression of macular edema and an increase in retinal thickness. Thus, the severity of DME is in direct correlation with the stage of CKD and the presence of CHD and morbid obesity in comorbidities.

Conclusion. Chronic kidney disease is almost twice as likely to develop in women with type 2 diabetes. A comparative analysis of the study groups showed statistically significant differences in the structure of comorbidities, such as coronary heart disease (CHD) and the presence of morbid obesity. In group 1, the proportion of CHD was 35.48%, in group 3, the proportion of CHD was 83.33%, which is statistically significantly higher ($p=0.0003$). When analyzing the structure of obesity, it was found that the proportion of morbid obesity correlates with the stage of diabetic kidney damage, so in the 1st group of patients, the proportion of morbid obesity was 19.3%, in the second group 24.5%, and in the third 37.5%, respectively, which is a statistically significant indicator ($p=0.001$).

The study of laboratory parameters revealed statistically significant deviations in the level of creatinine ($p=0.0003$) and GFR ($p=0.0005$) depending on the severity of CKD.

In patients of group 3 with a history of morbid obesity and coronary heart disease, after PRC, no positive dynamics was recorded, in some cases further progression of macular edema and an increase in retinal thickness were noted. Thus, the severity of DME is in direct correlation with the stage of CKD and the presence of CHD and morbid obesity in comorbidities.

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乳腺癌生存的病理形态学和免疫学评估
**PATHOMORPHOLOGICAL AND IMMUNOLOGICAL
ASSESSMENT OF SURVIVAL IN BREAST CANCER**

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注解。将肿瘤淋巴细胞浸润 (TIL) 作为预测性生物标志物纳入, 似乎是了解乳腺癌 (BC) 生物学的重要一步。该研究的目的是研究免疫活性细胞对乳腺癌肿瘤浸润的预后和预测价值。在该研究中, 之前未完全研究过的乳腺癌患者TIL的个体组分 (CD3+、CD4+、CD8+)、程序性细胞死亡免疫检查点蛋白PD-1及其配体PD-L1, 以及FoxP3及其对肿瘤的影响总生存期和无病生存期。T细胞 (CD8+等) 淋巴细胞浸润肿瘤及调节性T淋巴细胞 (T-regs) 水平对HER2阳性乳腺癌患者联合新辅助和辅助靶向抗HER2治疗的预测价值与细胞毒性化疗, 包括紫杉烷。阐明了免疫活性细胞对肿瘤浸润的预后和预测价值, 以及 PD-1 配体 PDL-1 在三阴性乳腺癌患者和接受新辅助化疗患者肿瘤细胞中的表达。评估不同乳腺癌表型中免疫活性细胞的肿瘤浸润严重程度。

关键词: 乳腺癌; 肿瘤浸润淋巴细胞; PD-1; PD-L1; 免疫疗法

Annotation. *The inclusion of tumor lymphocytic infiltration (TILs) as a predictive biomarker appears to be an important step in understanding the biology of breast cancer (BC). The purpose of the study is to study the prognostic and predictive value of tumor infiltration by immunocompetent cells in breast cancer. In the study, previously not fully studied individual fractions of TIL's in patients with breast cancer (CD3+, CD4+, CD8+), immune checkpoint protein of programmed cell death PD-1 and its ligand PD-L1, as well as FoxP3 and their effect on overall and disease-free survival. The predictive value of T-cell (CD8+, etc.) lymphocytic infiltration of the tumor and the level of T-regulatory lymphocytes (T-regs) in patients with HER2-positive breast cancer undergoing neoadjuvant and adjuvant targeted anti-HER2 therapy in combination with cytotoxic chemotherapy, including taxanes. The prognostic and predictive value of tumor infiltration by immunocompetent cells, as well as the expression of the PD-1 ligand PDL-1 in tumor cells in patients with triple-negative breast cancer*

and undergoing neoadjuvant chemotherapy, was clarified. Evaluation of the severity of tumor infiltration by immunocompetent cells in different breast cancer phenotypes.

Keywords: Breast cancer; tumor-infiltrating lymphocytes; PD-1; PD-L1; immunotherapy

As a result of the study of the archival material of the cancer registry of patients treated at the Institution of oncology named N.N. Petrov from 2000 to 2009 included 1240 patients. In total, TILs were evaluated in 1172 cases.

The degree of tumor infiltration by lymphocytes was quantified according to the recommendations of the International TILs Working Group 2014 (Salgado, 2014, 2015).

High long-term results were obtained in a study of patients with TNBC and an assessment of the ratio of CD8/FOXP3 at baseline and in the residual tumor. The five-year disease-free survival (FFS) was 72% in patients with a high CD8/FOXP3 ratio compared to 40% in patients with a low CD8/FOXP3 ratio ($p=0.009$). In our study, with a high ratio (more than 2), the relapse-free survival rate exceeded 80%, with a low CD8/FOXP3 ratio (0.68), the 10-year relapse-free survival rate decreased to 47% ($p=0.02$).

The pathogenetic pathway through the expression of PD1 and the PDL-1 ligand is the main regulator of the immune response to a growing tumor. In recent years, monoclonal antibodies have been developed that block immune “check-point proteins”. Atezolizumab (anti-PDL1 antibody) has been the most studied drug in breast cancer [3-9].

We have shown that pronounced (more than 10%) lymphocytic infiltration of CD 8+, as well as CD 3+ with low expression of PD-L1 and FOXP3, improves disease-free and overall survival of patients with breast cancer [1].

Approximately 80% of patients with breast cancer have low levels of tumor infiltration of CD8+ cytotoxic T-lymphocytes and CD3+ TILs. Expression of the PD-L1 gene was detected more frequently (29.5%) in triple-negative breast cancer, 1.5 times less frequently (18.2%) in HER2+ breast cancer, and extremely rarely (1.5%) in luminal A subtype.[1,2]

In patients receiving neoadjuvant systemic therapy, the baseline median level of TILs was 26.7% (range 5%-90%) for HER2+ breast cancer and 29.0% (range 5%-80%) for TNBC. Positive PDL-1 level was detected in 21.7% of HER2+ breast cancer and 25.0% of TNBC. After chemotherapy, the median PDL-1 decreased to 14.1% in HER2+ breast cancer and to 11.2% in TNBC. It was found that the level of intratumoral lymphocytes in all fractions of the T-cell response (CD3+, CD4+ [regulatory lymphocytes] and CD8+ [cytotoxic]) is affected by the presence of PDL1 expression both on tumor cell membranes and on the lymphocytes themselves.

Among the studied patients, 20% had a low percentage of CD4+. The 10-year overall survival of patients in the indicated groups reached 93%. In the remaining patients, the percentage of CD4+ exceeded the value of more than 50%. The 10-year overall survival of patients was significantly below 82%.

In triple-negative breast cancer [TNBC], PD-L1 expression was observed in 28 of 95 patients (29.5%), and 67 patients (70.5%) tested negative. In patients with HER2-positive breast cancer, PD-L1 expression was observed in 8 (18.2%) out of 44 patients. In 36 (81.8%) patients the PD-L1 test was negative. Thus, for the entire study group, PD-L1 gene expression was detected in 39 (11.7%) out of 333 patients of cases. Less often (1.5%) in Luminal A type, most often (29.5%) in triple negative breast cancer.

The recurrence-free survival (DFS) was significantly ($p=0.0027$) higher in the group of tumors without PDL1 expression and amounted to 70% vs. 41%, the divergence of survival curves according to Kaplan Meier ($p=0.02$). Overall survival (OS) was also higher in the group of tumors without PDL1 expression and was 75% vs. 50% ($p=0.04$) in the group with PD-L1 expression.

In our study, the achievement of pathomorphological complete regression (pCR) was observed in 77.7% of patients with no tumor cells in the intermediate core-biopsy versus 45.3% in their presence ($p = 0.023$). Atezolizumab “converted” PDL1-negative tumors observed in 45.4% to positive in 74.6% of patients. Conversely, patients who underwent one neoadjuvant chemotreatment (carboplatin + nab-paclitaxel) showed a decrease in PDL1-positivity from 52.1% to 37.9%. Atezolizumab complete pathological regression (pCR) was highest (86.9%) in patients in the “immune-enriched” group (PDL1-positive immune cells [PDL1IC+] or with stromal sTILs or intratumoral iTILs compared with the group of patients from the same group, but receiving one chemotherapy (72.0%, $p=0.02$) [1].

In a multivariate analysis of survival rates, a high level of FOXP3 TILs was significantly associated with poor survival in ER+ breast cancer with no CD8+ T-cell infiltrate (HR=1.3). However, ER-negative FOXP3 TILs tended to improve survival in the HER2+|ER- subgroup, especially those with high levels (>20%) of CD8+ T-cell infiltrate.

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cFLIPL在细胞中的含量决定了程序性细胞死亡的优先途径

THE CONTENT OF CFLIPL IN THE CELL DETERMINES THE PREFERENTIAL PATHWAY OF PROGRAMMED CELL DEATH

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抽象的。cFLIP 蛋白 (FLICE 抑制蛋白) 是 cFlar 基因的产物, 该基因编码无活性的 caspase-8 同系物 (cFLIPL) 或由两个模拟 caspase-8 前域的 DED 结构域组成的短 cFLIP 亚型。目前, cFLIP 蛋白被认为是免疫活性细胞中一种细胞死亡到另一种细胞死亡的主要开关分子, 这使我们可以将其视为开发靶向药物的有前途的细胞靶标。研究结果表明, cFLIPL 在调节 caspase-8 激活和凋亡复合物 II 的形成中发挥关键作用, 从而保护巨噬细胞免受 LPS 依赖性细胞焦亡。同样重要的是, cFLIPL 合成的增加使细胞在体内对 LPS 介导的细胞毒性具有抵抗力, 这强调了 cFLIPL 作为细胞死亡和炎症调节剂的重要性。

关键词: cFLIP 蛋白, 细胞凋亡, 细胞焦亡, 坏死性凋亡。

Abstract. *The cFLIP protein (FLICE-inhibitory protein) is a product of the cFlar gene encoding an inactive caspase-8 homologue (cFLIPL) or short cFLIPs isoforms that consist of two DED domains mimicking the caspase-8 prodomain. Currently, the cFLIP protein is considered as the main switch molecule of one type of cell death to another in immunocompetent cells, which allows us to consider it a promising cellular target for the development of targeted drugs. The results of the study show the key role of cFLIPL in the regulation of caspase-8 activation and the formation of apoptotic complex II in the protection of macrophages from LPS-dependent pyroptosis. It is also important that the increased synthesis of cFLIPL gives the cell in vivo resistance to LPS-mediated cytotoxicity, which underlines the importance of cFLIPL as a regulator of cell death and inflammation.*

Keywords: *cFLIP protein, apoptosis, pyroptosis, necroptosis.*

Programmed cell death and inflammation are interrelated processes of the body's response to infection and are extremely important for suppressing the de-

velopment of the pathogen and the survival of the infected organism. The pyroptotic pathway of programmed cell death is usually associated with caspase-1 and -11 mediated cleavage and activation of gasdermin D, which directly forms pyroptotic pores in the cell membrane [1, 2]. The release of IL-1 β and IL-18 from the cell causes an increase in temperature in the surrounding areas. In experiments *in vivo*, maturation and release of IL-1 β from the cell occurs in response to bacterial lipopolysaccharide (LPS), however, in mouse macrophages *in vitro*, two factors are required to obtain a similar effect: a signal to increase the amount of pro-IL-1 β through Toll-like receptors and any danger signal from the whole spectrum of inducing inflammasome oligomerization, including NLRP3 [3]. The NLRP3 inflammasome activates the apoptosis associated speck-like protein (ASC or PYCARD), and is also able to activate caspase-1 to cleave pro-IL-1 β to the active form, which subsequently leaves the cell through the pores formed by gasdermin D [4]. Despite the fact that the activation of gasdermin D is mainly described as a process dependent on caspase-1 and -11, recently there is evidence of the involvement of caspase-8 in the processes of pyroptosis. Thus, in the case of infection of mouse macrophages with bacteria of the genus *Yersinia*, pyroptosis mediated by caspase-8-dependent activation of gasdermin D was observed. Cell death in this case is associated with the action of the bacterial protein YopJ [5, 6]. This protein is capable of inhibiting MAP kinase TAK1 (TGF β -activated kinase) [7], and in macrophages and dendritic cells it inhibits MAP kinase signaling in general [8, 9], which ultimately leads to a decrease in the immune response to infection. A similar effect and activation of caspase-8 can be obtained with the combined use of LPS and the TAK1 inhibitor 5Z-7-oxosaenol (5z7), which makes it possible to simulate the effect of the YopJ protein upon infection with bacteria of the genus *Yersinia*. Caspase-8 mediated activation of gasdermin D has also been shown in TNF-stimulated macrophages from TAK1-inhibited mice [10]. In all cases, activation of caspase-3 and -7 was observed, which indicates the induction of different pathways of cell elimination, both apoptotic and pyroptotic [8-10].

The mechanisms of IL-1 β maturation mediated by caspase-1 and activation of the NLRP3 inflammasome are presented differently by individual research groups, which is explained by high interest and different approaches to the study of this problem. Thus, in one case, the NLRP3 inflammasome is activated by K⁺ leakage due to the pores formed by gasdermin D [6], while in the other case, a mechanism independent of gasdermin D mediated by pannexin-1 is assumed [10]. And although our studies failed to confirm the direct involvement of pannexin-1 in NLRP3 activation, it is highly likely to be involved through the formation of K⁺ channels leading to ion outflow. Differences in the described mechanisms of activation of the NLRP3 inflammasome may be associated with differences in the intervals for the introduction of activators (LPS, TNF, and 5z7). This phenome-

non may be associated with the weakening of NF- κ B and MAPK signaling (in turn, associated with the synthesis of pro-IL-1 β) upon inhibition of TAK1, which is consistent with our data on a more intense release of IL-1 β in the case of the introduction of activators with an interval of 4 hours than with their combined application [5, 11].

In addition, the timing of LPS addition has a significant effect on the kinetics of cell death, probably due to the induction of genes involved in caspase-8 mediated pyroptosis. It is noteworthy that among the genes whose expression changed both upon LPS activation and upon the combined addition of LPS and the TAK1 inhibitor, there was a gene encoding an enzymatically active caspase-8 homologue, cFLIP. Knockdown of the long form of this protein (cFLIPL), in contrast to the short form, allowed pyroptosis to be activated using only LPS without the addition of TAK1 inhibitors (Fig. 1), while caspase-8 activation and IL-1 β synthesis associated with the NLRP3 inflammasome were observed. Thus, we can safely speak about the important role of cFLIPL in cell resistance to LPS-induced cytotoxicity.

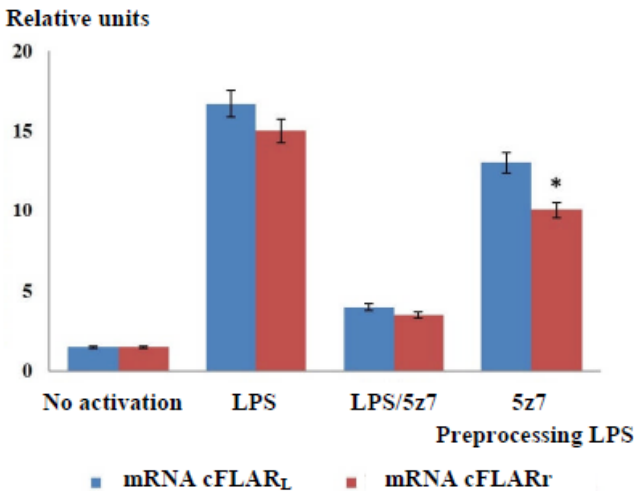


Figure 1. Relative amount of mRNA of cFLIP isoforms under different activation conditions. LPS pre-activation was carried out for 4 hours. The data are normalized to the Gapdh level. * - significant difference between the level of mRNA of long and short protein isoforms during sequential activation of cells

The use of macrophages with knockout cFLIPL makes it possible to obtain a cleaner model for studying the problem and considering its individual steps. Thus, activation of these cells by LPS leads to the formation of a complex of FADD,

RIPK1, and caspase-8, which confirms the fact that cFLIPL prevents pyroptosis by inhibiting pro-apoptotic complex II (Fig. 2). These data indicate the involvement of cFLIPL in the regulation of pyroptosis downstream of TAK1 inhibition.

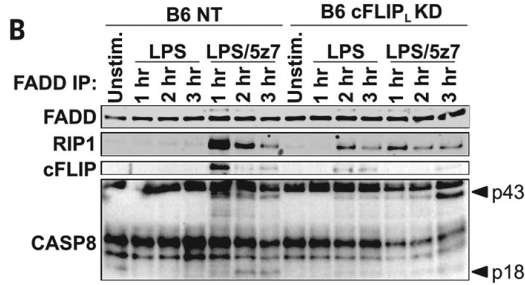


Figure 2. The content of various FADD components in normal and cFLIPL-deficient bone marrow macrophages at various time intervals after activation of LPS and 5z7

There are a number of studies suggesting alternative pathways for the activation of cell death and NLRP3 inflammasome in the absence of TAK1. Using TAK1-deficient macrophages as an example, the elimination of cells of a mixed type was demonstrated: with characteristic features of apoptosis, pyroptosis, and necroptosis [12, 13].

As in our work on *Yersinia*-infected macrophages, both spontaneous and TLR-mediated cell death and NLRP3 inflammasome activation were RIPK1 dependent. However, in TAK1-deficient macrophages, LPS-mediated cell death and inflammasome activation did not require RIPK1 kinase activity [5, 12, 13]. It is quite logical that the lack of TAK1 in the cell affects many types of cell death in various ways, given the wide range of functions of this protein in the regulation of cell death and inflammation, including the activation of NF- κ B and MAPK signaling, the regulation of RIPK1 activity by direct and indirect phosphorylation [14-17]. A summary of our results is presented in the table.

Table

The effect of cFLIPL on the components of the cellular response under the action of LPS

| Regulated process | The presence of cFLIPL in the cell | cFLIPL deficiency in the cell |
|----------------------|------------------------------------|-------------------------------|
| Apoptotic complex II | Inhibited | Functioning normally |

| | | |
|--|--|---|
| Substrate specificity of CASP8 upon inhibition of TAK1 | CASP3, CASP7, GSDMD | GSDMD |
| Pyroptosis activation | LPS + TAK1 inhibitor | LPS |
| LPS activation | IL-1 β is not released, no ASC spec formation and CASP1 activation | NLRP3-dependent IL-1 β release, ASC speck formation, and CASP1 cleavage |
| CASP8 dimers | cFLIPL and CASP8 heterodimers with low enzymatic activity | CASP8 and CASP8 homodimers with high enzymatic activity |

In summary, our results on cFLIPL-deficient macrophages demonstrate a clearer pattern of LPS-induced cytotoxicity and caspase-8-mediated pyroptosis in the absence of multiple effects associated with TAK1 inhibition.

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克罗恩病的眼部病变(文献复习、临床观察)
**EYE LESIONS IN CROHN'S DISEASE (LITERATURE REVIEW,
CLINICAL OBSERVATION)**

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抽象的。 本文回顾了关于克罗恩病眼部损伤的文献,并分析了在该病理学背景下对一名右眼突眼和角膜葡萄膜炎患者的观察结果。 患者自行取消长期基础治疗和胃肠病学家不定期监测会导致克罗恩病恶化(发作),并可能导致肠外表现的发展(在本临床病例中,是一种严重的眼科疾病)。 缺乏患者依从性,未能将疾病的全部病史告知相关专家,导致眼科医生进行长期治疗,无法稳定改善眼部病理(眼球突出、角膜葡萄膜炎),并发角膜穿孔和失明 基础疾病(克罗恩病)的治疗。

关键词: 克罗恩病, 眼科表现, 角膜葡萄膜炎, 眼眶受累。

Abstract. *The article presents a review of the literature on eye damage in Crohn's disease and an analysis of the observation of a patient with exophthalmos and keratouveitis of the right eye against the background of this pathology. Self-cancellation of long-term basic therapy by the patient and irregular monitoring by a gastroenterologist lead to an exacerbation (attack) of Crohn's disease and can lead to the development of extraintestinal manifestations (in the presented clinical case, a severe ophthalmic disease). Lack of patient compliance, failure to inform*

related specialists about the full history of the disease leads to long-term treatment by an ophthalmologist, does not provide a stable improvement in eye pathology (exophthalmos, keratouveitis) and is complicated by corneal perforation and blindness without treatment of the underlying disease (Crohn's disease).

Keywords: *Crohn's disease, ophthalmic manifestations, keratouveitis, orbital involvement.*

Crohn's disease (CD) - is a chronic, recurrent disease of the gastrointestinal tract of unclear etiology, characterized by transmural, segmental, granulomatous inflammation with the development of local and systemic complications. The disease develops as a result of a combination of several factors, including genetic predisposition, defects in innate and adaptive immunity, intestinal microflora and various environmental factors.

CD can affect any part of the gastrointestinal tract, from the mouth to the anus, but in the vast majority of cases, CD affects the ileocecal region. CD, unlike ulcerative colitis (UC), cannot be cured by either therapeutic or surgical methods. The peak incidence is observed between 20 and 30 years of age, and the second peak of incidence is described at the age of 60-70 years. The incidence is approximately the same in men and women.

The severity of the disease is generally determined by: the severity of the current exacerbation, the presence of extraintestinal manifestations and complications, the extent of the lesion, refractoriness to treatment, in particular, the development of hormonal dependence and resistance. Clinical manifestations of inflammatory bowel disease (IBD) are locally not limited to the gastrointestinal tract; a significant proportion of patients have damage to other organs and systems [1].

Extraintestinal manifestations of CD are detected in 6-23% of all patients. Among patients with IBD, eye lesions are more common in Crohn's disease (uveitis, iritis, iridocyclitis, episcleritis), occur in 4% and belong to the group of autoimmune manifestations associated with the activity of the inflammatory process, which appear along with the main intestinal symptoms of exacerbation and disappear along with them during CD treatment, control of the underlying bowel disease is important to prevent relapse [2,3].

Ophthalmic changes are of great clinical importance. Their symptoms are often non-specific, which leads to difficulty in timely etiological diagnosis and, in the future, to a decrease or complete loss of vision, the development of complications that can cause significant damage to the structure of the eye and, accordingly, to a deterioration in the quality of life of patients [5].

The most common eye lesions in CD are uveitis and episcleritis. Episcleritis is an inflammation of the abundantly vascularized connective tissue plate connecting the conjunctiva and the sclera of the eye. Clinical manifestations: redness of one

or both eyes, burning, irritation, severe sensitivity. Decreased visual acuity is not typical.

