



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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这些会议文集结合了会议的材料 – 研究论文和科学工作者的论文报告。它考察了职业化人格的技术和社会学问题。一些文章涉及人格职业化研究问题的理论和方法论方法和原则。

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重度伴发颅脑外伤对大龄儿童每分钟血液循环量的影响
**THE EFFECT OF SEVERE CONCOMITANT TRAUMATIC BRAIN
INJURY ON THE MINUTE VOLUME OF BLOOD CIRCULATION IN
OLDER CHILDREN**

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抽象的。1.3组SCTBI患儿最严重的情况是严重闭合性颅脑外伤、脑室出血、蛛网膜下腔出血。显示第2组受伤儿童血液循环的高动力特性占优势，每日波动更明显，CO的昼夜节律幅度较大。显然，第2组中相对更明显的偏差是由于在对大脑结构的损伤相对较小的情况下，通过过度交感神经的影响实现了更强大的代偿机制动员的结果。

关键词：重度伴发颅脑损伤，微量血液循环，儿童。

Abstract. *The most aggravating condition of children was exerted by severe closed craniocerebral trauma, hemorrhage in the cerebral ventricles, subarachnoid hemorrhage in 1.3 groups of children with SCTBI. The predominance of the hyperdynamic nature of blood circulation in injured children of group 2, more pronounced daily fluctuations, a large amplitude of the circadian rhythm of CO was revealed. Comparatively more pronounced deviations in group 2, apparently, are the result of a more powerful mobilization of compensatory mechanisms realized through hypersympathetic influences in conditions of relatively less damage to the brain structures.*

Keywords: *severe concomitant traumatic brain injury, minute volume of blood circulation, children.*

Relevance

The main factors aggravating mechanical trauma to the brain include hypoxia, disorders of systemic hemodynamics, as well as severe anemia. More than half of patients with severe TBI tend to have multiple lesions that result in significant blood loss, systemic hypotension, and hypoxia. Prevention or reasonable intensive care of these secondary pathological processes can significantly improve the outcome of TBI in most cases. The hyperkinetic type of blood circulation can

also be caused by a sharp increase in the concentration of adrenaline in the blood. Impaired oxygen delivery to the brain, with an increase in its oxygen demand, leads to the fact that the brain becomes more susceptible to the action of additional damaging factors, such as fluctuations in blood pressure, hypoxia, and impaired rheological properties of the blood. These secondary damaging factors complicate the condition of patients with TBI in more than 50% of cases [1-6]. Due to the lack of information, we made an attempt to study and assess the dynamics of the circadian rhythm of the cardiac output (CO) in the acute period of severe concomitant traumatic brain injury (SCTBI) in children.

Purpose of the work: to study the effect of severe concomitant traumatic brain injury on the minute volume of blood circulation in older children.

Material and research methods

We studied the indicators of a comprehensive examination of 18 school-age patients (7-18 years old) with severe concomitant traumatic brain injury (SCTBI) admitted to the intensive care unit (ICU) of the neurosurgical department of the Republican Scientific Center for Emergency Medical Aid (RSCEMA) in the first hours after a road traffic accident (RTA) - 15, catatrauma - 3 patients. Hourly monitoring of indicators of cardiac output (CO), systolic blood pressure (SBP), diastolic blood pressure (DBP), mean blood pressure (MBP), pulse blood pressure (PBP) was performed by calculating hemodynamic parameters using the formula: $CO=SV*HR/1000$ in l/minute, where SV - stroke volume of blood; HR - heart rate.

Results and discussion

Table 1.

Types of traumatic injuries

Damage types	Group 1 (4)	Group 2 (6)	Group 3 (8)
SCTBI	50% (2)	-	75% (6)
SCC	75% (3)	75% (4)	62% (5)
Light CC	25% (1)	-	25% (2)
SOTBI	50% (2)	83% (5)	25% (2)
SAH	50% (2)	50% (3)	62% (5)
Brain blood imbibition	50% (2)	33% (2)	37% (3)
Cerebral hematoma	50% (2)	18% (1)	37% (3)
Subdural hematoma	25% (1)	18% (1)	25% (2)
IVH	25% (1)	-	25% (2)
Dislocation syndrome	25% (1)	-	37% (3)
Facial bone fracture	50% (2)	75% (3)	25% (2)

Fracture of the pelvic bones	-	25% (1)	25% (2)
Fracture of the humerus, femur, shin bones	-	75% (4)	37% (3)
Lung contusion	50% (2)	33% (2)	-
Lung rupture		18% (1)	
Pneumothorax	25% (1)	18% (1)	-
Crushing injury of the liver	25% (1)	-	-
Ruptured kidney	25% (1)	-	-
Hemoperitoneum	25% (1)	-	-
Retroperitoneal hematoma	25% (1)	-	12% (1)
Laceration of the thigh	25% (1)	18% (1)	25% (2)

With a comparatively less pronounced traumatic effect on the brain, it was possible in a fairly short time to bring patients out of the state of severe traumatic shock, to carry out timely surgical correction of bone fractures, effective intensive therapy of bruises of parenchymal organs, and compensation of blood loss. A difference in the quantitative composition of some severe brain injuries was revealed (tab. 1). Thus, severe closed traumatic brain injury (SCTBI) was detected in 8 patients out of 12 in groups 1 and 3, subarachnoid hemorrhage (SAH) was diagnosed in 7; dislocation syndrome was observed in 4 children; IVH complicated STBI in 3 patients, while in group 2 SCTBI, IVH, dislocation syndrome was not revealed upon admission to the clinic (tab. 2).

Table 2.

Characteristics of patients with concomitant severe traumatic brain injury over 7 years old

Groups	1	2	3
Number of patients	4	6	8
Days at the ICU	7.7±1.7	14.8±2.2	34.6±14.1
Age, years	11.5±3	10.6±0.9	12.7±2.8
GS, points	10±0.4	8.2±0.9	7.8±0.7
ALV, days	2±0.9	10.7±2.6	22.2±4.5
PTS, points	4±0.2	1±0.3	1±0.25
ISS, points	52±8	60±13	47.8±8.5

Table 3.

Dynamics of the CO circadian rhythm mesor in the acute period of SCTBI

	Group 1	Group 2	Group 3
1	6.0±0.8	6.1±1.3	6.5±0.6
2	6.2±0.7	7.1±0.4	6.0±0.4
3	5.9±0.4	6.7±0.3*	6.6±0.4
4	4.7±0.4	7.0±0.5*	5.4±0.6
5	5.4±0.4	6.3±0.5	5.3±0.3
6	5.1±0.4	6.5±0.4*	5.3±0.3
7	5.0±0.5	6.5±0.4*	5.5±0.4
8	5.1±0.5	6.9±0.4*	6.1±0.5
9	5.4±0.4	6.8±0.4*	5.7±0.4
10		6.8±0.4	6.6±0.5
11		6.6±0.7	6.4±0.4
12		6.7±0.5	5.9±0.4
13		6.