Uveitis is a chronic inflammation of the choroid of the eye, often leading to a decrease and loss of vision. More common in women. Manifested by headache and eye pain, photophobia, usually accompanied by other extraintestinal symptoms of IBD (articular and skin manifestations). If uveitis is suspected, timely consultation with an ophthalmologist, the use of topical or systemic corticosteroids, immunosuppressants are necessary. In case of ineffectiveness, the appointment of infliximab is recommended.

Rarer ocular manifestations in IBD include central retinopathy, blepharitis, conjunctivitis, dry eye syndrome, cataracts, including steroid-induced cataracts, and involvement of the orbit, posterior segment, and optic nerve may also occur [5.6].

Purpose of the study. To present a clinical analysis of the dynamics of the course of ophthalmopathy in a patient with Crohn's disease.

Materials and methods. The course and treatment of keratouveitis (a condition after perforation of a purulent corneal ulcer) and exophthalmos of the right eye against the background of Crohn's disease in a 59-year-old woman treated in the rheumatology department of SBHCI TO "OCH № 1" were analyzed. Standard and in-depth ophthalmological research methods were used to detect changes in the eyes and adnexa.

A 59-year-old woman was hospitalized in the rheumatology department of SBHCI TO "OCH № 1" due to the severity of her condition on 27.12.2021, with complaints of weakness, arthralgia, ossalgia, pain and blindness of the right eye, exophthalmos, moderate discharge and the presence of bloody crusts in the nose, dryness, feeling of congestion in the nasopharynx, hearing loss, thirst, weight loss by 12 kg. From the anamnesis of the disease, it is known that the diagnosis of Crohn's disease with damage to the colon was verified for about 10 years, at the onset of the disease she received GCS, sulfasalazine. About 4-5 years ago, taking into account the good health and remission of the disease, she ceased to be observed by a gastroenterologist and independently stopped taking the drugs. For the last 3 years, she began to notice nasal congestion, later bloody crusts appeared in her nose, then redness and pain in her right eye joined. Since April 2019, she has been treated for inflammation of the right eye in a polyclinic at the place of residence, received antibacterial and anti-inflammatory therapy. Repeatedly consulted at the Oblast Ophthalmological Dispensary (OOFD) with a diagnosis of keratopathy of the right eye, ophthalmohypertension. In connection with the appearance of exophthalmos, computed tomography (CT) of the orbits was performed on 29.04.2019: "In the parabolbar region, a solid formation 13x24 mm

located on the superior rectus and lateral muscle”. Follow-up and local treatment on an outpatient basis by an ophthalmologist at the polyclinic at the place of residence and at the OOfD were continued without correction of local therapy, which led to an increase in exophthalmos. CT of the orbits in dynamics on 23.05.2021: “Formation in the projection of the right lacrimal gland, 15x24 mm in size”. The patient underwent a diagnostic orbitotomy on the right and a consultation with an onco-ophthalmologist, who, according to the morphological picture, ruled out a malignant process and recommended observation and additional examination by an ophthalmologist, infectious disease specialist, and rheumatologist in a planned manner. The infectious disease specialist ruled out an infectious etiology of the disease. Against the background of conservative anti-inflammatory therapy, there was a gradual decrease in vision in the right eye - up to 0.1, moderate pain syndrome. On 31.10.2021, the patient was taken by an ambulance to the emergency department of SBHCI TO “OCH № 2” with complaints of increased pain and loss of vision in the right eye. When examined by an ophthalmologist (fig. 1), corneal perforation with prolapse of the inner membranes of the right eye was revealed, a neoplasm of the right orbit was suspected.



Figure 1. Patient F., 59 years old. Photo of the orbital (adnexa and anterior surface of the eyeball) and partially nasal regions

In order to dynamically monitor changes in the right orbit, a CT scan of the brain and orbits was performed: “In the anterior-outer parts of the right orbit, a solid formation is determined, with an extra- and intracranial location, dimensions 24x17x34mm, with a defect in the adjacent soft tissues, closely adjacent to the eyeball. The right eyeball is displaced anteriorly, the shape is preserved” (fig. 2).

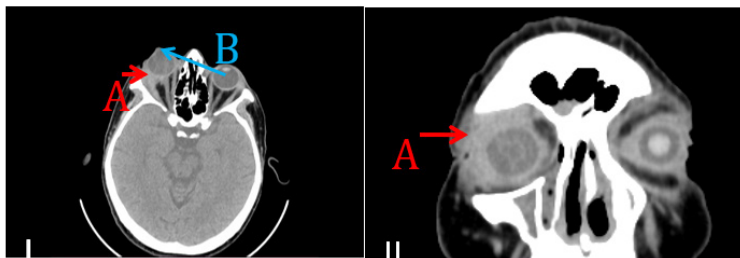


Figure 2. Patient F., 59 years old. CT images of the brain: I - in the axial projection: A - solid formation, with extra- and intracranial location; B - the right eyeball is displaced anteriorly (exophthalmos), the shape is preserved; II - in the coronal projection: A - solid formation

A second consultation with an onco-ophthalmologist was recommended and, if a malignant process in the right orbit was ruled out, a second visit to the emergency department of SBHCI TO “OCH № 2”. The patient could not get to the onco-ophthalmologist due to the lack of a specialist. The OOfD recommended an additional examination outside the Tyumen Oblast, which did not take place due to the acute illness of the patient with COVID-19, which she suffered in a mild form. After recovery from coronavirus infection, given the presence of prolonged exophthalmos, regarded as an orbital pseudotumor due to chronic inflammation (according to the results of the morphological conclusion) and uveitis, the patient was urgently hospitalized in the rheumatology department due to the severity of the condition with suspected prunulomatosis with polyangiinitis. An in-depth examination in the rheumatology department (laboratory diagnostics, colonoscopy with examination of the terminal ileum, CT enterography) by the decision of a council of rheumatologists, gastroenterologists, and therapists made it possible to verify the diagnosis: “Crohn’s disease in the form of ileocolitis with damage to the ascending and transverse sections of the colon, small intestine, chronic continuous course, moderate attack, stricture of the descending colon, with extraintestinal manifestations - sluggish keratouveitis, condition after perforation of a purulent ulcer of the cornea of the right eye. Damage to the upper respiratory tract - reactive polysinusitis, complicated by the destruction of the nasal concha, bilateral otitis media, hearing loss. According to the current clinical guidelines for the management of patients with Crohn’s disease [7], therapy with glucocorticosteroids (prednisolone) at a dosage of 1 mg/kg was prescribed, followed by a gradual decrease to complete withdrawal, basic therapy - azathioprine 50 mg per day, symptomatic therapy. To determine further tactics for the underlying disease, the results of the patient’s examination were sent (telemedicine consultation) to specialized federal centers (Moscow) - FSBI National Medical Research Center for Coloproctology

named after A.N. Ryzhykh and NMIC GB named after Helmholtz (ophthalmology). Before discharge, the patient was examined by an ophthalmologist SBHCI TO "OCH № 1" (figure 3) in dynamics, improvement was noted: the disappearance of exophthalmos, the absence of pain in the right eye, and the reduction of inflammation from the choroid.



Figure 3. Appearance of the patient F. 59 years old after the course of treatment (glucocorticosteroids and azathioprine)

After discharge, it is recommended to continue glucocorticoid therapy orally until it is completely canceled (total duration of GCS therapy is not more than 12 weeks) and locally (epibulbar in the right eye in the form of instillations), the issue of prescribing a genetically engineered biological therapy drug is decided [3]. The patient needs regular monitoring by a therapist, gastroenterologist, ophthalmologist, otorhinolaryngologist at the place of residence.

Discussion. Ophthalmic symptoms in IBD are mostly non-specific and their significance may not be recognized by the clinician; most ophthalmic manifestations are treatable and disappear without consequences with timely treatment, but at the same time they can be the first manifestation of the activity of the underlying disease (Crohn's disease, ulcerative colitis). Knowledge of the ocular manifestations of these systemic diseases and possible complications is essential for the successful interdisciplinary management of patients with IBD.

Thus, the given clinical example clearly demonstrates that with an exacerbation of the disease (CD) with nonspecific extraintestinal symptoms (ophthalmopathy), there are difficulties in timely diagnosis and the prognosis of the disease often worsens. The work of a multidisciplinary team, which includes a gastroenterologist, an ophthalmologist, an internist, a rheumatologist, and a coloproctologist, is increasingly needed for timely diagnosis and the appointment of effective treatment for patients.

Conclusions. Ophthalmologists, general practitioners, gastroenterologists, rheumatologists, in the event of ophthalmopathies in the form of exophthalmos and damage to the cornea with choroid (keratouveitis), must exclude the systemic process of the disease (inflammatory bowel disease, rheumatic and hemato-

logical). Ophthalmic manifestations may indicate the activity of the underlying disease (Crohn's disease). Comprehensive clinical examination, observation and treatment of patients with extraintestinal manifestations of Crohn's disease should be aimed at reducing the frequency of relapses of the underlying disease and the occurrence of extraintestinal manifestations.

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调节分子在肠道感染免疫发病机制中的作用
**ROLE OF REGULATORY MOLECULES IN
IMMUNOPATHOGENESIS OF INTESTINAL INFECTIONS**

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抽象的。目的 - 研究 IL-2 基因的 T330G 多态性变体对急性肠道感染中白细胞介素表达的影响。

材料和方法。对 62 例急性肠道感染患者的血清进行了研究。使用 CJSC “Vector-Best” (新西伯利亚) 的测试系统测定血清中细胞因子 (IL-1 β 、IL-2、IL-6、IL-10) 的水平。使用自动酶免疫分析仪 “Personal Lab” (意大利) 记录结果。使用来自 “Litekh” LLC (圣彼得堡) 的引物通过 PCR 确定 IL-2 基因的 T330G 多态性。对使用 DNA Express Blood 试剂从全血白细胞中分离的基因组 DNA 进行分析, 然后使用两对等位基因特异性引物进行扩增反应。

结果。作为这项工作的结果, 发现在患有细菌性 AII 的患者中, 启动子区 G 等位基因的携带者 - IL-2 基因的 330 TG, 这种炎症介质的产生水平较低, 如 IL-2、IL-6, 在病毒性腹泻组中未显示出这种模式。

结论。因此, 获得的结果可能表明 IL-2 分子的基因型对细菌肠道感染期间炎症介质产生的直接影响。

关键词: 肠道感染, 细胞因子, 多态性。

Abstract. *Purpose - to study the effect of T330G polymorphic variants of the IL-2 gene on the expression of interleukins in acute intestinal infections.*

Materials and methods. *The blood serum of 62 patients with acute intestinal infection was studied. The level of cytokines (IL-1 β , IL-2, IL-6, IL-10) was determined in the blood serum using the test systems of CJSC “Vector-Best” (Novosibirsk). The results were recorded using an automatic enzyme immunoassay analyzer “Personal Lab” (Italy). The T330G polymorphism of the IL-2 gene was determined by PCR using primers from “Litekh” LLC (St. Petersburg). Genomic DNA isolated from whole blood leukocytes using the DNA Express Blood reagent was subjected to analysis, then an amplification reaction was carried out with two pairs of allele-specific primers.*

Results. *As a result of the work, it was found that among patients with AII of a bacterial nature, carriers of the G allele of the promoter zone -330 TG of the IL-2*

gene, there was a lower level of production of such inflammatory mediators, as IL-2, IL-6, in the group of viral diarrhea this pattern was not revealed.

Conclusion. Thus, the results obtained may indicate a direct effect of the genotypes of the IL-2 molecule on the production of inflammatory mediators during bacterial intestinal infection.

Keywords: intestinal infections, cytokines, polymorphism.

Acute intestinal infections (AII) occupy one of the leading places in infectious pathology. Every year more than 1 billion people fall ill with AII in the world [1]. Against the background of the course of AII, the synthesis of pro-inflammatory cytokines IL-1, IL-6, IL-2 and anti-inflammatory IL-10 is induced. [2]. At the same time, a low level of IL-1 contributes to the dissemination of the infectious process, and hyperactivation of the production of TNF- α and IL-6 contributes to a “cytokine storm” with the development of infectious-toxic shock and an unfavorable course of the disease. These mechanisms are genetically determined and, therefore, in carriers of different variants of genes responsible for the synthesis of inflammatory mediators, the level of cytokine production will vary, which will undoubtedly affect the further development of immune processes [3,4,5].

Objective: to study the effect of *T330G* IL-2 gene polymorphism on the expression of pro-inflammatory and anti-inflammatory interleukins in patients with acute intestinal infection of bacterial and viral etiology.

Materials and methods. For laboratory tests - serological and immunological - the blood serum of 33 patients with acute intestinal infection (age 27.2 ± 8.7 years), bacterial etiology, 29 patients with viral diarrhea (age 23.2 ± 8.4 years) served as the material for the study). The main criteria for inclusion of patients in the study were: age from 15 to 55 years, the presence of a laboratory-confirmed intestinal infection in the acute period, the absence of concomitant diseases in the decompensation stage and/or during the exacerbation period, and the absence of other acute pathology. In all patients, the etiological factor AII was confirmed by bacteriological and serological studies: fecal culture for the intestinal group, feces for UPM, RIGA with the determination of AT titer in paired sera, and feces by PCR. As a result of laboratory tests in group 1, 82% (27/33) were diagnosed with Salmonellosis, 6% (2/33) with Shigellosis, 12% (4/33) with others; in group 2, rotavirus gastroenteritis was found in 24.1% (7/29) and norovirus RNA was found in 75.9% (22/29). In the blood serum taken with the written permission of the patients, the level of cytokines (IL-1 β , IL-2, IL-6, IL-10) was determined using the CJSC Vector-Best test systems (Novosibirsk, Russia). The results were recorded using an automatic enzyme immunoassay analyzer “Personal Lab” (Italy). The *T330G* polymorphism of the IL-2 gene was determined by PCR using primers from Litekh LLC (St. Petersburg, Russia). Genomic DNA isolated from whole

blood leukocytes using the “DNA Express Blood” reagent was subjected to analysis, then an amplification reaction was carried out with two pairs of allele-specific primers. Statistical processing of the data obtained was carried out using electronic programs Microsoft Excel 2010, Statistica 6.0, with the determination of the statistical significance of differences at the achieved significance level $p \leq 0.05$ using the Mann–Whitney test (U-test).

Work results. The T330G IL-2 mutation affects the promoter region of the gene and affects the rate of transcription and translation of the encoded IL-2 protein [4,5], which has a synergistic, pleiotropic, and paracrine effect. We have studied the effect of the T330G gene polymorphism of the IL-2 gene on the synthesis of not only IL-2, but also other inflammatory proteins in AII. In the course of the work, in the first group, bacterial AII, among carriers of the G allele, a lower production of pro-inflammatory cytokines was revealed, with the lowest indicators in the group of patients with the -330GG genotype: IL-2 (13.438 [12.188-15] and 13.126 [11.874-14.688] pg/mL, $p \leq 0.05$), IL-6 (1.345 [0-4.166] and 1.254 [0-4.032] pg/mL, $p \leq 0.05$) compared with the -330TT variant. The concentration of IL-1 \square , IL-10 in blood serum in patients with different variants of gene polymorphism, without pronounced fluctuations ($p \geq 0.05$). In the second study group, patients with viral diarrhea, there were no characteristic dynamic changes in the level of cytokines depending on the T330G IL-2 gene polymorphism ($p \geq 0.05$) (table 1).

Table 1

The level of cytokines in patients with AII of bacterial and viral etiology depending on the presence of a mutation in the T330G region of the IL-2 gene

| Indicators | The concentration of cytokines in patients with AII, viral etiology, depending on the T330G genotype of the IL-2 gene (n=29) | | | The concentration of cytokines in patients with AII, bacterial nature, depending on the T330G genotype of the IL-2 gene (n=33) | | |
|-------------------------|--|---|---|--|---|--|
| | genotype TT (n=14) | genotype TG (n=11) | genotype GG (n=4) | genotype TT (n=8) | genotype TG (n=18) | genotype GG (n=7) |
| IL-2 pg/ml | 13,594 [12,188-15,312] | 13,44 [12,188-15,218] $p \geq 0,05$ | 13,75 [11,95-14,30] $p \geq 0,05$ | 14,062 [12,5-15,312] | 13,438 [12,188-15] $p \leq 0,01$ $p^* \leq 0,05$ | 13,126 [11,874-14,688] $p^* \leq 0,05$ |
| IL-1 \square pg/ml | 0 [0-1,6] | 0 [0-10,25] $p \geq 0,05$ | 0 [0-0] $p \geq 0,05$ | 0 [0-1,6] | 0 [0-1,133] $p^* \geq 0,05$ | 0 [0-0,933] $p^* \geq 0,05$ |
| IL-6 pg/ml | 1,586 [0-4,66] | 1,434 [0-4,032] $p \geq 0,05$ | 1,344 [0,05-5,15] $p \geq 0,05$ | 1,972 [0,538-4,66] | 1,345 [0-4,166] $p^* \leq 0,05$ | 1,254 [0-4,032] $p^* \leq 0,05$ |

| | | | | | | |
|----------------|--------------------|------------------------------|--------------------------------------|-----------------------|-------------------------------|-------------------------------|
| IL-10 pg/ml | 5,518 [0-11,25] | 5,518 [0-10,25] p≥0,05 | 5,517 [0,345- 11,25] p≥0,05 | 6,896 [0,69-10,25] | 5,173 [0-9,804] p*≥0,05 | 4,828 [0-8,966] p*≥0,05 |
|----------------|--------------------|------------------------------|--------------------------------------|-----------------------|-------------------------------|-------------------------------|

Note. p – the reliability indicator of the level of inflammatory mediators in patients with viral diarrhea, in cases of mutation in comparison with carriers of -330TT of the IL-2 gene (non-parametric Mann-Whitney method - U - criterion, median, interquartile interval between 25 and 75 percentiles); p* is an indicator of the significance of the level of inflammatory mediators among patients with bacterial AII, in the case of a mutation in comparison with the -TT330 genotype of the IL-2 gene (nonparametric Mann-Whitney method - U - criterion, median, interquartile interval between 25th and 75th percentiles)

Thus, it can be assumed that the polymorphism of the IL-2 gene in the T330G promoter zone, with the replacement of a thymine nucleotide by a guanine nucleotide, in combination with other factors characteristic of a bacterial infection, affect gene expression, significantly reducing the production of IL-2, IL-6. Therefore, when assessing and predicting the severity and duration of the disease in patients with AII of a bacterial nature, we can assume a more protracted course of the disease, the development of complications among carriers of the hypoproductive allele G of the IL-2 T330G gene.

Conclusion.

- in patients with acute intestinal infection of a bacterial nature, who are carriers of the recessive allele G of IL-2 T330G, a lower production of pro-inflammatory IL-2 and IL-6 was determined.

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青少年焦虑、抑郁表现及应对压力策略的研究
**THE STUDY OF THE LEVEL OF ANXIETY, DEPRESSIVE
MANIFESTATIONS AND STRATEGIES OF COPING WITH
STRESS IN YOUNG PEOPLE**

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摘要：在现代条件下，在心理健康面临全球挑战的背景下，年轻人中不同程度的焦虑、抑郁和压力障碍有所增加。在某种程度上，这些与表现下降、情绪不稳定、食欲不振和睡眠相关的疾病症状不会引起年轻人的关注，也不是联系专家的理由。他们使用的认知、情绪和行为应对策略各不相同，但并不总是自适应的，这会影晌应对压力的成功与否。

关键词：焦虑、抑郁、压力、应对、认知应对策略、行为应对、年轻人的应对策略。

Abstract: *In modern conditions, against the backdrop of global challenges to mental health, there is an increase in anxiety, depressive and stress disorders of varying severity in young people. Until a certain point, the symptoms of these disorders associated with decreased performance, emotional instability, impaired appetite and sleep do not cause concern among young people and are not a reason for contacting specialists. The cognitive, emotional and behavioral coping strategies they use are variable, but not always adaptive, which affects the success of coping with stress.*

Keywords: *anxiety, depression, stress, coping, cognitive coping strategies, behavioral coping, coping strategies in young people.*

INTRODUCTION

According to the World Health Organization (WHO), “mental health is a state of well-being in which the individual realizes his or her own abilities, can cope with the normal stresses of life, can work productively and fruitfully, and is able to make a contribution to his or her community” [1]. The state of mental health con-

sists of a number of biological, psychological, social, spiritual and moral determinants and, of course, depends on socio-economic processes, geopolitical situation, presence of external threats and other challenges (for example, a pandemic) that change the usual way of life, requiring an individual to adapt quickly to changed living conditions. According to WHO, in 2020, every second young person aged 19–29 experienced anxiety or depression [2]. The WHO Bulletin of September 13, 2021 notes that 280 million people in the world suffer from depression, but since the early diagnosis of this disorder is difficult, over 75% of patients do not receive timely assistance [3]. The results of the NAFI study (March 2022), which involved 1,600 people from 53 regions of Russia aged 18 and older, indicate that 70% of the Russians surveyed experience anxiety of varying degree of severity [4].

Cognitive, emotional and behavioral coping strategies help with coping with stress. They contribute to the successful integration of the individual into the reality that has changed under the influence of stress factors and optimal adaptation to unexpected life difficulties. Thus, we consider the study of the level of anxiety and depression of young people, as well as the analysis of the coping strategies they use to be a relevant and practice-oriented area of scientific activity.

METHODS

The purpose of this work was to study the level of anxiety, depression and coping mechanisms, as strategies for coping with stress, among university students. This study was conducted in July 2022. The testing involved 38 people (17 girls and 21 boys), aged 18 to 25. Criteria for inclusion in the study were the presence of increased psycho-emotional and stress load due to intensive educational activities; no diagnosed psychiatric disorders.

The following methods were applied:

1) the PHQ-9 depression scale - a module from the Patient Health Questionnaire that allows to detect depressive manifestations [5]

2) scale GAD - 7 (Generalized Anxiety Disorder -7), designed to identify signs of anxiety

3) a technique for the psychological diagnosis of coping mechanisms according to E. Heim (E. Heim test). It contains a description of 26 variants of situationally determined coping mechanisms compared with three basic forms of mental activity (cognitive, emotional and behavioral), the study of which allows to assess the degree of adaptability of coping strategies [6, 7].

RESULTS AND DISCUSSION

As a result of testing using PHQ - 9, the following results were obtained: the number of points scored 0-4 (no depression) was observed with 8 (21.1%) students; a score of 5–9 was noted with 14 (36.8%) people. And although their scores were not so high, relative to the maximum possible 27 points, but this group of students correlates with the risk group for the development of depression.

Test results exceeding 10 points indicate the presence of depressive manifestations of varying degree of severity (the test is considered positive) and provide for the need to contact a specialist for subsequent therapeutic work or psychological support. According to the results of the survey: the sum of points 10–14, corresponding to a moderate risk of developing depression, was found with 10 (26.32%) students; a score of 15–19, correlated with a fairly high severity of depressive symptoms, was found in 5 (13.16%) students; the total score of 20–27 was determined with 1 (2.63%) respondent and indicated the need for an urgent consultation with a doctor and the start of therapy. In parallel, the level of anxiety was studied among the respondents. The results of testing using GAD - 7 were as follows: the sum of the points scored 0–4 (minimum level of anxiety) was observed with 16 (42%) students; the sum of points 5–9 - with 13 (34.2%) people, which indicated a moderate level of anxiety; a score of 10–14 was found in 6 (15.8%), which corresponded to the average level of anxiety; the total score of 15–21 was found in 3 (8%) students, which indicates a high level of anxiety. As part of the study of the characteristics of students' coping with stress, cognitive, emotional and behavioral coping strategies were studied.

Cognitive copings are reflections and cognitive patterns used by a person to cope with stress or a difficult life situation. Adaptive cognitive coping strategies aimed at analyzing emerging problems and finding optimal solutions based on the awareness of personal value (problem analysis, strategy for maintaining self-control, setting one's own value) were observed with 13 (34.2%) respondents. Relatively adaptive cognitive coping strategies (giving meaning to what is happening, religiosity, relativity) were found in 14 (36.8%) people. Non-adaptive cognitive coping, manifested by passive forms of activity, combined with low self-esteem and disbelief in one's own ability to overcome difficulties, was found in 11 (29%) students.

Emotional coping strategies are emotional reactions to stress that allow a person to function in changed conditions of life without a significant deterioration in their own psycho-emotional state or using previously worked out emotional response patterns. Adaptive copings (optimism, protest), due to an active life position, unwillingness to put up with the difficulties that have arisen and confidence in the surmountability of problems, were identified in 20 (52.6%) of the respondents. Relatively adaptive emotional coping strategies aimed at getting rid of the psycho-emotional tension that has arisen or at delegating responsibility for making a decision to another person were observed with 3 (7.9%) people. Non-adaptive emotional strategies, perceived as suppressed emotional tension (anger, irritation) that did not find a way out, along with self-blame, were found in 15 (39.5%) of the respondents.

Behavioral coping strategies are based on the ability to transform one's own behavior in accordance with changing events and stressful situations in every-

day life in order to overcome the problems that have arisen. Adaptive behavioral copings (altruism, seeking help, cooperation), which allow relying on interaction with others and actively offering one's help to others in solving problems, were chosen by 12 (31.6%) people. Relatively adaptive behavioral copings (distraction, compensation), which imply the possibility of temporary suspension from solving problems using means and methods acceptable to the individual, were noted in 13 (34.2%) students. Non-adaptive behavioral copings (solitude, active avoidance), which contribute to the formation of an avoidant type of activity and behavior that allows avoiding solving the problem, were chosen by 13 (34.2%) students.

CONCLUSION

As a result of the study, it was found that depressive manifestations of mild, moderate and significant degree of severity were found in 16 (42%) students; an increased level of anxiety was observed in 22 (57.9%) students. All respondents, being confident in the absence of mental health problems, did not consider the received answers and scores as manifestations of dysfunction or illness. Such characteristics of their mental status as a decrease of working capacity and concentration of attention, a violation of vital functions (sleep and eating behavior), as well as the actual depressive and anxiety manifestations that require the attention of specialists, did not become the reason that forced the students to seek psychological or medical help, and were interpreted by them as a "tribute" to intensive and energy-consuming study.

The study of coping mechanisms in the study group demonstrated variability both in the specifics of coping strategies and in the degree of their adaptability. Cognitive coping strategies that provide for a passive attitude towards overcoming problems were chosen by 65.8% of students. 34.2% of students chose an active position through perception of the causal relationship of the problem and assessing their capabilities based on previous experience. 60.5% of students used adaptive and relatively adaptive emotional strategies. 39.5% of students used maladaptive coping methods, which can negatively affect their ability to cope with stress in the future. Adaptive behavioral copings, which allow to act effectively in a stressful situation, were observed in 32.6% of students. In stressful situations, 68.4% of students used coping options focused on evading problem solving and taking responsibility for their actions or strategies aimed at ignoring stress in order to "legitimize" their inaction.

Thus, the study of the test results of students, who do not have diagnosed mental disorders and who function on the background of a high stress load due to educational activities, has demonstrated the use of coping mechanisms by them, which are often relatively adaptive or non-adaptive. Identified depressive and anxiety manifestations, being not recognized and corrected in a timely manner, carry the risks of developing a more serious mental pathology. It is possible to

increase this symptomatology up to clinical manifestation, or its “masking”, followed by somatization of mental disorders, or the search for getting rid of a negative psychoemotional state through impulsive actions or addictions. Considering the urgency of the problem and its social significance, we consider it appropriate to continue this study with a wider audience coverage and to conduct such tests (as part of screening) in educational institutions, followed by “feedback” and specific recommendations (or routing) for participants.

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运载火箭分离部件坠落次数与阿尔泰边疆区儿童患病率的关系
**THE RELATIONSHIP BETWEEN THE NUMBER OF FALLS
OF SEPARABLE PARTS OF LAUNCH VEHICLES AND THE
PREVALENCE OF DISEASES AMONG CHILDREN OF THE ALTAI
KRAI LIVING NEAR THE FALL AREAS**

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抽象的。阿尔泰边疆区的部分地区被用作从拜科努尔航天发射场发射的运载火箭分离部分的坠落区。火箭和太空活动对影响区、邻近领土和邻近领土的人口造成负面影响。该研究的目的是确定生活在火箭和太空活动区的阿尔泰边疆区儿童中某些疾病的流行与运载火箭分离部件坠落次数之间可能存在的相关性。对于大多数类别的疾病，首次揭示了直接的强相关性和中等相关性。该结果来自于 1999 年、2006 年、2011 年和 2015 年对阿尔泰边疆区恰雷什区儿童的调查。

关键词：火箭和太空活动，运载火箭的分离部件，儿童健康，疾病流行，相关性。

Abstract. *Part of the territory of the Altai Krai is used as fall areas for the separated parts of launch vehicles launched from the Baikonur Cosmodrome. Impact areas, adjacent territories and the population of adjacent territories are negatively affected by rocket and space activities. The aim of the study is to identify possible correlations between the prevalence of certain diseases among the children of the Altai Krai living in the zone of rocket and space activity, and the number of falls of the separating parts of launch vehicles. For most classes of diseases, a direct strong and medium correlation was revealed for the first time. The results were obtained from a survey of children in the Charysh district of the Altai Krai in 1999, 2006, 2011 and 2015.*

Keywords: *rocket and space activities, separating parts of launch vehicles, children's health, prevalence of diseases, correlation.*

For many years, rocket and space activities (RSE) have firmly entered almost all spheres of human activity. However, RSE provides not only great benefits for humanity, but also creates serious problems associated with its negative impact on environmental objects and, possibly, on public health. The Altai Krai is exposed to RSE, since more than one and a half thousand square kilometers of its territory are involved as impact areas (IA) for separable parts of launch vehicles (SPLV) of the Yu-30 zone (IA № 306, 307, 309, 310), launched from Baikonur Cosmodrome. IA SPLV and territories adjacent to them are areas of increased environmental risk, the most important indicator of anthropogenic impact is the health of the population [1-6, 8, 13-15, 17, 19, 20, 22-25].

The purpose of this work was to identify possible correlations between the prevalence of diseases among the child population of the Altai Krai territories adjacent to IA SPLV and the number of SPLV falls.

Material and method

Since 1999, with the financial support of the Roscosmos State Corporation, the KGBU “Research Institute of Regional Medical and Environmental Problems” has been regularly conducting in-depth medical examinations of residents of the Altai Krai territories living in the RSE zone [9-12, 25]. In 1999, 2006, 2011 and 2015, the child population (0-17 years old) of the Senteleksky village council of the Charyshsky district was surveyed.

An in-depth medical examination of the population was carried out by the expeditionary method, by a specially formed mobile medical team, the composition of which was determined empirically. The team was equipped with mobile diagnostic and laboratory equipment [16].

Statistical processing of the received materials included coding the diagnoses established during the survey based on the tenth revision of the International Classification of Diseases and Related Health Problems (ICD-10), entering these data into a personalized electronic database, calculating intensive indicators of the prevalence of diseases in general for all examined children, for boys and girls, according to ICD-10 classes and individual nosologies. Statistical processing of identified cases excluded data for two classes – “External causes of morbidity and mortality. Class 20” (V01-Y98) and “Factors influencing health status and visits to healthcare facilities. Class 21” (Z00-Z99).

Subsequently, during the statistical analysis of the obtained materials, due to the difference in the age composition of the examined children in different years of the study, standardization of intensive indicators was carried out. Using the direct standardization method, standardized indicators of the overall prevalence

of diseases and the prevalence of diseases in general by ICD-10 classes were calculated with a detailed analysis of individual groups of nosologies from Class II “Neoplasms”, Class IV “Diseases of the endocrine system, eating disorders and metabolic disorders” and Class VII “Diseases of the eye and its adnexa” for all examined children, for boys and girls. These indicators were used to determine possible relationships between disease prevalence rates and the number of SPLV falls.

When estimating the number of fallen SPLVs, information was used on the total number of launches of launch vehicles of various types, since this is clearly related to the number of metal fragments of the second stage that fell and the amount of propellant residues and its components that entered the atmosphere and fell on the territory of IA and adjacent territories. In addition, the data we have on a significant spread of the separating parts of launch vehicles beyond the calculated contours IA contributed to the fact that when determining the number of fallen SPLVs, i.e., in fact, the number of launches of launch vehicles, we took into account all launches at the time of the examination of the children of the Senteleky village council Charyshsky district in 1999, 2006, 2011 and 2015, as residents of the territory adjacent to IA SPLV.

After studying the statistical methods designed to identify the relationship between phenomena [7, 18, 21, 27], a statistical method was selected that allows solving the tasks - Spearman's rank correlation coefficient ($\rho - r_o$). The errors of the correlation coefficients (m) were also calculated. The statistical significance of the obtained coefficient is assessed using Student's t-test. In our case, there were 4 pairs of initial data, which corresponds to the number of degrees of freedom 2. According to the Plokhinsky table, $p < 0.05$ with a value of $t > 4.3$; $p < 0.01$ at $t > 9.9$ [27].

It should be noted that the correlation coefficients obtained by us in the course of this work are for the most part not statistically significant ($p > 0.05$). The main reason for this is that the calculations used the original data from the results of four surveys of the population, i.e. the initial data in the calculations were presented in four pairs of figures. The presence of the fifth pair of data would have made it possible to obtain more reliable results, but after 2018 field surveys of the population were not carried out, which was mainly due to the anti-epidemic restrictive measures associated with the COVID-19 pandemic.

Results and its discussion

According to the rank correlation coefficients obtained for the first time on this material, the direction and strength of the revealed correlation were determined. A fairly large list of ICD-10 classes and individual diseases has been identified with a direct strong relationship between the standardized prevalence rates of these diseases among children and the number of SPLV falls in the fall areas adjacent

to the territories of residence of this population. That is, with an increase in the number of launches, the level of prevalence of diseases also increased. A direct strong connection was found with “Diseases of the skin and subcutaneous tissue. Class XII” (L00-L99) - $p = +0.92$; “Diseases of the ear and mastoid process. Class VIII” (H60-H95) - $p = +0.87$; diseases of the muscles of the eye, disorders of friendly eye movement, accommodation and refraction (H49-H52) - $p = +0.77$; obese (E66) - $p = +0.75$; “Diseases of the respiratory system. Class X” (J00-J99) - $p = +0.72$.

In addition, there is a part of diseases where a direct average relationship with the number of SPLV falls was revealed. These include “Diseases of the eye and its adnexa. Class VII” (H00-H59) - $p = +0.66$; “Diseases of the nervous system. Class VI” (G00-G99) - $p = +0.65$; total number of diseases - $p = +0.55$; “Congenital anomalies [malformations], deformities and chromosomal abnormalities. Class XVII” (Q00-Q99) - $p = +0.47$; “Diseases of the musculoskeletal and connective tissue. Class XIII” (M00-M99) - $p = +0.37$; malignant neoplasms (C00-C97) - $p = +0.33$.

An analysis of the correlation coefficients obtained for the examined boys also revealed the presence of correlation coefficients (p), indicating that for most ICD-10 classes and individual diseases in boys, a direct correlation was found. At the same time, the presence of a direct strong relationship was noted for “Diseases of the skin and subcutaneous tissue. Class XII” (L00-L99) - $p = +0.87$; obesity (E66) - $p = +0.82$; “Diseases of the ear and mastoid process. Class VIII” (H60-H95) - $p = +0.81$.

In addition, boys have a part of the ICD-10 classes and individual diseases, where a direct average relationship was found with the number of SPLV falls. These include: “Diseases of the nervous system. Class IX” (G00-G99) - $p = +0.64$; “Diseases of the respiratory system. Class X” (J00-J99) - $p = +0.61$; “Congenital anomalies [malformations], deformities and chromosomal abnormalities. Class XVII” (Q00-Q99) - $p = +0.58$; total number of diseases - $p = +0.49$; “Diseases of the eye and its adnexa. Class VII” (H00-H59) - $p = +0.38$; malignant neoplasms (C00-C97) - $p = +0.33$; “Diseases of the musculoskeletal and connective tissue. Class XIII” (M00-M99) - $p = +0.33$; diseases of the eye muscles, disorders of friendly eye movement, accommodation and refraction (H49-H52) - $p = +0.30$.

An analysis of the correlation coefficients obtained for the surveyed girls showed that for most ICD-10 classes and individual diseases, a direct correlation was found. At the same time, the presence of a direct strong relationship was noted for “Diseases of the skin and subcutaneous tissue. Class XII” (L00-L99) - $p = +0.94$; diseases of the eye muscles, disorders of concomitant eye movement, accommodation and refraction (H49-H52) - $p = +0.93$; “Diseases of the ear and mastoid process. Class VIII” (H60-H95) - $p = +0.90$; “Diseases of the respiratory

system. Class X”(J00-J99) - $p = +0.79$; obesity (E66) - $p = +0.70$; “Diseases of the eye and its adnexa. Class VII”(H00-H59) - $p = +0.70$.

In addition, girls have a part of the ICD-10 classes and individual diseases, where a direct average relationship was found with the number of SPLV falls. These include: “Diseases of the nervous system. Class IX“(G00-G99) - $p = +0.66$; total number of diseases - $p = +0.58$; “Diseases of the musculoskeletal and connective tissue. Class XIII“(M00-M99) - $p = +0.42$; “Congenital anomalies [malformations], deformities and chromosomal abnormalities. Class XVII”(Q00-Q99) - $p = +0.40$.

The cases of inverse correlation revealed in children are random. For the most part, these diseases were detected during medical examinations in isolated cases or were recorded in separate years. Among them are neoplasms (C00-D48); “Diseases of the genitourinary system. Class XIV”(N00-N99); “Diseases of the blood and hematopoietic organs and certain disorders involving the immune mechanism. Class III”(D50-D89); “Pregnancy, childbirth and the postpartum period. Class XV“(O00-O99); “Separate conditions arising in the perinatal period. Class XVI”(P00-P99).

Conclusions

1. In the course of the study, a methodology adequate to the goals and objectives of the study was developed, which made it possible for the first time to reveal a correlation between standardized indicators of the prevalence of diseases among the child population of the territories of the Altai Krai adjacent to the SPLV impact areas and the number of launch vehicles.

2. When identifying possible relationships between data on the prevalence of diseases by ICD-10 classes and individual nosologies among all examined children with the number of SPLV falls, most of the obtained correlation coefficients correspond to a direct strong and medium correlation, i.e. with an increase in the number of launch vehicles, the level of disease prevalence increases.

3. When identifying possible relationships between data on the spread of diseases among the examined boys with the number of SPLV falls, most of the obtained correlation coefficients correspond to the presence of a direct strong and medium correlation, i.e. with an increase in the number of launch vehicles, the level of disease prevalence increases.

4. When identifying possible relationships between data on the prevalence of diseases among the examined girls with a drop in SPLV, for most classes of diseases, a direct strong and medium correlation was determined, i.e. with an increase in the number of launches of launch vehicles, the level of prevalence of diseases increases.

To increase the reliability of the research results, medical examinations of the population of the territories adjacent to the RSE zone should be continued.

The results obtained can be used to make management decisions in healthcare, in planning and implementing social protection measures for residents of the territories adjacent to the RSE zone, as well as for scientific purposes.

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rTMS 方法与认知训练在 COVID-19 后患者康复中的多模式应用
**MULTIMODAL APPLICATION OF RTMS METHODS TOGETHER
WITH COGNITIVE TRAINING IN THE REHABILITATION OF
PATIENTS AFTER COVID-19¹**

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抽象的。文章讨论了联合使用经颅节律磁刺激 (rTMS) 和神经心理训练在 COVID 后患者认知障碍康复中的有效性。使用 rTMS 刺激区域的选择是在扩展的神经心理学检查的基础上进行的,其目的是确定大脑的形态功能状态并识别功能失调最严重的区域。根据确定的疾病,为每位患者单独编制认知训练。

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关键词：COVID-19、认知训练、神经心理学检查、rTMS、神经康复、多模式刺激。

Abstract. *The article discusses the effectiveness of the combined use of transcranial rhythmic magnetic stimulation (rTMS) and neuropsychological training in the rehabilitation of cognitive disorders in post-COVID patients. The choice of stimulation zones using rTMS was made on the basis of an extended neuropsychological examination, the purpose of which was to determine the morpho-functional state of the brain and identify the most dysfunctional areas. Cognitive training was compiled individually for each patient, depending on the identified disorders.*

Keywords: *COVID-19, cognitive training, neuropsychological examination, rTMS, neurorehabilitation, multimodal stimulation.*

Introduction. Cognitive disorders are one of the important medical and social problems of modern medicine. According to statistics, every third person on the planet as a result of brain diseases of various etiologies manifests disabling disorders, including movement, sensitivity, speech disorders and, in the vast majority of cases, cognitive deficits. Cognitive deficit is a violation of higher mental functions: memory, attention, gnosis, praxis, executive functions and various types of thinking. In the absence of timely treatment and correction, these disorders inevitably progress, leading to maladjustment of a person and his dependence on others. Some modern diseases can provoke cognitive deficits even in young apparently healthy individuals. And the total number of patients with impaired higher mental functions of varying severity is 22% of all people on the planet over 50 years old.

Cognitive impairments slow down the process of physical rehabilitation, reducing functional capabilities and rehabilitation prognosis, prevent the formation of motivation for treatment, and are directly related to restrictions in everyday life, social and professional life.

Currently, the goal of rehabilitation treatment is to bring the rehabilitation period as close as possible to the acute stage of treatment using the strategies of induction and escalation of functional capabilities when they are limited. At the same time, one of the important principles is the personalization of influences, which combines the topical correspondence of stimulating influences (targeted stimulation) with the use of multisensory afferentation, taking into account the modality of the identified functional disorders.

At the moment, the search continues for effective methods for improving brain functions that can be used in the rehabilitation of patients with diseases and injuries of the nervous system.

However, the most interesting is transcranial magnetic stimulation (TMS), a method of non-invasive stimulation of the cerebral cortex by means of an alternat-

ing magnetic field. Under the action of a magnetic field, activation and modulation of neuroplastic processes occur (at the same time, intact but functionally inactive motor neurons are activated and sprouting processes are stimulated), a decrease in cerebral blood flow dyscirculation, opening of reserve capillaries, and an improvement in shunt function. rTMS is also capable of modulating higher cortical functions – facilitating learning, visual pattern recognition, improving memory, analog thinking, and decision making; regulate the function of the zone that is directly affected, as well as influence other brain structures functionally related to it - that is, TMS allows you to reorganize neural networks by modulating their connections and can be used for neurocognitive rehabilitation.

To create a protocol, an important issue is the choice of stimulation frequency. Comparison of high-frequency and low-frequency stimulation showed the effectiveness of high-frequency stimulation and its more pronounced effect compared to low-frequency stimulation. In addition to choosing the frequency of stimulation, it is equally important to determine the zone of influence.

Target. Make an individual program of cognitive training taking into account the general “cognitive profile” of the post-COVID patient and conduct topically oriented cognitive training in conjunction with rTMS.

Materials and methods. At the first stage, all patients selected to participate in the study (27 people) underwent a screening neuropsychological examination, the purpose of which was to determine the presence of a cognitive deficit in relation to the average norm. For this, quantitative diagnostics was used using the MoCA and FAB screening scales. If the patient had a mild or moderate cognitive deficit, he underwent an extended neuropsychological examination. Its goal was to conduct a topically-oriented neuropsychological diagnostics, namely, the determination of the morpho-functional state of the brain, a qualitative analysis of the state of higher mental functions and their topical correlation with certain areas of the brain. For this, the Luria-Nebraska Neuropsychological Battery was used. n=15 people underwent this diagnosis (6 men, 9 women, median age was 37.7 years). The patients were then divided into two study groups. The main group included patients who underwent topically oriented cognitive training in conjunction with rTMS (n=7 people, 3 men, 4 women, median age 39). The patients of the second group underwent only cognitive training without the use of stimulating techniques (n=8 people, 3 men, 5 women, median age 37.5).

Results. As a result of extended diagnostics, the neuropsychologist compiled an individual “cognitive profile” for each patient, in which the most impaired cognitive functions were identified and the localization of this function in the brain was indicated. In total, we identified 6 zones that were affected: occipital, parietal, temporal lobes, parietal-temporal-occipital region (TPO zone), premotor region, prefrontal region. Each patient had his own, identified as a result of the diagnosis,

a combination of the above zones, the number of which varied from 1 to 3-4. In 100% of patients, dysfunction in the work of the frontal parts of the brain was revealed. Also, 66% of patients had dysfunction in the work of the temporal lobes. The frequency of occurrence of violations in the work of other areas was evenly distributed. To work with each of them, the neuropsychologist selected a number of tasks and exercises.

So, to work with dysfunction of the occipital parts of the brain, manuals were used aimed at developing and restoring visual perception (superimposed images, noisy images, chimerical pictures), memory (memo games) and attention (“Double”, “find and show”). To work with the prefrontal sections, tasks aimed at working with performing functions were used: labyrinths, rebuses, various encryption, games with self-test. To work with the TPO zone, the neuropsychologist used constructors, graphic dictations, various options for oral and written counting, and games for training quasi-spatial representations. When working with the premotor area, in addition to training the assimilation of successively organized motor actions, we also used variations of a graphic test, tasks to establish patterns and sequences. When correcting violations of tactile perception and kinesthetic praxis (parietal areas), manuals with stimulus material of different shapes, sizes, made of different materials, as well as exercises for working with hand positioning were added to the work. When working with the temporal region, the work differed depending on the hemisphere. When working with the temporal region of the dominant hemisphere, accompanied by speech disorders in the patient, speech therapy tasks and manuals were used. When working with the temporal region of the non-dominant hemisphere, the work was focused on non-speech sounds, prosodic, exercises with rhythms.

During the correction, a physiotherapist and a neuropsychologist worked with patients of the first group at the same time. In advance, the specialists discussed the sequence of moving the TMS coil between the zones defined for each particular patient. While the physiotherapist was stimulating one of the zones, the neuropsychologist was conducting cognitive training aimed at correcting this particular zone. rTMS procedures were carried out according to the following protocol: relative amplitude 90% of PMO, stimulus frequency in a series 10 Hz, number of stimuli in a series 20, number of series 20, pause between series 30 sec, total time up to 30 minutes, number of procedures 10-15.

As a result, in patients of the main group, with whom the above described multimodal stimulating measures were carried out, a pronounced positive trend was observed in the form of an increase in the average score on MoCA by 3.4, on the FAB scale by 2.1 points. There were also improvements in individual tests: fluency of speech, reciprocal coordination, problem solving, establishing analo-

gies. Patients of the control group, with whom only neuropsychological sessions were performed during rehabilitation, also noted positive dynamics, but to a lesser extent: an increase in the average score on MoCA by 1.8 points, on the FAB scale by 1.6 points.

Conclusions. Each patient has his own cognitive impairment profile, which can be identified using topic-oriented neuropsychological diagnostics. This makes it possible to form an individual rehabilitation program, including targeted stimulation together with training in neuropsychological correction. Common to all patients who have had a new coronavirus infection are disorders of the frontal lobes of the brain. Multimodal application of rTMS methods together with personalized cognitive training is a more effective method in the rehabilitation of patients with post-COPD cognitive disorders than monomodal rehabilitation measures. Such a personality-oriented approach makes the rehabilitation process the most personalized and effective.

现代牙科的口干问题

THE PROBLEM OF XEROSTOMIA IN MODERN DENTISTRY

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抽象的。口干症或口干症是现代牙科中的一个实际问题，各专业的医生都会遇到。口干症是一种以唾液腺分泌活动减少和唾液分泌减少或完全停止为特征的病症。1889年哈登首次引入“口干”一词，他认为这不是一种独立的疾病，而是一种症状。口腔干燥会对患者的生活质量产生负面影响，是牙科实践以及医学各个领域中的一个实际问题。根据一些文献来源，已知有 10% 到 25% 的年轻患者抱怨口干。而在老年患者中，表现频率为 43% 至 52%。已经确定，到 50 岁时，唾液分离率可能会下降。口干症导致口腔龋齿过程的发展、粘膜创伤的增加、唾液腺结构的变化和口腔粘膜的生态失调。此外，口干综合症有助于口腔炎、牙周炎和口腔感染性病变的发展。

关键词：口干，口干症，口干症。

Abstract. *Xerostomia or dry mouth syndrome is an actual problem in modern dentistry, which is encountered by doctors of various specialties. Xerostomia is a condition that is characterized by a decrease in the secretory activity of the salivary glands and a decrease or complete cessation of salivation. For the first time the term “dry mouth” was introduced by Hadden in 1889, who believed that it was not an independent disease, but a symptom. Dryness in the oral cavity negatively affects the quality of life of patients and is an actual problem in dental practice, as well as in various fields of medicine. According to some literature sources, it is known that 10 to 25% of young patients complain of dry mouth. And in elderly patients, the frequency of manifestation is from 43 to 52%. It has been established that by the age of 50, the rate of saliva separation may decrease. Xerostomia contributes to the development of a carious process in the oral cavity, increased traumatism of the mucous membranes, changes in the structure of the salivary glands and dysbiosis of the oral mucosa. Also, xerostomic syndrome contributes to the development of stomatitis, periodontitis and infectious lesions of the oral cavity.*

Keywords: *dry mouth, xerostomia, xerostomia syndrome.*

Relevance

Dry mouth develops gradually. There are three stages of xerostomia: initial, clinically pronounced and late. In the initial stage, dryness in the oral cavity may disturb the patient periodically, most often during a long conversation. There may also be complaints of burning in the mouth. According to the results of laboratory studies, there is no decrease in the level of salivation [1]. In the stage of clinical manifestations, dry mouth bothers patients during meals and when talking quite often. The late stage is characterized by constant dryness in the oral cavity, soreness, while patients are forced to eat food with water [2].

According to research, depending on the sensations and clinical manifestations, true and imaginary (false) xerostomia are distinguished. True xerostomia is associated with a violation of the secretory function of the salivary glands due to a number of reasons: a consequence of chemotherapy and radiation therapy, autoimmune diseases, HIV infection, Alzheimer's disease, herpetic stomatitis, periodontal tissue diseases, etc. True xerostomia can be divided into the first and second types. The first type is a combination of xerostomia with a normal state of the oral mucosa; the second type is a combination of dryness with damage to the oral mucosa. True xerostomia is characteristic, for example, of Sjögren's disease and radiation injuries [6].

Studies have established that the epithelium of the salivary glands is very sensitive to radiation. In the first 3-5 days, an increase in the process of salivation was noted, followed by the onset of persistent hyposalivation. After 12-14 days, the development of xerostomia accompanied by dysphagia, as well as perversion and loss of taste sensations were observed. It is known that radiation changes in the salivary glands are largely reversible. In 2-3 weeks after the cessation of irradiation, the mucous membrane of the oral cavity returns to a relative norm. However, scientists' data indicate that with a large absorbed dose (5000-6000 rad), irreversible changes in the salivary glands may occur [8].

Literature data indicate that with imaginary (false) xerostomia, the discomfort associated with a feeling of dry mouth, as a rule, is not due to a real decrease in salivation. It occurs in neurological conditions such as stress and depression. People with impaired nasal breathing (polyps, adenoids, deviated septum, swelling of the nasal mucosa, allergic diseases) are forced to constantly breathe through the mouth. In this case, xerostomia is due to increased evaporation of fluid from the oral cavity - false hyposalivation. Dry mouth only at night can be the result of sleeping with your mouth open. During sleep, saliva is released 8-10 times less than during wakefulness, which is more common in old age. In the elderly and senile age, there is a decrease in salivation [7].

An analysis of the literature data shows that patients may have varying degrees of severity of dry mouth. In the first group of patients, dryness in the oral cavity is

constantly present, in the other - periodically, for example, during and after eating or when talking. To get rid of dryness, patients drink water while eating or talking. With chronic dryness of the oral mucosa, it is rather difficult for the patient to speak, chew, swallow, there is a violation of the sense of taste, there is a sharp pain when eating spicy and hard foods, there is a burning sensation, roughness of the mucous membrane, there are difficulties with wearing removable dentures, as well as discomfort during sleep [3].

It is noticed that patients with xerostomia find it difficult to chew and swallow food, since saliva no longer washes and softens it. Because of this, food lumps are formed incorrectly, which leads to provoking diseases of the gastrointestinal tract, liver and kidneys. After stopping the flow of saliva into the oral cavity, it ceases to saturate the teeth with minerals and protect the oral mucosa from bacteria. A bacterial process begins in the oral cavity and oropharynx, leading to the development of viral and fungal diseases, such as tonsillitis, stomatitis, caries, etc. Drying out of the oral mucosa is a common cause of complaints in the elderly. At the same time, in elderly patients, the quality of life deteriorates and various psychoneurotic disorders occur. Due to severe stress, they try to communicate less with other people and withdraw into themselves [5].

Literature evidence suggests multiple and extensive causes of xerostomia. There are transient xerostomia caused by such causes as taking medications (retinoids, sympathomimetics, antihistamines, etc.), a state of mental agitation, acute or chronic inflammation of the salivary glands, as well as fluid loss against the background of general exsiccosis with a general fever, bleeding, diarrhea or diabetic coma. Persistent xerostomia occurs in the elderly, in postmenopausal women, with aplasia or hypoplasia of the salivary glands, after radiation therapy, in systemic diseases such as diabetes mellitus and hyperthyroidism. Also, persistent xerostomia is observed in patients with primary diseases of the salivary glands, such as a tumor, Sjögren's syndrome, actinomycosis, etc.; with lesions of the salivary glands in systemic diseases, for example, malignant lymphomas and progressive scleroderma; poisoning, iron deficiency anemia, cachexia and other diseases associated with deficiency [9].

It has been noted that xerostomia syndrome has a rather negative effect on the quality of life of patients and is an urgent problem in dental practice, otorhinolaryngology, oncology, and other areas of medicine. Scientists subdivide xerostomia into sialogenous and aialogenic. Sialogenic xerostomia is characterized by dryness of the mucous membrane of the oral cavity and pharynx in the absence of dryness of the tongue, dysfunction or structural changes in the salivary glands. With aialogenic xerostomia, there is a lesion of the tongue with a strong sensation of thirst. With prolonged symptoms of xerostomia, hyperemia and atrophy of the tongue, as well as the oral mucosa, may develop. Soon, small cracks appear, a light

brown coating on the tongue, a feeling of dryness in the oral cavity, difficulty in speech and swallowing due to pain.

At the same time, a number of studies have confirmed that as a result of a decrease in the amount of saliva, a mature biofilm is formed rather quickly, which leads to enamel demineralization, the development of a carious process, and inflammation of periodontal tissues. More pronounced and severe clinical signs may be as follows: dry lips and the appearance of dry crusts, loss of gloss of the oral mucosa, the appearance of fissures and lobules on the back of the tongue, angular cheilitis, candidiasis, inflammation and ulceration of the oral mucosa, difficulty in communication, soreness when eating (especially spicy and sour), the inability to swallow food without liquid. Also, patients have hyperemia and swelling of the mucous membrane, while saliva can be quite viscous, dental sticking to the oral mucosa is noted. In such patients, there are seizures in the corners of the lips, dryness and cracks, the mucous membrane of the oral cavity with elements of keratinization, inflammation and hyperemia, there is no free saliva in the oral cavity. It has been established that in patients with imaginary xerostomia in 60% of cases, a decrease in the amount of oral fluid by more than half was revealed, which requires the appointment of replacement therapy, which, first of all, should include proper individual oral hygiene care.

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用于分析三维声场的 FPGA 系统
**FPGA SYSTEM FOR ANALYZING THREE-DIMENSIONAL
SOUND FIELDS**

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译注: 本文描述了数字MEMS麦克风阵列的并行轮询系统的实现。介绍了系统的结构和功能描述, 给出了各个模块和软件的操作原理。该研究并未追求创建统一块和模块的目标, 在这方面, 开发的 IP 块非常严格地绑定到麦克风阵列的给定配置和麦克风模型。

关键词: MEMS 麦克风, 音频信号的注册, Zynq, QM-Tech Zynq, IP 核, 音频流的并行处理。

Annotation: *This article describes the implementation of a parallel polling system for an array of digital MEMS microphones. The structural and functional description of the system is presented, the principles of operation of individual blocks and software are given. The research did not pursue the goal of creating unified blocks and modules, and in this regard, the developed IP blocks are quite rigidly tied to a given configuration of the array of microphones and to the microphone model.*

Keywords: *MEMS microphones, registration of audio signals, Zynq, QM-Tech Zynq, IP cores, parallel processing of audio streams.*

Introduction

Recording and analysis of sound waves can be of interest in a number of scientific and practical tasks, such as:

- analysis of the sound passage through inhomogeneous media;
- determination of the direction to the sound source and the power level of the

source;

- modeling or verification of models of the functioning of the hearing organs of biological objects.

The goals are to develop a system for recording and visualizing sound fields.

The tasks are as follows:

- development of IP cores for receiving signals from an array of microphones;
- development of IP cores for parallel audio preprocessing;
- development of appropriate software for data storage, visualization of sound fields.

Due to a rather high degree of uncertainty in the final and intermediate data processing algorithms, a possible change in the number of microphones involved in sound recording, the system will be developed on programmable logic chips. The basic system-on-a-chip (S-on-C) was selected for the Zynq family of chips, which contain, in addition to sufficiently large blocks of programmable logic, two ARM Cortex-A7 processor cores. Processor cores can work both under the control of the embedded program and under the control of the operating system. In most cases, Linux is chosen as the operating system for Zynq. The usage of Linux OS looks promising in terms of the development of the software ecosystem of the device, and we also solve a lot of issues concerning the user interface, software support and development, and many others.

Block diagram of the audio signal reception system.

The block diagram of the audio signal reception unit is shown in *Figure 1*. It includes an array of microphones placed in the order of the lattice (in this case, a 3x7 microphone array with one separate microphone is used to compensate for its own noise). Audio channels should be received as much as possible in parallel mode to avoid the occurrence of a system phase difference due to sequential polling by a multichannel ADC. The synchronicity of the sound channel readouts is realized due to digital MEMS microphones (in this case, INMP441 with I2S interface), united by common synchronization circuits. The output data signals from the microphones are combined into a bus of eleven consecutive lines. Two microphones are connected to each of the lines, forming a stereo pair of right and left channels according to a typical connection scheme.

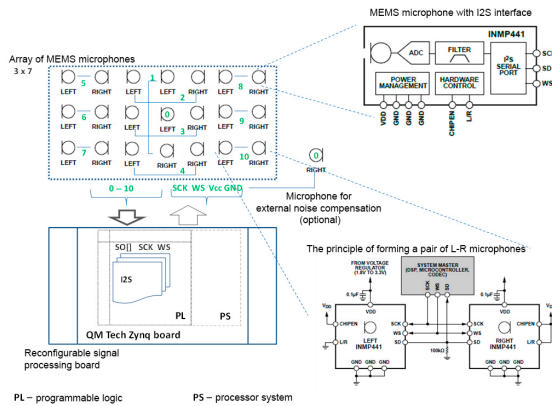


Figure 1. Block diagram of the audio signal reception and processing system

The synchronization and data lines of the array of microphones are serviced by logic implemented in the programmable logic block S-on-C Zynq (Fig.2).

A deserializer block (DES) has been created for polling the array, which:

- generates clock sequences on WS and CLK lines;
- receives 48-bit audio report sequences from each pair of microphones;
- packs samples into a 504-bit output vector;
- generates a reference number (cyclically ranging from 0 to 2047);
- generates a confirmation clock signal for each finished output vector;
- generates an interrupt signal every 1024 references.

The output vector of the DES block, the reference number and the confirming clock signal arrive at port A of the dual-port memory block (512_RAM) with the organization 512x2048 (2048 512-bit cells), which is essential. Thus, during operation, the DES unit automatically writes audio signal references to the buffer memory.

The second memory port is connected to the processor subsystem (PS) via the AXI bus memory controller. The interrupt signal from the DES unit via the AXI bus I/O controller is also connected to the processor subsystem.

512_RAM memory is organized in such a way that writing to it from the DES block is carried out with 512-bit words, while reading from the processor subsystem is implemented by using the AXI controller with 64-bit words (theoretically, 8/16/32-bit reading is also possible, but, as preliminary testing has shown, such methods lose in speed).

In the mock-up version of the system, a control unit for LEDs and switches (as AXI peripherals) were added as peripherals for debugging purposes.

For each of the devices in the memory space of the processor system, its own pool of addresses is allocated and for the application program they are available simply as memory cells. At the moment, direct reading of data from buffer memory to the main memory of the processor system is being implemented, potentially it is possible to implement this operation through direct access to memory via the AXI-DMA controller.

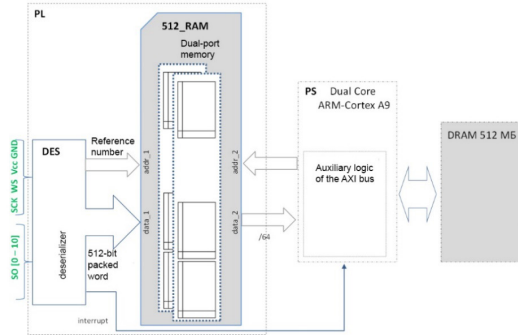


Figure 2. Structural and functional diagram of the interaction of logic blocks and processor subsystem

Implementation of the system by means of FPGA Zynq 70**

The structure described above is implemented by means of the block design of the Vivado IDE (**Fig.3**). The DES, 512_RAM blocks are written in Verilog, the AXI bus blocks are I/O line controllers, the BRAM memory controller is from the standard Vivado component library for S-on-C Zynq.

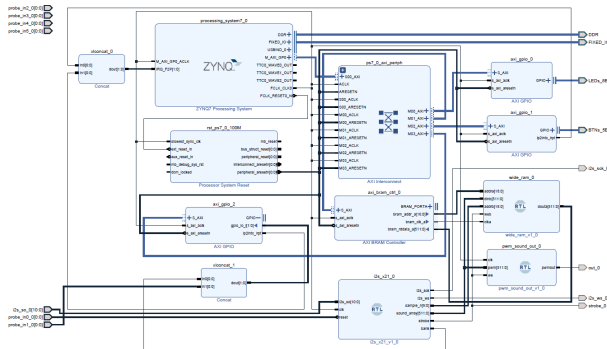


Figure 3. Block Design of sound channel processing system in Vivado environment

Figure 4 shows an example of how the DES module works when reading signals from digital MEMS microphones.

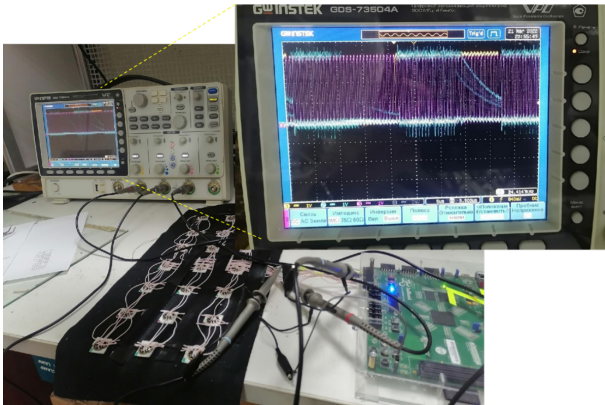


Figure 4. An example of the operation of polling an array of microphones using the ZedBoard debugging board

The operation of the DES module begins after the reset signal is removed, the clocking of the array of microphones and the reception of digitized sound begins. After recording 1K samples by the DES module, an interrupt signal is generated, according to which the processor system begins reading the buffer into RAM, and the module itself continues writing to the buffer in the higher addresses. When the 2K-word boundary is reached, the interrupt signal is sent again, the recording of samples continues to the lower buffer addresses (recording goes continuously and cyclically). Even in the mode of direct reading of buffer memory by the processor, due to reading 64-bit words, there is a guaranteed time margin between two consecutive interrupts. The process continues until the recording of sound samples of the required duration is obtained (set by the application program). Further, arrays with records of signals of individual channels are formed from the resulting array – byte-by-byte reading and packing of three bytes that make up the original 24-bit reference into 32-bit words for subsequent processing.

Conclusions

As a result, IP cores were developed and tested to control an array of MEMS microphones with an I2S interface, methods of reading data and formatting them for subsequent processing were also approved. Testing was carried out on the ZedBoard debugging board, the target board in the final device is a budget board from QMTech – Xilinx Zynq XC7Z010 SoC FPGA. The differences from the

test board are in a slightly smaller amount of RAM and a block of programmable logic, but for this project these parameters are not critical. Further development of the system is the addition of modules for preliminary digital signal processing (primarily noise filtering), integration of modules with Petalinux to simplify the implementation of the user interface, expansion in the functionality of the system as a whole and simplification of the modification and support of software.

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从二恶英中净化气体的方法
METHODS OF GASES PURIFICATION FROM DIOXINS

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抽象的。介绍了有关二恶英的特性、毒性和结构的信息。介绍了世界上发达国家二恶英类物质销毁的基本原理和技术。

关键词: 二恶英, 销毁方法。

Abstract. *Information on the properties, toxicity and structure of dioxins is presented. The basic principles of the destruction of dioxins and technologies adopted in the highly developed countries of the world are described.*

Keywords: *dioxins, destruction methods.*

Properties of dioxins

The term dioxins is commonly used to refer to a family of compounds whose structure is based on Polychlorinated dibenzo-p-dioxins (PCDD) and polychlorinated dibenzofurans (PCDF). Each compound contains two benzene rings linked by oxygen atoms. In the case of PCDD, the rings are connected by two oxygen bridges; in the case of PCDF, the rings are connected by a C-C bond and an oxygen bridge. Figure 1 shows the structural formulas of PCDD and PCDF indicating the position of hydrogen atoms that can be replaced by a Cl or other halogen atom.

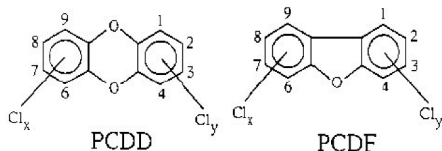


Figure 1. *Structure of PCDD and PCDF. [1]*

Dioxins are by-products of the production of chlorophenols, their formation also accompanies the combustion of compounds containing C, H, O and Cl (or Br) atoms. Dioxins and furans (PCDDs and PCDFs) form in the temperature range of 250-450 °C. There is also evidence of the formation of such compounds in the

range from 150 to 240 °C. Dioxins and phenols are formed more easily, so the temperature in the smoke filters is kept below 200 °C.

The content of dioxins in waste gases, waste water or solid residues is highly dependent on the choice of technology and equipment. The literature distinguishes between primary and secondary sources of dioxins. According to this classification, sources of dioxins that are released into the environment and/or in places other than the place of waste processing are classified as secondary sources. For example, anthropogenic dioxins that are prevented from entering gaseous emissions by purification systems may remain in adsorbents and yet enter the food chain and increase human consumption. The average half-life of dioxins in the soil is 10-12 years, and in the human body 6-8 years. Dioxins are sparingly soluble in water, are not destroyed by acids, are resistant to alkalis, and strongly bind to solid carriers. [1]

Much is known **about the toxicity** of dioxins. Let's note that out of the known 75 dioxins and 135 furans, the toxicity of only a small number of compounds of this class has been seriously studied. The action of 2,3,7,8-tetrachlorodibenzodioxin has been most intensively studied. Very low doses of 2,3,7,8 TCDD cause weight loss, reduced immunity, decreased testosterone, skin and liver disease. [11] The average lethal dose for humans, obtained by calculation, is 0.05-0.07 ppm for a single oral intake. [2].

The MAC criterion for dioxins is completely unacceptable. This follows from the well-established fact that there is no dose of dioxin so low that it would be safe. The allowable daily dose established in Russia is 10 pg/kg of body weight/day, the American norm is 6 femtograms (10^{-15} g) per kilogram of body weight per day. These norms are set out of impotence, since the already existing dioxin pollution in Western countries is so high that these norms are easily exceeded. [2] In Europe in 2012, the norm for the concentration of dioxins is 0.1 ng/m³. The norm of dioxin content in sediments is 1-2 ng/kg (Europe). [1]. Table 1.

Table 1.
MAC or SRLI for polychlorinated dibenzo-p-dioxins (PCDDs) and dibenzofurans (PCDFs).*

| An object | Dioxins DE (PCDD+PCDF) | Σ PCB | Regulatory document (for dioxins) |
|---|------------------------|---------------------|--|
| Atmospheric air | 0.5 pg/m ³ | 1 µg/m ³ | GN 2.1.6.014-94 |
| Air emissions | 0.1 ng/m ³ | | European norm |
| Drinking water, ground and surface water, withdrawal points | 20 pg/l 1 pg/l | 1 µg/l | <u>Order of the Ministry of Health of the USSR No. 142-9/105 dated 05.05.1991</u> ----- GN 2.1.5.2280-07 |

| | | | |
|----------|------------|----------|--|
| The soil | 0.33 ng/kg | 60 ng/kg | Order of the Ministry of Health of the USSR dated 08.09.86 No. 697 DSP |
|----------|------------|----------|--|

* Estimated safe exposure level

Ways of formation of dioxins have not yet been fully identified. It is believed that in the process of MSW processing, they are formed at temperatures of 700-1000 °C. The volume of their formation depends on the conditions of the process and the feedstock, and, above all, the presence of Cl- and Br-containing components in it. Factors that increase the formation of dioxins are temperatures above 150 °C, alkaline reaction medium, the presence of carbon, CO, chlorides and copper compounds as catalysts.

Destruction of PCDD and PCDF.

Numerous methods have been developed for soil disinfection and disposal of waste from dioxinogenic technologies, based on various principles - physical, chemical, biological, and more often combined. Efficient and economical methods for disinfecting soils and chemical industry waste from dioxins have been developed in the USA, as well as in Germany, Italy, and France.

“Burnout” of PCDDs and PCDFs is the most accepted method for their destruction. According to the standards of the European Union, the geometry of the hot zone of the burner must ensure that gases stay in the zone with a temperature of at least 850 °C for at least 2 s (two seconds rule) at an oxygen concentration of at least 6%. This is a very strict requirement and it is not easy to withstand it. It is especially difficult to achieve a high oxygen content in the combustion zone. These incinerators are equipped with additional heaters to maintain this temperature at all times. The fuel in them is oil, and usually only some of its fractions are active. Most modern incinerators use factory filters (often with Teflon membranes) that allow submicroparticles to be collected and thus can trap dioxins from the solid phase [4].

Compliance with the rule of two seconds means the complete destruction of dioxins when this requirement is met, which is completely untrue. The requirement of two seconds means that under these conditions the concentration of dioxins in the exhaust gases will be acceptable for their purification to the required 0.1 ng/m³ (at 11% oxygen in the gases). This implies that the degree of purification will not be lower than “six nines”, that is, 99.9999 96; [5-7].

The method of “burnout” dioxins is criticized. The notion that “everything will burn” at high temperatures is a mistake. This does not take into account the special property of dioxins - the ability to new synthesis in the cold zone (there is a so-called “de novo synthesis” - the synthesis of complex molecules from simple ones). A lot of evidence indicates the inefficiency of this method for reducing the concentration of products of incomplete combustion (PIC). PIC also includes

dioxins. It is reported in [4] that when examining waste incinerators, it was shown that dioxins are formed during the combustion process, and that their formation occurs in the cooling zone, therefore, an increase in temperature during combustion does not lead to the destruction of dioxins. Hot electrostatic filters, which are so common in all cleaning schemes, generate dioxins themselves. Thus, during the examination of the incinerator in Florida on one incinerator, the following results were obtained: at a temperature of 242n°C on an electrostatic filter of 242 °C, dioxin emissions amounted to 893 ng/nm³, at a temperature of 282°C - 2100, and at 347 °C - 8533. [8-10]

It is shown that the emissions of 15 toxic substances (PIC) from various types of combustion furnaces do not improve with a change in temperature from 700 to 1500 °C, with a change in the residence time of gases in the furnace from 2 to 6 s and a change in oxygen concentration from 2 to 15%. In addition, high temperatures lead to an increase in the volatility of the components, resulting in an increase in emissions, including hazardous metals. [9]

It is a common notion that quenching the off-gases (“quenching”) will reduce the formation of dioxins. True quenching involves lowering the temperature many hundreds of degrees in a fraction of a second to freeze the thermodynamic equilibrium position at high temperature. This is difficult to achieve in real conditions of the WIP. But even if it were possible to freeze the hot mixture of gases, they would not achieve a decrease in concentration, since “new” dioxins are formed not in vapors, but on the surface of fly ash particles.

A typical “quenching” scheme: flue gases with a temperature of more than 850 °C enter either the water injection chamber or the waste heat boiler, where they are cooled to approximately 320 °C. [9]. These are precisely the temperature conditions under which secondary dioxins are formed. Thus, the waste heat boiler in the scheme under consideration is an ideal reactor for the formation of secondary dioxins. It is believed that reducing the oxygen content of the off-gases (European Union regulations require at least 6% O₂ in the gases during combustion) could improve the performance of this reactor in terms of secondary dioxin production.

Other dioxin removal methods are known and are detailed in the Annex. Let’s take a quick look at some of the most effective ones.

Disinfection of waste **using infrared heating**. The process involves two processing. Decontamination efficiency 99.9999 %. Destruction of organic components of highly toxic waste, achieved instead of oxidation by electric **pyrolysis**. The temperature in the heat treatment zone is maintained at the level of 2200-2500 °C, the processing time is milliseconds. The gases after pyrolysis undergo additional purification in a cyclone and in an adsorber with activated carbon. Stationary and mobile installation options have been developed. The main products formed during the treatment of soils contaminated with dioxins are hydrogen, chlorine and

HCl. Only materials that are homogeneous in phase (not sludge) can be processed in the plant. Dioxin disinfection efficiency $\rightarrow 99.999\%$.

The method of destruction of organic substances by melts, mainly sodium and potassium carbonates, with simultaneous air blowing has been known since 1969 and was originally used for coal gasification. Hydrocarbons are oxidized to carbon dioxide and water. Chlorine atoms of organochlorine substances are absorbed by the melt. The advantage of the process is a relatively low temperature (about 800-1000 °C) and the absence of nitrogen oxides in emissions. Both solid and liquid wastes with low water and ash content can be processed. Destruction efficiency has been demonstrated on poisonous substances and herbicides. Impurities of highly toxic dioxin I are destroyed by 99.96-99.98%.

A dechlorination process was developed in an inert gas atmosphere at 600-800 °C using calcium oxide fixed on silica gel. The process takes place in an electrical-stirred reactor. Dioxins and furans are destroyed by more than 99.99%.

Several effective technologies have been created for the disinfection of highly toxic liquid wastes by high-temperature **pyrolysis in pyroplasm**. The processed waste is introduced directly into the plasma arc (> 5000 °C). In this case, complex organic molecules decompose into atoms, which later recombine into the simplest molecules - H_2 , N_2 , CO, CO_2 , HCl, ethylene, acetylene, etc. With this technology, not only liquid wastes are treated, but also suspensions of solids.

Several chemical methods of disinfection from dioxins and related compounds have been proposed and implemented. These include **dechlorination, oxidation and ozonolysis, reduction, chlorolysis**, etc. Some of them have not received industrial implementation, such as the destruction of dioxins with the help of quaternary ammonium base chlorides, as well as chlorolysis and oxidation with the help of ruthenium tetroxide. The treatment of dioxin-containing waste with alkaline reagents is considered, for example, in the USA to be particularly effective.

Oxidation of dioxins by atmospheric oxygen under **non-catalytic conditions** is effective only at temperatures above 500 °C. A number of methods have been developed that make it possible to oxidize dioxins and related compounds of various kinds with powerful oxidizing agents. In addition, catalysts are being developed that allow the oxidation of dioxins at temperatures below 100°C. The possibility of disinfection of dioxin-containing waters using **ozonation, RuO_4** , an aqueous solution of **hydrogen peroxide**, and a number of other technologies has been shown.

Photoexposure is one of the most effective methods for the destruction of dioxins. Successful photodegradation of dioxins must be preceded and/or accompanied by the use of any other methods - extraction, oxidation, dechlorination, etc. A number of combined disinfection methods have been developed. The most effective, however, is the destruction of dioxins by catalytic oxidation and photode-

gradation after their preliminary extraction from soils by solvents or sublimation into solutions at 500-600 °C.

A number of technologies combine the energy of **UV radiation and the action of oxidizers - ozone or hydrogen peroxide**. The process is carried out in water and is suitable for the destruction of halogenated solvents, pesticides, etc.

An effective means of **decomposing dioxin I is the photolysis** of its aqueous suspensions. The method of heterogeneous photochemical destruction of chlorine-aromatic compounds, including dioxins, under catalytic conditions is based on their irradiation in the presence of aqueous suspensions of semiconductors (TiO_2 is most effective). In these systems, dioxins are rapidly destroyed and substances are mineralized with the formation of HCl , CO_2 and other non-toxic products.

Methods are being developed for the **catalytic destruction** of dioxins and furans, which make it possible to drastically reduce the temperature, energy intensity, and cost of the process. It turned out, for example, that copper effectively catalyzes dechlorination and hydrogenation. The degree of destruction is 99.9999%. The method was used to neutralize liquid laboratory waste containing dioxins and furans. It is believed that low-temperature catalytic decontamination of these substances can become an alternative to high-temperature thermal decomposition.

Institute of Catalysis SB RAS (IC SB RAS), Novosibirsk is engaged in the development of technology for the neutralization of PCDD and PCDF and other highly toxic organochlorine compounds in exhaust gases based on **new generation glass fiber catalysts** with the Research Triangle Park (RTP), North Carolina, USA. The authors of the project believe that, compared with traditional catalytic processes, a significant increase in the efficiency of dioxin conversion can be expected, first of all, the elimination of the formation of secondary dioxins and other highly toxic products (phosgene, elemental chlorine), as well as a reduction in capital and operating costs due to a decrease in the cost of the catalyst and increase its service life. The method assumes high selectivity for the oxidation of organochlorine compounds into safe products (CO_2 , H_2O , HCl), as well as the virtual absence of toxic by-products and secondary waste

Dioxin extraction technologies are based on sorption, extraction, coagulation and flocculation. A 93-98% reduction in dioxin emissions from solid waste is achieved by using sorbalite. Efficiency is improved by the addition of activated carbon. In Germany, a technology has been developed for the sorption of PCDD and PCDF from flue and flue gases using lignite coke filters. In this case, it is possible to reduce the concentration of dioxins in the purified gas by at least 2 orders of magnitude, bringing it up to acceptable standards. Zeolite-like natural montmorillonite chemically modified with aluminum hydroxide, natural smectite treated with copper salts, etc. were tested [1,2].

For the effective extraction of trace amounts of highly toxic PCDD and PCDF from industrial wastewater and liquid waste, their **sorption** using effective sorb-

ents has been proposed. The method for removing trace amounts of PCDD and PCDF from sewage ponds and wells is based on **coagulation and flocculation with aluminum salts. Coagulants and polymeric substances introduced into wastewater from pulp and paper industries** contribute to the release of their lignin, tannin and dioxins. To do this, the effluent is passed through a suspended sediment - flocculated lignin and tannin. A pilot plant of continuous operation ensures the release of wastewater from dioxins and other substances by 90-95%.

The sorption properties of PCDD and PCDF are also used in modern waste incineration plants (WIP).

The level of emissions into the atmosphere depends on the specific combustion technology and gas cleaning system, but there are general principles for solving this problem. Usually the first step is dust cleaning with an electrostatic dust collector. This is followed by chemical, adsorption and/or catalytic treatment using appropriate equipment.

Only some of the listed technologies are able to meet the standard adopted in civilized countries. Specifically, in the United States, 40 CFR 264.343, established by the EPA, must ensure the destruction and disposal of 99.99% of all major hazardous components, and for the most hazardous organic components of toxic waste, such as PCDD, PCDF and PCBs, destruction and annihilation of 99,9999% [2,3]. It is obvious that the development of new and improvement of the presented technologies is necessary and is on the agenda.

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脱水原料在蜂蜜酒制备技术中的应用前景

THE PROSPECT OF USING DEHYDRATED RAW MATERIALS IN THE TECHNOLOGY OF MEAD PREPARATION

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注解。在现代蜂蜜酒制备技术中,经常将各种原料添加到经典产品中以增加品种的多样性。新鲜水果或浆果经常用作添加剂,但它们含有一定量的水分,这会以某种方式稀释成品。为避免降低蜂蜜酒中干物质的含量,可以使用冷冻干燥和辛辣芳香的原料

在这项工作中,重点将放在脱水原料的添加上,它对蜂蜜酒的制备和感官有什么影响。

本发明的目的是扩大基于脱水原料获得的低酒精度饮料的范围。

关键词: 发酵, 蜂蜜酒, 脱水原料, 辛香原料, 冻干原料, 感官。

Annotation. *In modern technologies of mead preparation, various raw materials are very often added to the classic product to increase the variety of the assortment. Very often fresh fruits or berries used as an additive, but they contain a certain amount of moisture, which somehow dilutes the finished product. To avoid lowering the amount of dry substances in the mead, it is possible to use freeze-dried and spicy-aromatic raw materials*

In this work, the emphasis will be on the addition of dehydrated raw materials, what effect does it has on the preparation and organoleptic of mead.

The objective of the invention is to expand the range of low-alcohol beverages obtained on the basis of dehydrated raw materials.

Keywords: *fermentation, mead, dehydrated raw materials, spicy-aromatic raw materials, freeze-dried raw materials, organoleptic.*

Technology of mead production

The main technology of mead production is the fermentation of honey wort with the addition (/ without addition) of spicy-aromatic raw materials, fruit and berry raw materials, juices, fruit drinks, infusions and other raw materials.

The main stages of the production of honey drinks are:

- Preparation of honey wort for fermentation;
- Fermentation of wort;
- Beverage processing.

At the first stage honey is diluted with water or a mixture of juice and water. The ratio of honey: liquid component can be from 1:2 to 1:10 [1]. One of the simplest options for the production of mead is the dilution of honey with water without boiling and yeasts addition to the resulting wort. After the wort is left to ferment. This method does not heat-treat honey, therefore it is more practical from the point of view of the functionality of the drink. Anyway it has a bad effect on the stability and safety of the product.

A possible stage is the boiling of honey. This stage is performed to prevent contamination of honey wort by harmful microorganisms. Boiling may be accompanied with spicy-aromatic raw materials or hops. It is recommended to stir the wort and remove the resulting foam while the wort is boiling. After cooking, the wort is cooling down and getting set for fermentation. At this stage, any semi-finished product can also be added: kvass wort, malt extract, spicy-aromatic raw materials, herbs, etc.

There may be differences at the fermentation stage. Yeasts are often used to ferment honey wort. They can be both bakery and wine, alcohol, beer, etc. Researches have been done on the fermentation of honey wort with lactic acid and alcoholic yeast like in kvass technology [2]. Also, fermentation can occur with the help of perga without the addition of yeast. Perga is a plant pollen, packed into honeycomb cells filled with honey and preserved with the resulting lactic acid.

At the stage after fermentation the honey wort is removed from yeasts. Pasting is possible. After that, it is also possible to add other components of the recipe to the honey drink – spices, herbs, aromatic alcohols and infusions.

What is a freeze-dried raw material?

To begin with, the sublimation process is a transition from a solid state to a gaseous state, while bypassing the liquid stage. Sublimation drying of wet material involves evaporation of ice. Mechanically bound moisture is converted under a pressure of less than 4.58 mmHg due to the pressure of the vapor-gas mixture on the material. Then evaporation of supercooled adsorption-binding liquid inside the material at a temperature above 0 ° C. [3]

Water is well suited for sublimation. It determines the widespread use of this process as one of the drying methods. In industrial sublimation it is first frozen and then placed in a vacuum or a chamber filled with inert gases. Physically, the sublimation process continues until the concentration of water vapor in the room

reaches a normal level for a given temperature. Therefore the excess water vapor is continuously pumped out.

One of the methods of cleaning solids is based on this effect. At a certain temperature, one of the substances in the mixture sublimates and the other does not. The vapors of the cleaned substance condense on the cooled surface. The device used for this method of purification is called a Lyophilizer (sublimator). [4]

Sublimation is also used in the food industry. Freeze-dried products are significantly superior to dried ones in terms of nutritional value, because only water can be sublimated and many useful substances are lost during thermal evaporation.

Sublimation is an aqueous extract obtained from fresh products by the vacuum method. It allows you to preserve up to 98% of useful substances when consuming food as well as the natural taste and smell of original products. Freeze-dried products quickly return back, when they are immersed in water. This technology allows you to store freeze-dried products for up to five years. [5]

Freeze-dried products are used as a basis for dietary and baby food. Most importantly, the raw materials for the production of freeze-dried foods are only fresh products.

The technological process of freeze-drying food production includes the following stages:

- Selection and pre-processing of raw materials;
- Freezing;
- Freeze drying;
- Packaging of dried products. [6]

There are three stages of removing moisture from the material:

- self-freezing;
- Sublimation;
- Evaporation of residual moisture.

The disadvantage of food sublimation is the use of freezing. It leads to the destruction of cells that expand when frozen with water. The costs of traditional atmospheric drying are two times less than the costs of sublimation.

The process of preparing fruit mead (melomel) with the addition of freeze-dried raw materials in secondary fermentation.

Using freeze-dried raw materials prevents excess moisture. Thereby reduces the risk of increasing the degree of mead by diluting it with fructose juice from fruits.

If we turn to the methods of preparing fruit mead (melomel) the main attention should be allocated to the methods. There are two fundamentally different ways of making melomel from traditional mead: add fruit during the main fermentation or make it during the secondary fermentation. This is a widely discussed issue, because both approaches have both pros and cons. Adding fruit during the main fermentation seems like an obvious solution. In this variant, berries and fruits add nutrients to honey that are necessary for yeast. It also help regulate the pH of the wort. Fermentation is fast and vigorous, which only benefits the mead. [7]

However, more and more honey producers prefer to add fruit during secondary fermentation. There are several good reasons for this:

1. The fast fermentation process greatly changes the taste of the fruit. Sometimes these changes are positive, sometimes not, but in any case they happen. If the goal were to capture the taste of fruits or berries, adding them during the main fermentation would not be the best idea.

2. Carbon dioxide is actively released during the main fermentation. It destroys the volatile aromatic and flavoring substances of the added ingredients.

3. The high alcohol content, low pH and nutrients in the already partially fermented mash wort create a difficult environment for the growth of pathogens. A secondary fermenter would be a much safer place to add fruit.

4. Additives during secondary fermentation allow you to fully control the main fermentation of the base mead. When honey and fruits are mixed together, a number of variables appear during the main fermentation process that are difficult to control. For example nutrient levels, pH and acidity changes, etc. [8]

This approach has perhaps the most interesting advantage: you can cook several melomels and even mead of different styles at once. You need to dump the traditional mead in sufficient quantity. Then divide it into smaller batches into which you can add freeze-dried raw materials.

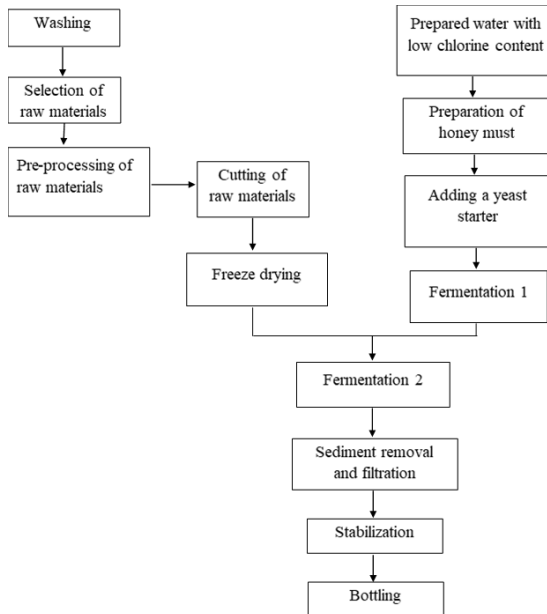


Figure 1. Technological scheme of preparation of fruit mead (melomel) from freeze-dried raw materials.

What is a spicy-aromatic raw material?

Spicy-aromatic raw materials are cultivated and wild plants with a high content of volatile substances with a pleasant smell. They are used in the production of essential oils and to add flavor to food products. [9]

The benefits of spicy-aromatic raw materials are undeniable. In addition to the obvious creation of a rich organoleptic drink, such raw materials have a pharmacological effect – improves mood, gives a feeling of vivacity, improves breathing, relieves fatigue and improves sleep quality [10]. Among other advantages, it is worth highlighting phytoncidal, antiseptic and bactericidal properties. [11]

There is the following classification of spicy-aromatic raw materials [9, 12]:

- Balsamic (St. John's wort, oregano, tarragon, lavender, etc.)
- Astringent (badan, cherry, etc.)
- Burning (red pepper, ginger, cinnamon, etc.)
- Bitter (cinchona bark, wormwood)
- Camphor-resinous (roots and rhizome of valerian and peony, rosemary, etc.)
- Nutmeg (vanilla, clove, cardamom, etc.)
- Sweet (licorice roots, stevia leaves)
- Citrus fruits (lemon, tangerine, orange roots, mint grass, etc.)

Recipe for mead with the addition of spicy-aromatic raw materials

Spicy-aromatic raw materials are processed to extract soluble substances (pectins, mono-, di- and trisaccharides, dyes, tannins, cyclic alcohols, organic acids and some mineral compounds [9]). They are extracted at room temperature. When it increases, the yield of coloring and flavoring substances increases. But at the same time the yield of volatile and some biologically active components decreases.

Extraction methods [9, 12]:

- Maceration – the infusion of crushed vegetable raw materials in a certain amount of extractant. Maceration time ranges from 15-30 minutes to several days. For a longer infusion in the form of an extractant, an aqueous alcohol solution is used.

- Vortex extraction is an extraction by using very intensive stirring. Mixers are used. They additionally grind the raw materials. But this method is not always suitable for obtaining high-quality extracts.

- Percolation is an extraction with continuous change of the extractant in the percolator. This method accelerates extraction and provides a complete output of the contents of the raw material.

- Repercolation is a sequential passage of a solvent with a certain amount of extracted substance through fresh raw materials. In this way, highly concentrated extracts are obtained with minimal solvent consumption

Raw materials can be added to the mead when they are extracted. Spicy-aromatic raw materials can be applied at any stage. The main thing is to separate various

solid residues of leaves, roots or stems before bottling. Some manufacturers skip the extraction stage and add dry plants to the mead. The most popular stage for adding various flavoring additives is the fermentation of mead. Thus, more substances that are volatile will pass into the finished drink.

It is important to use a good source of water that does not contain chlorine and chloramines. If the water is too hard, it is better to dilute it with distilled water to reduce the alkalinity and mineral content. At this stage, it is possible to add spicy-aromatic raw materials as an aqueous extract. [8]

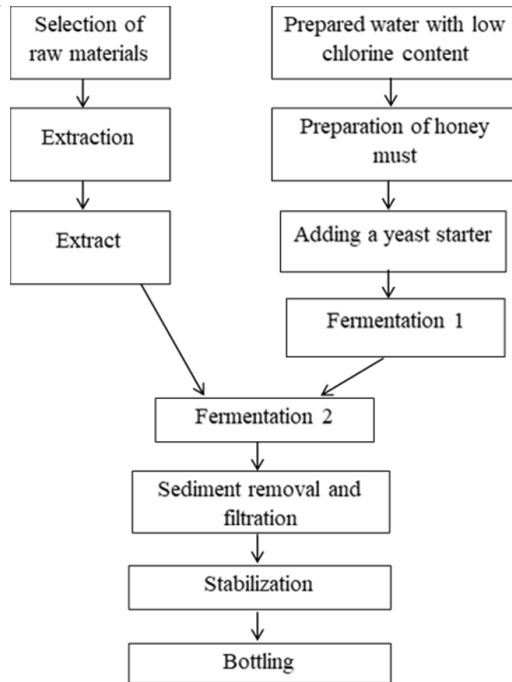


Figure 2. Technological scheme of preparation of mead with spicy-aromatic raw materials.

Conclusion

The article presented the prospect of using dehydrated raw materials. Namely: spicy-aromatic and freeze-dried raw materials.

Also, there was information about what mead is and how we can cook it using dehydrated raw materials.

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有机锗的来源——概述

SOURCES OF ORGANIC GERMANIUM – AN OVERVIEW

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抽象的。自上世纪 60 年代以来，含有锗的膳食补充剂 (DS) 和化妆品的受欢迎程度一直在不断增长。与此同时，对这些产品的安全性进行了许多研究。一些研究人员谈到了锗的一些有用特性，而另一些研究人员则分享了锗对人体的毒性作用的结果。在这篇文章中，考虑了锗在产品中的主要使用形式，给出了有机锗的植物来源，并考虑了富含锗的食品。

关键词: Ge-132, 锗, 有机锗, 二氧化锗, 食品, 膳食补充剂。

Abstract. *Since the 1960s of the last century, the popularity of dietary supplements (DS) and cosmetic products containing germanium has been constantly growing. In parallel with this, many studies were carried out on the safety of these products. Some researchers spoke about a number of useful properties of germanium, while others shared the results of its toxic effect on the human body. In this article, the main forms of germanium used in products are considered, plant sources of organic germanium are given, and foodstuffs enriched with germanium are considered.*

Keywords: *Ge-132, germanium, organic germanium, germanium dioxide, food, dietary supplement.*

The effect of germanium on the body

For the first time, the addition of germanium to cosmetics and food began to be discussed in the 60s of the last century. Then in Japan, Dr. Asai Kazuhiko synthesized the first form of organic germanium, now known as Asai-germanium or Ge-132. It was positioned as a dietary supplement.

Most of the physiological effects of Ge-132 were discovered through a series of clinical trials in the 70-80s of the last century, which are described in the book

“Organic germanium - the miracle cure” by Dr. Kazuhiko Asai [11]. These include an oxygen transport process similar to human hemoglobin and antioxidant properties. More recent research points to anti-cancer, anti-tumor, anti-aging, anti-viral, and anti-inflammatory properties. [1-3, 7]

At the end of the last century, a lot of DS and cosmetics with germanium appeared on the market. Such products quickly gained popularity around the world. In the same period, medical reports began to appear on the toxic effects of germanium on the human body.

The article “Nephrotoxicity of germanium compounds: report of a case and review of the literature” describes the clinical case of a 55-year-old woman who presented with complaints of general malaise, muscle weakness, anorexia, and weight loss. The woman ingested a specific germanium compound for 19 months. According to the results of the tests, she was found to have kidney failure, damage to muscle and nerve tissues. Treatment did not improve, resulting in death [9].

Similar cases are described in the article “Hazard assessment of germanium supplements”. By 1997, 31 cases were reported in which long-term use of products containing germanium was associated with kidney failure: signs of kidney dysfunction, degeneration of the renal tubules and accumulation of germanium in the body were observed [6].

According to the data presented in “Nephrotoxicity and neurotoxicity in humans from organogermanium compounds and germanium dioxide”, 18 cases of renal failure were reported from 1982 to 1991 caused by the intake of germanium elixirs containing germanium dioxide [8].

In 2008, the report “Dermal absorption of inorganic germanium in rats” was published, which states that subchronic and chronic oral exposure to germanium dioxide, a popular chemical form of inorganic germanium, causes severe germanium toxicosis, including impaired renal function and possible death in humans and experimental animals [5]. Also in this report are the results of a study of absorption through the skin of ointments containing germanium dioxide ions, which showed that this form of germanium can be absorbed through the skin, accumulate in tissues and have a toxic effect on the body.

All of these medical reports dealt with the effects of preparations of inorganic germanium in the form of dioxide (GeO_2) or artificially synthesized organic germanium. At the same time, there are modern studies of the effects of organic germanium on the human body.

The largest clinical study was conducted in 2020, which examined the change in immune profiles after administration of germanium [7]. A group of 130 people was divided into two parts: for 8 weeks, the first was given the drug bio-germanium, the second - a placebo. Anthropometric measurements, blood sampling, a general biochemical blood test, urinalysis, natural killer cell (NK-cell) activity, as

well as cytokines and immunoglobulins were carried out. The results of the study showed that the mechanism of bio-germanium immunostimulation is associated with the activation of NK cells and immunoglobulin. The immunostimulatory ability shows that bio-germanium increases the activity of NK cells, one of the key markers of immune strength.

In 2011, an article was published on the study of Ge-132 and the development of an oral anticancer drug from it. The results showed that organic germanium enhances pro-inflammatory responses by enhancing interferon-g (IFN-g) and NK cell activity, and is significantly less toxic than other commonly used metal-based anticancer drugs [2].

In 2020, a toxicological assessment of organic germanium was carried out [1]. The studies were carried out according to the requirements of the OECD (Organization for Economic Co-operation and Development) and GLP (Good Laboratory Practice). The results showed that germanium dioxide and germanium citrate-lactate (the inorganic form of germanium) caused kidney failure, while germanium sesquioxide (the organic form of germanium) was safer. No mutagenic effect was detected in the bacterial reverse mutation test and in the mammalian chromosome aberration test in vitro. No genotoxic activity was observed in the in vivo mammalian micronucleus test at concentrations up to the dose limit. No observed side effect level (NOAEL) was defined as 2000 mg/kg body weight per day.

In 2018, a study was conducted to identify the antioxidant activity of Ge-132. The results showed that Ge-132 has antioxidant activity against oxidative stress. It is believed to be caused by hydrogen peroxide and is associated with many chronic diseases such as cancer, diabetes, cardiovascular disease, inflammation, aging, and other neurodegenerative diseases in humans.

Plant sources of organic germanium

Based on the above medical reports and studies, it can be concluded that in the production of food products, dietary supplements and cosmetics, it is preferable to use sources of organic germanium, rather than its artificially synthesized forms.

The book “Organic germanium - the miracle cure” contains the following list of products containing germanium [11]:

- Cinnabar polypore (*Trametes cinnabarina Fr.*) – 800-2000 mg/kg (ppm)
- Ginseng (from Shimane Prefecture, Japan) – 250 mg/kg (ppm)
- Ginseng (from the Shinano region, Japan) – 320 mg/kg (ppm)
- Tangshen bellflower (*Codonopsis Tangshen*) – 257 mg/kg (ppm)
- Fluffy Angelica (*Angelica pubescens Maxim.*) – 262 mg/kg (ppm)
- Japanese rogan (*Trapa Japonica Flerov*) – 239 mg/kg (ppm)
- Chinese dereza (*Lycium Chinense mill*) – 124 mg/kg (ppm)
- Blooming Wisteria (*Wisteria floribunda*) – 108 mg/kg (ppm)

- Pearl barley (*Coicis Semen*) – 50 mg/kg (ppm)
- Sparrow (*Lithosemi Radix*) (*Lithospermum officinale*) – 88 mg/kg (ppm)

This information is current as of 1980. Now the content of germanium in vegetable raw materials may differ, since fertile soils are depleted every year.

More recent data was published in 2006. The study describes a method for determining the total germanium content for the identification of foods and over-the-counter products containing germanium, as well as information on the total germanium content in the studied samples [15]:

- Tomato - 0.36 mg/g
- Bulb onion - 0.29 mg/g
- Green pepper - 0.16 mg/g
- Yellow pepper - 0.28 mg/g
- Red pepper - 0.48 mg/g
- Garlic - 2.78 mg/g
- Carrot - 0.6 mg/g
- Potato - 1.85 mg/g
- Aloe vera (tablets) - 20.83 mg/g
- Ginseng (in tablet form) - 5.48 mg/g
- Ginger (in tablet form) - 9.96 mg/g
- Peppermint (leaves) - 2.56 mg/g
- Chinese angelica - 0.43 mg/g
- Echinacea - 5.21 mg/g
- Siberian ginseng (*Eleutherococcus*) - 0.38 mg/g
- Ginseng (root) - 0.38 mg/g
- Bamboo sprouts - 0.42 mg/g
- Soy flour - 3.64 mg/g
- Soy mince - 9.29 mg/g
- Pearl barley - 1.64 mg/g

In this work, the relationship that food coloring has on germanium uptake and retention was investigated by comparing its content in three colored peppers. The pigments found in peppers are beta-carotenes. Green pepper was found to contain the least amount of germanium (0.16 mg/g), followed by yellow pepper (0.28 mg/g), and red pepper contains the most germanium (0.48 mg/g). The relationship between beta-carotenes and germanium uptake is confirmed by its high concentration in carrot samples. It is also noted that garlic, which contains a large amount of germanium (2.78 mg/g), has a number of medicinal properties, in particular the ability to strengthen the immune system.

A 1995 study presents the results of a study of the Reishi mushroom (*Ganoderma Lucidum* and *Ganoderma Tsugae*) for biologically active substances and its medicinal effects. Natural and cultivated samples of *Polyporales* mushrooms and

cultivated Reishi mushroom were analyzed for germanium content using the ICP (Inductively-Coupled Plasma) method. None of the samples contained high concentrations of germanium, however, it was found that the content of germanium in the Reishi mushroom was significantly higher when it was cultivated on a log that had absorbed Ge-132 [14].

Germanium enriched foods

Based on the results of several works and the book of Dr. Asai [11, 13-14], it can be assumed that polypore fungi can absorb germanium and accumulate it in fruiting bodies, spores, and mycelium.

This conclusion is confirmed by the existing patents for the production of food products enriched with Ge-132 [4, 10, 12]:

1. CN103749694A “Beverage rich in organic germanium Ge-132 and preparation method thereof”. The composition of the drink includes Reishi mushroom, ginseng, Chinese cordyceps, common beans, glutinous rice, curly griffin, red cereberry seed powder, potatoes, carrots, banana, sweet potato, citric acid, xylitol, excipients and water. Due to the fact that the drink contains a large amount of ingredients rich in Ge-132, it can improve human immunity, protect the liver, prevent and suppress the development of cancer.
2. CN102613628A “Original ecological coconut germanium juice and producing method thereof”. The basis of the drink is coconut water containing organic germanium, also contains extracts of medicinal plants and mushrooms, such as Reishi mushroom, American ginseng, etc.
3. CN101053437A “Organic germanium Ge-132 glossy ganoderma beverage and processing method”. The composition of the drink includes extracts of Reishi mushroom and gray tinder, flavor enhancer and Ge-132 as an additive. Using this drink as an example, a method for introducing organic germanium into food products is disclosed. This functional drink can enhance human immunity, prevent and suppress cancer, protect the liver, and have a detoxifying effect.

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陆内水体中的人造地球化学屏障、研究、问题和后果
**MAN-MADE GEOCHEMICAL BARRIERS IN
INTRACONTINENTAL WATER BODIES, THEIR STUDY,
PROBLEMS AND CONSEQUENCES**

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抽象的。考虑了技术地球化学障碍的知识问题及其对水资源的影响，众所周知，水体涉及人类活动领域，它们被用作家庭、工业和农业供水的资源来源，能源和食物资源的来源，以及交通要道和娱乐需求。世界各地的环境问题“迫使”识别和研究技术障碍并研究与之相关的过程。

在本文中，以贝加尔湖和安加尔斯克水电站（HPP）梯级为例，考虑了技术地球化学障碍的出现条件，分析了其建设过程中出现的问题，因为建设河流上的水力发电站导致河流的水和水动力状况发生急剧变化，这主要影响水质。

关键词：水资源，技术地球化学屏障，HPP 级联，安加拉河，贝加尔湖，养分，迁移，水交换。

Abstract. *The problems of knowledge of technogenic geochemical barriers and their consequences for water resources are considered, as it is known, water bodies, being involved in the sphere of human activity, they are used as a source of resources for domestic, industrial and agricultural water supply, a source of energy and food resources, as well as transport arteries and for recreational needs. Environmental problems around the world “force” to identify and study technogenic barriers and study the processes associated with them.*

In this article, on the example of lake Baikal and the cascade of Angarsk hydroelectric power plants (HPP), the conditions for the emergence of technogenic geochemical barriers are considered, an analysis of problems is given, arising during their construction, since the construction of hydroelectric power stations on rivers leads to a sharp change in their water and hydrodynamic regimes, which primarily affects water quality.

Keywords: *water resources, technogenic geochemical barriers, HPP cascade, Angara river, lake Baikal, nutrients, migration, water exchange.*

The question of the structure, formation and functioning of technogenic geochemical barriers in inland water bodies and their influence on the internal circu-

lation of substances and the material exchange of a water body with the external environment, to date, remains insufficiently studied. At the same time, significant material has been accumulated in limnology and hydrochemistry on the transfer, differentiation, concentration, and dispersion of matter in water bodies, its internal circulation, which makes it possible to approach the analysis and interpretation of the data obtained based on the concept of technogenic geochemical barriers. Of particular interest, in this regard, is the consideration of the conditions for the migration of substances that limit the vital activity of an aquatic ecosystem and have a significant impact on the quality of water masses. These, first of all, include biogenic elements (phosphorus, nitrogen, silicon). As well as toxic substances of various nature (phosphorus and organochlorine compounds, heavy metals, radionuclides, oil products) and other substances polluting water bodies.

The study of technogenic geochemical barriers is based on modern ideas about the mechanisms of chemical exchange between the bottom and water, which were formed under the influence of the classical works of C. Mortimer [9-12]. This author has developed the concept of a barrier oxidized layer that forms on the surface of bottom sediments under aerobic conditions and prevents free chemical exchange in the water-bottom system. During the last two decades, materials have been obtained that indicate the incompleteness of the concept of the barrier layer [2, 8]. In this regard, an alternative interpretation of the results of Mortimer's experiments and natural observations on English lakes was proposed, based on the concept of transient processes in the bottom sediments of water bodies with a temporary catastrophic oxygen deficiency in the hypolimnion [3]. B.V. Perfiliev and D.R. Gabet et al. developed capillary microbial landscape methods and applied them to establish the role of microorganisms in the formation of ferromanganese lacustrine ores [5]. S.I. Kuznetsov [1] summarized the accumulated information on the role of microorganisms in the migration, dispersion, and concentration of chemical elements in lakes. A significant contribution to the establishment of the regularities of mechanical differentiation of terrigenous and autochthonous suspensions deposited in a reservoir, the processes of chemical and biological circulation and the development of the theory of chemical differentiation of matter in modern reservoirs was made by N.M. Strakhov [6, 7]. In the 90s, work was carried out on Baikal on the processes of material exchange in the water-atmosphere system [4]. All these studies paved the way for subsequent work on the description and analysis of formation, properties, structure and functioning of geochemical barriers in inland water bodies, elucidation of their role in the intra-aquatic cycle of matter, the activity of the aquatic ecosystem, the processes of self-purification and secondary pollution, the formation of the trophic status of the reservoir and the quality of its waters.

Both natural geochemical barriers and technogenic ones can have absolute geometric dimensions and differ by orders of magnitude, and therefore it makes

sense to consider macro-, meso-, and micro-barriers. In this regard, any large body of water itself is a macro-barrier on the paths of transport of material suspended in water and entrained sediments. Favorable conditions are created on such barriers for the precipitation of chemical elements migrating as part of a terrigenous suspension and in the form of forms adsorbed on it. It is here that, under a certain physical and chemical situation, the accumulation of various elements and, above all, heavy metals, such as mercury, cadmium, lead and other polluting components, can occur.

The main reason for the emergence of technogenic geochemical barriers are hydraulic structures of various designs and purposes (dams, dams, port facilities, water intakes, spillways), which act as the main technologies for exploiting water resources. Due to the fact that water is one of the main resources that ensure human existence, conflicting interests of many consumers, the population and sectors of the economy intersect at water bodies. An uncoordinated strategy for the exploitation of water resources among consumers often leads to environmental disasters. Examples of this are the Aral Sea and the acute problem of drinking water in a number of regions of the world.

Thus, hydraulic structures change the system of currents in water bodies, the intensity of vertical and horizontal water exchange, which inevitably affects the values of internal flows of matter. In zones where the flows of any substance undergo drastic changes, conditions arise for the formation of technogenic geochemical barriers. The latter are the hydraulic structures themselves, coastal shallow waters of reservoirs, backwater zones, and the water-bottom sediment boundary. Based on this, it can be said that the study of the formation and functioning of geochemical barriers in water bodies is the study of the influence of these technologies on the processes that determine water quality.

Pursuing pragmatic goals, humanity concentrates the substances it needs on technogenic geochemical barriers, subject them to technological processing and inevitably disperse them, since none of these barriers is absolute. This circumstance gave rise to the problem of anthropogenic pollution of the environment and the need to develop theoretical and methodological principles of rational nature management, as well as to provide measures and methods for their practical application. The lack of coordinated strategies for the use of natural resources and their implementation in the form of specific technologies has led to the fact that the actions of some users of natural resources to achieve their narrow production goals often cause damage to others.

Technogenic macro and meso geochemical barriers owe their origin to the creation of HPP cascades on rivers, which transform the latter into a system of reservoirs, significantly changing their state as water bodies. For example, the implementation of this technology in the Irkutsk Oblast is the Angarsk HPP cascade

with a system of reservoirs including Lake Baikal, which is the largest natural reservoir of clean fresh water on the planet. The creation of reservoirs affected not only the level regime of Lake Baikal, but also led to a radical transformation of the Angara River for more than 1000 km and a profound change in its hydrological, hydrochemical and hydrobiological regime.

The most important hydrological consequences of the construction of the Angara hydroelectric power stations, which are of direct practical interest, include an increase in the duration of the ice period and the formation of ice-free areas up to 10-20 km long in the HPP downstream. A change in the water level in the reservoirs of the cascade during their partial activation and filling under conditions of significant fluctuations in water content leads to periodic drainage and flooding of vast areas of shallow water, which entails a deterioration in water quality in coastal zones where water is withdrawn, and for this reason, which are of particular interest to water users.

The formation of deep water reservoirs with large volumes of water slowed down the rate of water exchange in the river system and reduced the ability of water masses and bottom sediments to self-purify. This circumstance exacerbated the negative consequences of the ingress of industrial wastewater (chemical, petrochemical, timber processing, metallurgical), thermal power plants, agriculture and utilities into the Angarsk reservoirs.

Under conditions of slow water exchange and unfavorable oxygen conditions in the hypolimnion of reservoirs, their bottom sediments have become a source of secondary pollution of water masses. The occurrence of secondary pollution processes associated with the interaction of water masses with bottom sediments and the involvement of toxic components in the biological cycle in a reservoir poses a serious danger both to the totality of aquatic organisms and the life of the aquatic ecosystem as a whole, and to humans. Bottom sediments as an open physical and chemical system are characterized by material exchange through the interface with the environment. Chemical exchange between the water column and bottom sediments is one of the most important problems of limnology, hydrochemistry, and geochemistry of water bodies. This problem is complex and multifaceted, has a history of half a century and, despite the significant number of works devoted to it, is still far from its final solution. All this reduces the quality of water resources.

The negative consequences of the Angarsk HPP construction can be grouped into two groups. The first of them is a consequence of the adoption of economic and political decisions. Thus, the drawdown of the level below the design mark leads to the fact that infiltration water intakes are in the coastal zone with lower water quality, and often become unusable. Significant drops in the water level create difficulties for navigation.

The second group is determined by ignorance or ignorance of the processes occurring in reservoirs and their immediate environment. For example, when

designing the Bratsk HPP, it was assumed that a sharp increase in the free water surface during the filling of the reservoir would lead to an increase in evaporation and moistening of the adjacent territory (decrease in aridity). However, misconceptions about the processes of formation of the thermal regime of deep water bodies did not allow us to take into account that in the first half of summer the temperature of the near-water air will be below the dew point and condensation will prevail instead of evaporation. The consequence of this was an increase in the degree of aridity of the climate and a one-week delay in the sowing of crops, which is of no small importance in the conditions of the zone of risky farming in Eastern Siberia.

When designing the HPP, due to the lack of the necessary scientific materials, the geochemical and biochemical processes in the bottom sediments of the back-water zones and the coastal strip of reservoirs could not be taken into account, which changed the conditions for the migration of chemical elements, redox and alkaline-acid conditions in sediments. Ignorance of these processes and conditions led to the fact that the quality and availability of water resources did not match the design ones. These examples show that in order to correct the mistakes made and develop more efficient methods and technologies for nature management, deep knowledge of the patterns of the totality of processes that form natural water resources is required. For example, the Angara HPP cascade replaced a water-course with a chain of reservoirs with greater depths, which led to a sharp slow-down in vertical water exchange and nutrient turnover, which sharply reduced the self-cleaning capacity of the pelagic part of the reservoirs.

In the light of the above, one of the urgent tasks is the development of a theoretical and practical study of the technogenic and geochemical consequences of the use of various technologies for involving water resources in the system of nature management.

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黑松 (PINUS CONTORTA LOUD.VAR. LATIFOLIA S. WATS.) 作为俄罗斯欧洲北部人工林栽培的速生树种

LODGEPOLE PINE (PINUS CONTORTA LOUD.VAR. LATIFOLIA S. WATS.) AS FAST GROWING SPECIES FOR PLANTATION CULTIVATION IN THE EUROPEAN NORTH OF RUSSIA

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抽象的。俄罗斯联邦在人工林方面积累了相当多的经验。在国家任务的框架内开展了一项关于在俄罗斯欧洲北部建立目标人工林的研究。就针对性种植栽培的树种选择做出了有根据的结论。应优先考虑土著树种（欧洲赤松、欧洲云杉）。然而，适合温带国家纸浆和造纸工业的有前途的速生树种之一是黑松（*Pinus contorta* Loud.var. *latifolia* S. Wats.），它在北美自然生长。在长期研究的基础上，选择了最适合的黑松产地——位于加拿大最北部的原产地（育空地区），它生长在森林物种分布的北端。在工业化人工林中生长时，小黑松相对于当地针叶树种的优势得以体现，在 40–50 年树龄时，它形成 250–300 立方米/公顷的低树脂木材，适用于硫酸盐和亚硫酸盐制浆和比本地云杉和松树的生产力高出 70%。在研究过程中，制定了俄罗斯欧洲北部种植园作物的基本要求，在这些要求下，种植园证明了其目的。

关键词：黑松、苏格兰松、北方森林、人工林、俄罗斯北部欧洲

Abstract. *The Russian Federation has accumulated quite a lot of experience in plantation forestry. A research on the creation of targeted forest plantations in the European North of Russia was carried out within the framework of a state assignment. Well-grounded conclusions on the choice of species for targeted plantation cultivation were made. Preference should be given to aboriginal species (Scots pine, European spruce). However, one of the promising fast-*

growing species suitable for the pulp and paper industry in temperate countries is Lodgepole pine (*Pinus contorta* Loud. var. *latifolia* S. Wats.), naturally growing in North America. On the basis of a long-term research, the most suitable origins of Lodgepole pine were selected – located in regions of the most northern Canadian origin (Yukon), where it grows at the northern limit of the distribution of forest species. The advantage of Lodgepole pine over local coniferous species was revealed while growing on industrial forest plantations, where by the age of 40-50 years old it forms 250-300 m³/ha of low-resinous wood, suitable for both sulfate and sulfite pulping and is 70% more productive than local spruce and pine. In the research process, the basic requirements for plantation crops in the European North of Russia were developed, under which plantations justify their purpose.

Keywords: Lodgepole pine, Scotch pine, boreal forests, forest plantations, European North of Russia

Introduction

Lodgepole pine (*Pinus contorta* Loud. var. *latifolia* S. Wats) naturally growing in western North America, is one of the promising fast growing species on plantations. Its wood is suitable for the pulp and paper industry in countries with a temperate climate. Numerous studies, mainly in Sweden and Finland, confirm that Lodgepole pine is superior to native pine in growth and biomass production [1, 2, 3, 4].

The Lodgepole pine cultures in the Russian Federation have been created since the 1920s, mainly in Karelia Republic, the Leningrad Region and the Baltic Republics [5]. Subsequently, Lodgepole pine has been spread south to the forest-steppe and north to the Arkhangelsk Region. However, its cultivation was rather spontaneous, almost without regard to the origin of the raw material. Research and creation of experimental trials were carried out by industry and academic research institutions without any coordination, based on their capabilities.

Northern Research Institute of Forestry, which is situated on the European North of the Russian Federation, provides a research on Lodgepole pine introduction and cultivation during more than 40 years (since 1979). Experimental plantations of Lodgepole pine on a total area of 53 hectares were created in various regions of the European North of the Russian Federation (Arkhangelsk, Vologda Regions, Komi Republic). It was learned that Lodgepole pine of the most northern Canadian origin (Yukon), where it grows in permafrost on the northern limit of forest distribution, is of great interest for introduction into the European North of Russia [6].

The aim of the work is the feasibility of the Lodgepole pine (*Pinus contorta* Loud. var. *latifolia* S. Wats.) use for plantation cultivation in the boreal forests. The overall measurements of the diameters at breast height, the Lodgepole pine trees

height measurements and model trees cutting were carried out on the coniferous plantations.

Methodology

European North of the Russian Federation is located in the north of the East European Plain. Most of the territory is of the Far North regions; it is a vast plain with a weak slope towards the White and Barents Seas, where the plain is somewhere disturbed by terminal moraine hills formed as a result of the activity of an ancient glacier.

The climate of the region is transitional between marine and continental. Winter is usually long (up to 250 days) and cold, with a low average temperature -26 degrees Celsius and strong winds. Spring comes to the southern regions in April, to the northern ones in May. The average summer temperature is about +15 degrees C. The duration of the period with average daily negative temperatures in the south is 160 days, in the north \square about 200.

The annual amount of precipitation in the forest zone varies from 400 to 700 mm with the number of days with precipitation up to 200. Relative air humidity in winter and autumn is 85-95% and in summer and spring 70% -90%. This is due to low temperatures and a large number of cloudy days. In winter, a 60-70-cm-thick snow cover is formed on the territory of the region.

In terms of vegetation, the European North of Russia is entirely part of the natural zone of the taiga, which is subdivided into subzones: the subzone of the northern taiga (north of the 64-65th parallel), middle (the main part of the region) and south taiga.

The objects of research were Lodgepole pine plantations located in the European North of Russia (Arkhangelsk, Vologda regions and the Komi Republic) on a total area of 53 hectares.

Plantations were created by seedlings with an open root system. Lodgepole pine seeds were obtained from its natural range, as well from the most northern Canadian (Yukon) origin.

The study of the growth and productivity of Lodgepole pine was carried out according to the generally accepted method: complete counting of trees with measurement of height and diameter at a height of 1.3 m with an accuracy of ± 1 mm. The measuring plug "Mantax Precision 11-100-1032" was used for diameter measurement; the measuring pole "MODEL - 202 12 m" and the laser range finder "Vertex Laser VL 400" were used for height measurement. The growth progress in diameter was studied by selecting 5 cores at a height of 1.3 m (d1,3) using an incremental drill on each thickness level. Studying growth progress in height (h) on three medium-tall trees by whorl counting, the age was determined at $\frac{1}{4}$; $\frac{1}{2}$ and $\frac{3}{4}$ heights.

Methods of mathematical analysis and applied computer programs were used to determine the average growth indicators (average value, coefficient of variability, experimental accuracy, reliability of the average value). The stands stocks were determined using standard formulas and tables. Due to the lack of standard materials for Lodgepole pine for the European North of Russia, tables for Scots pine were used. Periodic surveys and analysis of these plantations state were carried out.

Results and its discussion

Particular attention is paid to the growth of Lodgepole pine (*Pinus contorta* Loud. var. *latifolia* S.Wats) compared to Scots pine (*Pinus sylvestris* L.) in the same growing conditions. The average taxation indicators of Lodgepole pine in height and stem diameter, obtained from the results of continuous counting, are presented in table 1. The data indicate the successful growth of Lodgepole pine, which, even in conditions of ameliorated swamp (P-83), it continues to grow intensively and exceeds Scots pine in terms of taxation indices (twice in stem volume).

Table 1
Average Lodgepole pine taxation indices

| Plantation number | Forest type | Area, ha | Species | Age at year of surveys | Stem volume, m ³ /ha | Average diameter, cm | Average height, m |
|-------------------|--------------------------------|----------|----------------|------------------------|---------------------------------|----------------------|-------------------|
| P-83 | Sphagnetosum ameliorated swamp | 1,12 | Lodgepole pine | 37 | 85,5 | 12,6±0,5 | 12,1±0,3 |
| | | | Scots pine | 36 | 48,0 | 10,4±0,3 | 10,3±0,4 |
| P-82-84 | Fresh spruce myrtillosum | 0,48 | Lodgepole pine | 36 | 220,7 | 18,3±0,4 | 15,1±0,3 |
| | | | Scots pine | 35 | 190,0 | 10,4±0,8 | 10,3±0,4 |
| P-85 | Floodplain | 0,05 | Lodgepole pine | 33 | 240,9 | 20,3±1,2 | 11,5±0,3 |
| P-1-88 | Former nursery | 2,7 | Lodgepole pine | 30 | 104,2 | 14,9±0,2 | 12,1±0,3 |
| P-2-85 | Pine lichenosum | 1,24 | Lodgepole pine | 34 | 109,0 | 9,4±0,1 | 9,2±0,2 |
| | | | Scots pine | 34 | 93,0 | 11,2±0,5 | 8,7±0,6 |
| P-3-93 | Pine vaccinsum, former nursery | 2,9 | Lodgepole pine | 25 | 163,0 | 14,7±0,2 | 12,9±0,4 |
| P-4-93 | Pine lichenosum | 2,4 | Lodgepole pine | 26 | 113,0 | 10,8±0,2 | 8,0±0,3 |
| P-1-90 | Fresh spruce myrtillosum | 1,8 | Lodgepole pine | 29 | 226,0 | 15,1±0,1 | 14,9±0,3 |
| | | | Scots pine | 29 | 163,0 | 10,7±0,4 | 11,9±0,4 |

| | | | | | | | |
|---------------|--------------------------|------|----------------|----|-------|----------|----------|
| P-1-93 | Spruce oxalisum | 9,9 | Lodgepole pine | 26 | 226,0 | 14,2±0,2 | 14,9±0,3 |
| | | | Scots pine | 26 | 182,0 | 12,7±0,7 | 13,3±0,5 |
| P-2-88 | Fresh spruce myrtillosum | 0,9 | Lodgepole pine | 31 | 42,5 | 12,3±0,3 | 10,8±0,4 |
| P-88 | Fresh spruce myrtillosum | 3,0 | Lodgepole pine | 32 | 196,0 | 16,0±0,2 | 12,1±0,4 |
| P-2-93 | Fresh spruce myrtillosum | 11,0 | Lodgepole pine | 27 | 167,0 | 12,9±0,3 | 10,8±0,5 |
| P-1-97 | Pine vacciniosum | 7,0 | Lodgepole pine | 23 | 98,0 | 9,7±0,1 | 9,1±0,1 |
| P-1-87 | Pine lichenosum | 1,0 | Lodgepole pine | 32 | 138,5 | 12,7±0,4 | 12,0±0,4 |

The presented results on the average growth indicators of Lodgepole pine of Yukon origin (P-1-88, P-2-88, P-88) show that this pine responds well to improved soil conditions and, undoubtedly, to pre-plant soil preparation.

The Lodgepole pine on plantation P-2-88, created on a site without soil preparation, is significantly behind in growth. As calculations show, the wood stock of 26-year-old Lodgepole pine per hectare has been determined between 113 and 163 m³/ha in different growing conditions. Lodgepole pine significantly exceeds Scots pine in growth in stem volume under similar growing conditions. The best growth both in diameter and height was noted at the Lodgepole pine plantations P-82-84, P-85, P-1-88, P-88, P-1-90, P-1-93, p-2-93 and P-3-93.

An urgent issue of returning unused agricultural land to economic circulation can be solved by creating plantations of fast-growing coniferous species that lead to rural development. As noted, Lodgepole pine responds well to improving soil conditions, which allows us to conclude that the creation of its plantations on lands that have come out of agricultural use will be successful. The creation of fast-growing forest plantations supports the reverse of the loss of forest cover through sustainable forest management, including protection of natural forests and afforestation of unused agricultural land.

The study of experimental Lodgepole pine cultures has demonstrated their high safety and good condition, indicating the proper selection of ecotypes of this species for planting. It was assigned that the Lodgepole pine exceeds the Scotch pine in current increment in diameter, volume and in range of mean volume increment. The most northern Canadian origin (Yukon) of Lodgepole pine appeared to be the most suitable origin for the European North of Russia. The advantage of Lodgepole pine over local coniferous species was revealed while growing on industrial forest plantations, where, by the age of 40-50 years old, it forms 250-300 m³/ha of low-resinous wood, suitable for both sulfate and sulfite pulping and is 70% more productive than local spruce and pine. In the research process, the

basic requirements for plantation crops in the European North of Russia were developed, under which plantations justify their purpose.

Conclusions

As a result of the study, it can be concluded that Lodgepole pine planting is recommended to be carried out in productive forest types of the *hylocomiosa* group (*oxalidosum* and *fresh myrtillosum*). At the same time, soil preparation and mineral fertilizing before planting are of great importance in increasing the productivity of the Lodgepole pine plantations.

Based on the research results, it can be concluded that the European North of Russia is a promising area for the Lodgepole pine cultivation.

The research contributes to the achievement of the Sustainable Development Goals through sustainable forest management, including protection, restoration, afforestation and reforestation.

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含矿物添加剂的塑化水泥系统的物理和机械性能——光催化剂的潜在载体
**PHYSICAL AND MECHANICAL PROPERTIES
OF PLASTICIZED CEMENT SYSTEMS WITH MINERAL
ADDITIVES – POTENTIAL CARRIERS OF PHOTOCATALYTIC
AGENTS**

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抽象的。不同成分矿物添加剂（硅粉、偏高岭土、膨胀硫铝酸盐改性剂、微方解石）增塑水泥体系物理力学性能的研究结果，可作为“核-壳”合成中光催化剂的潜在载体作曲，在作品中呈现。结果发现，所研究的有机矿物改性剂组合物在 3 天和 7 天的水泥石抗压强度增加率方面存在差异，特别是在 48–69% 和 71–83% 的抗压强度年龄分别为 28 天。同时，与不含矿物添加剂的对照组合物相比，28 天龄期改性水泥石的相对抗压强度在 0.9 至 1.2 相对单位之间变化，证实了提高强度指标的可能性水泥复合材料由于使用了最佳的矿物复合物。

关键词：矿物添加剂，水泥体系，物理机械性能，“核-壳”光催化组合物，颗粒载体。

Abstract. *The study results of the physical and mechanical properties of plasticized cement systems with mineral additives of various compositions (silica fume, metakaolin, expanding sulfoaluminate modifier, microcalcite), which could act as potential carriers of photocatalytic agents in the synthesis of “core – shell” compositions, were presented in the work. It was found that the studied compositions with organic-mineral modifiers differed in high rates of compressive strength gain of cement stone at the age of 3 and 7 days, in particular, 48–69 % and 71–83 % of the compressive strength at the age of 28 days, respectively. At the same time, in comparison with the control composition without mineral additives, the relative compressive strength of the modified cement stone at the age*

of 28 days varied in the range from 0.9 to 1.2 relative units, which confirmed the possibility of increasing the strength indicators of cement composites due to the use of optimal mineral complexes.

Keywords: *mineral additive, cement system, physical and mechanical properties, “core – shell” photocatalytic composition, particulate carrier.*

Introduction

The development of multicomponent high performance cement systems, the achievement of the required level of properties of which can be achieved through the use of modifiers of various nature and action mechanism, is an important area of modern building materials science [1, 2, 3, 4, 5]. Photocatalytic additives are special type of modifiers that contribute to the creation of photocatalytically active cement materials characterized by a complex of positive properties, in particular, the ability to self-clean, neutralize and remove pollutants, eliminate unwanted odors, etc. under the influence of light. [6, 7, 8, 9, 10].

It is known that “core – shell” compositions, obtained by depositing photocatalyst particles on particulate carriers (substrates), while mineral raw materials of various genesis can act as substrate, are one of the effective types of photocatalytic additives for cement systems [11, 12, 13].

According to the study results, the promising raw materials for carriers of photocatalytic agents was established:

- natural and technogenic pozzolans with high content of amorphous silica or alumina, in particular, diatomite, silica fume, metakaolin, fly ash, zeolite, granulated slags, polymineral clays, etc. [13, 14, 15, 16, 17], characterized by high activity in cement systems and chemical affinity with crystalline hydrates of cement stone;
- expanding sulfoaluminate additives that stimulated the formation process of phases increased in volume (ettringite, etc.), which made it possible to control deformations of cement stone [18, 19];
- carbonate rocks (limestone, chalk, marble, dolomite) with a predominant calcite content, which was able to act as a center of phase crystallization and thereby regulate the rate of structure formation of cement systems [20, 21].

It should be noted that in the development of effective photocatalytic compositions, an important task was the choice of mineral raw material – carrier of photocatalyst based on a set of requirements, among which its activity in the cement system was the main one.

The purpose of this study was to establish the influence regularities of mineral additives (MAs) of various compositions (silica fume, metakaolin, expanding sulfoaluminate modifier, microcalcite) on the physical and mechanical properties of plasticized cement systems to identify the most effective modifiers for further use as carriers of photocatalysts in the “core – shell” compositions.

Materials and methods

In the studied compositions the primary component of binder was Portland cement CEM I 42.5R (PC) produced by Mordovtsement PJSC. At the same time, studies were conducted on cement systems with total dosage of mineral additives of 20 % by weight of the binder (PC+MAs) at fixed water-binding ratio $W/(PC+MAs)=0.24$. Composition without mineral additives with equal water content and dosage of plasticizer of 1 % by weight of Portland cement was adopted as control composition.

Table 1.
Experimental study plan in coded values

| Composition number | Variable factors in coded values | | | | |
|--------------------|----------------------------------|--------------|--------------|--|-------------|
| | First group of factors | | | Second group of factors | |
| | Type and content of AMA | | | Content of superplasticizer and carbonate filler | |
| | v_1 (SF) | v_2 (HAMK) | v_3 (ESAM) | x_1 (PS) | x_2 (MCC) |
| 1 | 1 | 0 | 0 | -1 | -1 |
| 2 | 0 | 1 | 0 | -1 | -1 |
| 3 | 0 | 0 | 1 | -1 | -1 |
| 4 | 0.5 | 0 | 0.5 | -1 | 0 |
| 5 | 0 | 0 | 1 | -1 | 1 |
| 6 | 0.5 | 0.5 | 0 | -1 | 1 |
| 7 | 0 | 1 | 0 | 0 | 1 |
| 8 | 0 | 0.5 | 0.5 | 0 | -1 |
| 9 | 0.5 | 0.5 | 0 | 1 | 0 |
| 10 | 0.333 | 0.333 | 0.333 | 0 | 0 |
| 11 | 1 | 0 | 0 | 1 | -1 |
| 12 | 0 | 0 | 1 | 1 | -1 |
| 13 | 0.5 | 0 | 0.5 | 1 | 0 |
| 14 | 0 | 0.5 | 0.5 | 1 | 1 |
| 15 | 1 | 0 | 0 | 1 | 1 |
| 16 | 0 | 1 | 0 | 1 | -1 |
| 17 | 0.5 | 0 | 0.5 | 0 | 1 |
| 18 | 0.5 | 0.5 | 0 | 0 | -1 |
| Control (C) | 0 | 0 | 0 | 0 | -1 |

The experimental study was planned based on a specially synthesized plan containing 18 experimental points (Table 1). Two groups of factors varied:

- type and content of active mineral additives (AMAs): v_1 (condensed non-compacted silica fume produced by Kuznetskie Ferrosplavy JSC

- (SF)); v_2 (highly active metakaolin produced by Plast-Rifey LLC (HAMK)); v_3 (expanding sulfoaluminate modifier produced by Parade-Rus LLC (ESAM));
- content of plasticizing additive and carbonate filler: x_1 (Melflux 1641 F polycarboxylate superplasticizer (PS)); x_2 (microcalcite (MCC)).

Table 2.

The variation levels of the first group of the studied factors

| Factors | | | Variation levels | | | |
|---------------------------------|-------|--------------------------------------|------------------|--------------|-----------|-----------|
| | | | 0 | 0.333 | 0.5 | 1.0 |
| Type of active mineral additive | v_1 | SF, % by weight of binder (PC+MAS) | 0 | 6.67/5/3.33* | 10/7.5/5* | 20/15/10* |
| | v_2 | HAMK, % by weight of binder (PC+MAS) | 0 | 6.67/5/3.33* | 10/7.5/5* | 20/15/10* |
| | v_3 | ESAM, % by weight of binder (PC+MAS) | 0 | 6.67/5/3.33* | 10/7.5/5* | 20/15/10* |

Note. *The amount of AMAs at the content of the carbonate filler (MCC), respectively, equal to 0/5/10 % by weight of the binder (PC+MAS).

Table 3.

The variation levels of the second group of the studied factors

| Factors | | | Variation levels | | |
|-------------------|-------|-------------------------------------|------------------|-----|-----|
| | | | -1 | 0 | +1 |
| Type of component | x_1 | PS, % by weight of binder (PC+MAS) | 0.5 | 1.0 | 1.5 |
| | x_2 | MCC, % by weight of binder (PC+MAS) | 0 | 5 | 10 |

Studies of the effect of mineral additives on the main physical and mechanical parameters of cement stone (average density in normal humidity conditions at the age of 28 days, compressive strength at the age of 3, 7 and 28 days) were carried out using standardized methods and verified equipment.

The compressive strength of cement stone was determined using the WilleGeotechnik® press (13-PD/401 model). The primary parameters were configured and obtained experimental results were recorded using the GEOSYS 8.7.8 software.

Results and discussion

Table 4 shows the study results of the main physical and mechanical parameters of cement stone.

Table 4.
Physical and mechanical parameters of cement stone of the studied compositions

| Composition number | Average density in normal humidity conditions at the age of 28 days, kg/m ³ | Compressive strength, MPa, aged | | |
|--------------------|--|---------------------------------|--------|---------|
| | | 3 days | 7 days | 28 days |
| 1 | 2103 | 56.8 | 79.1 | 96.2 |
| 2 | 2064 | 51.1 | 69.1 | 88.7 |
| 3 | 2184 | 56.8 | 79.5 | 96.1 |
| 4 | 2154 | 77.0 | 88.6 | 111.9 |
| 5 | 2183 | 63.3 | 82.4 | 100.3 |
| 6 | 2136 | 58.8 | 75.8 | 100.6 |
| 7 | 2145 | 61.7 | 79.2 | 105.0 |
| 8 | 2173 | 71.9 | 88.6 | 117.5 |
| 9 | 2139 | 47.7 | 73.3 | 99.1 |
| 10 | 2163 | 65.4 | 85.4 | 106.4 |
| 11 | 2107 | 48.5 | 76.4 | 95.9 |
| 12 | 2186 | 55.4 | 83.2 | 103.7 |
| 13 | 2142 | 70.5 | 88.2 | 111.1 |
| 14 | 2154 | 62.7 | 84.7 | 106.5 |
| 15 | 2138 | 60.2 | 73.8 | 103.5 |
| 16 | 2139 | 60.5 | 78.0 | 103.7 |
| 17 | 2186 | 59.4 | 80.0 | 109.6 |
| 18 | 2142 | 67.2 | 87.6 | 115.5 |
| Control (C) | 2150 | 60.0 | 77.1 | 98.3 |

It was found that the studied plasticized compositions with mineral additives SF, HAMK, ESAM differed in high rates of compressive strength gain of cement stone at the age of 3 and 7 days, in particular, 48–69 % and 71–83 % of the compressive strength at the age of 28 days, respectively (Table 4).

In comparison with the control composition, the relative compressive strength of the modified cement stone at the age of 28 days varied in the range from 0.9 to 1.2 relative units, which confirmed the possibility of increasing the strength indicators of the developed composites by purposefully controlling the pore space and the mineral-morphological state of the cement stone structure through the use of optimal complexes of chemical and mineral additives. The highest values of cement stone strength at the age of 28 days equal to 117.5 MPa and 115.5 MPa were recorded for compositions without microcalcite (No. 8 and 18) with complexes of mineral additives (HAMK+ESAM), (SF+HAMK) and superplasticizer content of 1 % of the binder weight (PC+MAAs), respectively (Table 4), which was 19.5 % and 17.5 % higher than the same indicator of the reference composition without

mineral additives (98.3 MPa). Another effective complex of mineral additives was the combined use of microcalcite, microsilica and sulfoaluminate modifier, which allowed increasing the strength indicators at the project age for cement systems of compositions No. 4, 13 and 17 to the appropriate levels equal to 111.9 MPa, 111.1 MPa and 109.6 MPa (11.5–13.8 % higher than the corresponding parameter of control composition).

Conclusions

The following results were obtained in the work:

- the effect of dosages of mineral additives of various compositions (silica fume, metakaolin, expanding sulfoaluminate modifier, microcalcite) was established on the main physical and mechanical parameters of cement stone (average density in normal humidity conditions at the age of 28 days, compressive strength at the age of 3, 7 and 28 days);
- the most effective complexes of modifiers were revealed that allowed directionally control the physical-mechanical properties of cement systems.

According to the study results, the increased chemical activity of SF, HAMK and ESAM in cement systems was established, which indicated the potential prospects of their use as mineral substrate in the “core – shell” photocatalytic compositions.

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哈萨克斯坦过境运输潜力的开发
**DEVELOPMENT OF TRANSIT AND TRANSPORT POTENTIAL OF
KAZAKHSTAN**

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抽象的。 本文讨论了影响哈萨克斯坦运输和过境潜力发展的因素。 作者提供了描述该国交通系统特征的数据。 分析了改善和协调国家运输和过境潜力发展的可能性。

关键词： 运输、过境潜力、货物运输、运输、运输和物流系统。

Abstract. *The article discusses the factors influencing the development of the transport and transit potential of Kazakhstan. The authors present data characterizing the country's transport system. The possibilities of improving and coordinating the development of the country's transport and transit potential are analyzed.*

Keywords: *transport, transit potential, cargo transportation, transportation, transport and logistics system.*

Kazakhstan today has a high transport and transit potential. Transport flows from the People's Republic of China to Europe and back through the territory of the republic make it possible to unlock this potential. According to various estimates, the republic can territorially serve up to 20% of these transcontinental flows. Realizing this, since 2000 the leadership of Kazakhstan began to pay special attention to the development of the transport industry in connection with the large-scale processes of economic integration of the republic into the global and regional economies. Appropriate sectoral programs have been developed to unlock this potential. The most significant intersectoral programs aimed at realizing the transport and transit potential of Kazakhstan are the State Program for the Development and Integration of the Infrastructure of the Transport System of the Republic of Kazakhstan until 2020, which was preceded by the Program for the Development of the Transit and Transport Potential of the Republic of Kazakhstan for 2004-2006 and the Program for the Development of Transport Infrastructure in Republic of Kazakhstan for 2010 - 2014, the State Program for Infrastructure Development "Nurly Zhol" for 2015-2019. The concept of the "Nurly Zhol" program until 2025 has been developed.

The services of the transport industry are needed at almost every stage of production and consumption of products, from the extraction and processing of raw materials and resources to the delivery of finished products to their final consumer, including foreign markets.

Transport makes a huge contribution to the formation of value chains and production costs and, thus, has a significant impact on the competitiveness of products and the economy of the state as a whole. At the same time, the functioning of the transport industry is impossible without providing the population and business with an effective and sufficient public transport infrastructure, which is a direct responsibility and function of the state.

There are factors influencing the development of the country's transport potential: political, economic, social, technological, environmental and legal.

Accession to new intergovernmental agreements contributes to the growth of cargo flows, requiring an increase in the throughput and service level of the transport system of Kazakhstan.

Fluctuations in energy prices lead to instability in the activities of transport companies. For the transport system of Kazakhstan, which is an important link in the Asia-Europe transport corridor, the growth of trade contributes to an increase in cargo flows. Thanks to digitalization, a significant proportion of commercial transactions in the field of transport and logistics are executed electronically.

Growing competition in the market of transport and logistics services dictates new requirements for economic efficiency and competitiveness. Small transport companies will be forced out by large ones. Transport and logistics companies will

expand cooperation in the field of sharing warehouse space, terminals, as well as rolling stock on the basis of rental and operating leasing mechanisms.

The rapid introduction of “green technologies” and the reduction in the consumption of petroleum products will make significant changes in the volume and structure of supply and demand for energy carriers and the resources and materials created from them, which will lead to an increase in the unpredictability of price fluctuations and exchange rates.

The global trend of transition to green technologies with the tightening and widespread implementation of restrictions on greenhouse gas emissions will increase, causing the inevitable transition of the transport and logistics complex to the use of more environmentally friendly and safe solutions and technologies (“green logistics”). At the same time, existing technologies will be gradually banned and forced to be replaced by new ones.

Global climate change leads to changes in the historically established weather background in various regions of the Earth, including Kazakhstan. This trend will intensify, changing the usual operating conditions for various transport industries and may disrupt established schedules and supply chains due to weather conditions.

The depletion of natural resources will result in a reduction in the availability of familiar natural resources used in the production of vehicles, components, equipment, building materials, fuels, etc., which will inevitably lead to an increase in market prices for such resources and will necessitate a widespread transition to the disposal and processing of materials for recycling purposes.

The introduction of new information and telecommunication technologies based on access to personal data (for example, tracking and forecasting cargo flows based on data from mobile operators) may face restrictions imposed by personal data protection legislation. It is necessary to assess the benefits and threats in each specific case with the development of corrective measures at the national level, without infringing on the guaranteed rights and freedoms of citizens of Kazakhstan.

To reduce the technological gap of Kazakhstan in the transport industry, it is necessary to more actively develop the knowledge base and improve the institutional environment for the introduction of cutting-edge and highly intelligent technologies with a minimum delay in time from their introduction in more developed countries.

To fully participate in the competition for attracting transit cargo flows, the transport and logistics complex of Kazakhstan must develop ahead of the curve, including the creation of a logistics infrastructure of sufficient capacity (capacity) and the provision of high-quality services.

To minimize the damage from restricting the operation of rolling stock and technologies that do not comply with global environmental trends, Kazakhstan

should carry out timely harmonization of national legislation and technical regulations in order to ensure the systematic compliance of national operators with new requirements in the field of emission reduction and environmental protection. An important task is also the introduction of “green technologies” at the stage of implementation of projects for the construction of transport infrastructure.

Improving the accuracy of weather forecasts and constantly monitoring the dynamics of changes is an important condition for minimizing the effects of adverse weather events. Keeping vehicle operators informed of changing and dangerous weather conditions in a timely manner through the deployment of relevant elements of the intelligent transportation system in Kazakhstan, along with improving the effectiveness of restrictive and preventive measures, will help prevent an increase in weather-related incidents.

Kazakhstani legislation should stimulate the development of technologies and a culture of waste recycling among the population and business, since this brings not only environmental, but also economic benefits to society.

Strict tariff regulation of the activities of transport companies in some cases creates insurmountable obstacles to the development of their business and limits investment opportunities. To improve the efficiency of operators and provide them with opportunities for timely technological modernization, it is necessary to review the existing mechanisms in Kazakhstan with the introduction of a new model of market relations, at least in certain segments of the transport industry.

In addition, the outstripping pace of development of market relations dictates the need for a timely response on the part of the state through the formation of appropriate institutional conditions in order to avoid distortions in sectoral development.

The length of public roads of international, republican, regional and district significance in Kazakhstan is 95.9 thousand km.

The network of highways of international and republican significance has a length of 24.3 thousand km, of which 87% is in good and satisfactory technical condition (2019 data).

Along with the trend of improving the state and level of financing for the development and operation of roads, a number of systemic issues remain that require further improvement of the system for improving the efficiency of road repair planning, ensuring the required level of quality of roads at all stages of the life cycle, introducing new materials and technologies, as well as bringing the regulatory and technical base to the best international standards.

The deployed length of the railways of Kazakhstan in single-track terms is 21 thousand km (19th place in the world), of which 11.1 thousand km are single-track (69%), 4.9 thousand km are double-track (30.6%), 32.3 km - more than 2 tracks, 4.2 thousand km of electrified lines (26%). The operational length of the main railway network is 16.1 thousand km.

The provision of Kazakhstan with a railway network in comparison with other countries of the world shows a significant lag in the density of the network per 1000 sq km of territory. Accordingly, the transport policy in the field of railway transport in recent decades has been focused mainly on the formation of a new architecture of railway transport corridors through the construction of new ones, including directing lines.

In the field of railway infrastructure, the formation of an optimal railway network has almost been completed, with an emphasis on optimizing the routes of intra-republican transportation by creating direct connections between regions, as well as increasing the attractiveness of Kazakhstani routes for transit shippers.

Water transport in Kazakhstan is represented by three seaports on the Caspian Sea, several navigable rivers and reservoirs with a network of inland water ports and hydraulic infrastructure.

In recent years, a number of large-scale projects have been implemented to modernize and develop the infrastructure of water transport, primarily aimed at increasing the throughput of seaports and improving cargo handling technologies.

The development of inland water transport is closely connected with the industrial development of the country's rich natural resources. Navigation in Kazakhstan is possible along such rivers as the Irtysh, Ural, Ili and Ishim, Lake Balkhash. Of the main problems of river transport, it is necessary to single out the insufficient number and high wear and tear of coastal transport infrastructure facilities, the long service life of shipping locks without major repairs and equipment replacement. The state technical fleet and private transport vessels are largely worn out.

For the development of the Eurasian transport corridors, taking into account container technologies, over the past 10 years, Kazakhstan has invested about 30 billion US dollars in key transport and logistics infrastructure projects. New railway lines "Zhetygen - Altynkol", "Zhezkazgan - Saksaulskaya - Shalkar - Beineu" were built, which reduce transit routes by 1000 km and provide communication between the regions of the country from East to West. The new railway line "Uzen - Bolashak" provided a connection with the railway network of Turkmenistan and access to the ports of the Persian Gulf, and in the future - access to trade flows in India.

Favorable geographical position of Kazakhstan and targeted investments in the development of international transit corridors over the past 10 years. Favorable geographical position and historically established trade cargo flows between Russia and Central Asia formed the basis for the realization of the transit potential of Kazakhstan. The implementation of state programs for the development of transit and transport and logistics infrastructure, the Transport Strategy of the Republic of Kazakhstan until 2015 gave impetus to the realization of the transit potential and attraction of transcontinental container traffic between Asia and Europe, including

through the modernization and construction of new railways and roads, railway stations with multimodal terminals and transshipment areas, as well as the creation of a Caspian logistics hub in Aktau (Kuryk).

An active foreign policy of Kazakhstan on the development of Eurasian transport links and the integration of the transport and logistics system of Kazakhstan into the international one. Since the independence of Kazakhstan, the state has been pursuing an active domestic and foreign policy to develop the transport and infrastructure complex, which contributes to the realization of the transit potential.

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农村电网电网设备检修策略分析
**ANALYSIS OF ELECTRIC GRID EQUIPMENT MAINTENANCE
STRATEGIES IN RELATION TO RURAL ELECTRIC GRIDS**

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抽象的。本文考虑了农村电网电网设备维护策略实施的特点。从技术和经济的角度分析了具有参数控制的维护策略在哪些条件下是有益的。根据国家电网元件可靠性水平的评估，确定了阻碍农村电网设备维护策略实施的情况，并概述了解决这些问题的方法。

关键词：运行措施，电网设备，检修策略。

Abstract. *The article considers the features of the implementation of strategies for the maintenance of electrical grid equipment in rural electrical networks. The conditions under which the maintenance strategy with the control of parameters can be beneficial from a technical and economic point of view are analyzed. The circumstances that impede the implementation of the equipment maintenance strategy in rural electric networks according to the state with an assessment of the level of reliability of the elements of the electric network are determined, and ways to solve them are outlined.*

Keywords: *operational measures, power grid equipment, maintenance strategy.*

The length of rural electrical networks with a voltage of 0.38-35 kV on the territory of Russia is more than 2 million km [1]. To date, more than 500 thousand transformer substations with a voltage of 6-35 / 0.4 kV are in operation in networks of this class with a total provided power of 90 million kVA [2]. Obviously, for high-quality and reliable power supply to consumers, power grid equipment

must be in working condition for a long time. However, during the operation period, under the influence of a significant number of external and internal factors, the technical condition of the elements of electrical networks may deteriorate. The normal functioning of power grid equipment, the properties of which deteriorate during operation, can be ensured by timely maintenance and repairs. In this case, the definition of a maintenance strategy is important, which establishes the basic technical principles of maintenance, determines the costs of labor, funds and time for carrying out operational activities.

The “*zero strategy*”, in which the operation of electrical equipment is carried out to failure without taking preventive measures, causes low reliability indicators and is not implemented in rural electrical networks.

The strategy with the calendar principle of planning operational activities provides for a system of preventive maintenance (PM).

The basic principles of the PM system are as follows [3]:

- equipment reliability management during its operation is ensured by carrying out scheduled, periodically recurring maintenance and repairs of the established volume;
- the frequency and scope of maintenance are established by the requirements of the normative and technical documentation (NTD) for each type of equipment;
- the frequency and scope of maintenance and repair can be adjusted based on the results of monitoring the technical condition. In this case, in accordance with the requirements of NTD, the volume and frequency of diagnostic checks are planned.;
- optimal management of the reliability and performance of equipment is provided by a sufficient amount of technical and economic information about the operation of existing equipment and its analogues.

The main advantage of this strategy is the ease of planning maintenance and repairs. However, such a system has outdated standards, does not provide optimal values of resources before repair, the frequency and scope of work that would ensure optimal efficiency and safety of equipment operation. In this case, the main thing is the fact that the actual operating conditions of the equipment and its actual state are ignored.

Rural electrical networks operate in specific conditions associated with the impact of a significant number of external and internal factors. These include climatic conditions, wind loads, ice formation on wires, exposure to dust and chemicals, overloads, etc.

In such a situation, the flow of faults that occur in networks is random in nature and it makes no sense to talk about a strictly regulated list of work performed during a particular event, as is done when using PM. Because of this, a somewhat

modified maintenance system is used in electrical networks, in which operational activities are carried out at predetermined dates, and the list of faults is taken from the defect log, which is compiled based on the results of control measures.

This approach has the right to be used, but it is not without drawbacks, because due to the random nature of the appearance of defects, the volume and degree of complexity of work to eliminate them are not known in advance and there are problems with material support and the formation of the staff of the electric grid enterprise.

The equipment maintenance strategy according to the technical condition provides for the use of the frequency and the list of work performed depending on the technical condition of the facility. The equipment is operated until a pre-failure level is reached, which must be predicted. At the same time, the frequency of control measures will be individual for each of the considered products.

Depending on the used initial information about the state of the elements of the electrical network, the maintenance system can have two possible versions - with parameter control and with an assessment of the object reliability level.

When using the equipment maintenance strategy according to technical condition with parameter control, it is necessary to establish permanent or periodic monitoring of the technical condition of an electrical network element in order to establish the timing of putting the facility into service or repair. At the same time, only those products that have parameter deviations that go beyond the established tolerances are subject to maintenance, and serviceable equipment is used for its intended purpose.

Thus, the approach under consideration is based on such important measures as diagnosing the state of network elements and predicting the timing of proactive operational measures to restore the facility's operability before a failure occurs.

The method is planned and preventive, but unlike the PM method, which strictly regulates the timing and scope of the activities performed, here we are talking about planning diagnostic work in order to establish the drift of controlled parameters for subsequent clarification of the timing of the necessary operational activities.

In a condition-based strategy with parameter monitoring, an indication of an impending failure is the value of a diagnostic equipment parameter. At the same time, the permissible value of this parameter is established by calculation or empirically and is indicated in the NTD. The effectiveness of a parameter-controlled service system depends on a significant number of factors. Taking into account the fact that when assessing the technical condition of electrical equipment, erroneous decisions may occur, the control tools used acquire the leading role.

If, when using a preventive maintenance system for electrical network equipment, the decision to carry out certain operational activities is made a priori with-

out establishing the actual state of electrical equipment, then when using a maintenance strategy based on technical condition with parameter control, maintenance or repair is preceded by the phase of assessing its actual state. And at the same time, if the checks indicate the normal condition of the equipment, then the need for operational maintenance is eliminated. This is the fundamental advantage of the considered approach, since when using the PM system, operational activities are carried out without fail.

The strategy of maintenance of electrical equipment according to the technical condition with the control of parameters can be beneficial from a technical and economic point of view if a number of conditions are met. Equipment status may change randomly. When assessing the technical condition of electrical equipment using control devices, errors are not excluded. Therefore, it is necessary to take into account the probabilistic nature of the control measures. The conclusion about the state of the equipment is presented in the form of table 1.

Table 1
Initial data for evaluating the effectiveness of maintenance of electrical equipment

| Condition of electrical equipment | Probability of state | Solution | Conditional risk |
|-----------------------------------|----------------------|-------------|------------------|
| Serviceable | P | serviceable | C_o |
| | | faulty | $C_o + C_M$ |
| Faulty | Q | serviceable | $C_o + C_D$ |
| | | faulty | $C_o + C_M$ |

In table 1, the costs are taken as conditional risks: C_o – to determine the technical condition of network elements, C_M – for maintenance operations, C_D – damage from power outages.

In accordance with the initial data given in Table 1, the average value of the conditional risk can be determined by the formula

$$R = P[(1 - \alpha) \cdot C_o + \alpha \cdot (C_o + C_{TO})] + Q[\beta \cdot (C_o + C_y) + (1 - \beta) \cdot (C_o + C_{TO})]. \quad (1)$$

A distinctive feature of the planned preventive maintenance system is the fact that such a value as the cost of maintenance C_M remains constant. As a result, by dividing it by the value of the conditional risk, we can obtain a criterion for the effectiveness of the service system:

$$\Theta = \frac{C_{TO}}{R}. \quad (2)$$

Using the data in table 1, the formula for the efficiency criterion E will look like this:

$$\vartheta = \frac{C_{TO}}{P[(1-\alpha) \cdot C_0 + \alpha \cdot (C_0 + C_{TO})] + Q[\beta \cdot (C_0 + C_Y) + (1-\beta) \cdot (C_0 + C_{TO})]} \quad (3)$$

where α and β – probabilities of erroneous decisions, depending on the characteristics of the product in question and the control system used.

In the event that the determination of control parameters is carried out without errors, the advantages of the technical condition control system will be even more obvious, since the indicators $\alpha = \beta = 0$ and expression (3) will take the form:

$$\vartheta = \frac{C_{TO}}{C_0 + Q \cdot C_{TO}} = \frac{1}{\frac{C_0}{C_{TO}} + Q} \quad (4)$$

As effective means of monitoring the technical condition of electrical network elements are created and implemented, the costs of such equipment and control measurements will be reduced. In such a situation, when the cost of assessing the technical condition can become significantly less than the cost of carrying out operational activities ($C_0 \ll C_M$) and the value of the equipment maintenance efficiency indicator will be even higher, since ($E = Q^{-1}$).

The results of the conducted research indicate that it is desirable to apply the strategy of maintaining the elements of electrical networks with the control of parameters at objects with high reliability of the elements. The practice of operating rural distribution networks has made it possible to establish that most elements of the electric grid economy are related to such products [4]. Another important aspect necessary for the implementation of this method is the development of effective systems for monitoring the technical condition, for example, in the form of automated complexes.

The equipment maintenance strategy according to the state with an assessment of the level of reliability of the elements of the electrical network is characterized by the fact that the products are operated until the actual level of their reliability does not go beyond the permissible limits.

The use of this approach presupposes that the enterprise has a subdivision well trained in matters of reliability of complex technical systems. To this end, it is necessary to carry out a number of organizational and technical measures in the organization that allow performing the following work:

- organize the accumulation of statistical data on failures of electrical network equipment;
- carry out machine processing of statistical materials to assess equipment reliability indicators;
- learn to determine the permissible values of the reliability of electrical network elements and compare them with the actual level;

- develop recommendations for maintaining the required level of reliability indicators of power grid equipment. When developing recommendations aimed at improving the reliability of electrical network equipment, one should focus not only on improving the circuit design solutions of networks and the use of modern equipment, but also on the large-scale use of operational measures.

The issues of a wider implementation of the equipment maintenance method, taking into account the level of reliability, are hampered by the difficulties of solving a number of organizational problems, the need to use computers to control the level of reliability, the need to have specialists of sufficiently high qualification, the possibility of organizing the rapid collection of information on the reliability of individual elements of the network, etc.

When conducting a comparative feasibility study of various strategies for the maintenance of electrical networks, it is necessary to take into account the fact that the main advantages of using methods based on the condition of the equipment are the most complete use of the resource of network elements and the possibility of canceling some maintenance activities. However, in the latter case, such a situation is possible only if there is no significant damage to consumers due to interruptions in the power supply.

Of the considered maintenance strategies for electrical equipment of electrical networks, the most preferable is the maintenance method according to technical condition with parameter control. At the same time, the use of this method in rural electrical networks has not found proper distribution. The reasons for this situation are the lack of the necessary diagnostic tools, poor methodological support for this area of activity, and the lack of highly qualified specialists to organize and carry out such work.

In general, it should be noted that the strategy of maintenance of electrical equipment according to the technical condition is more progressive and further work is needed to implement it as soon as possible in all sectors of the economic mechanism of our country. As one of the priority tasks, it should also be considered in relation to electric grid enterprises operating rural electric networks.

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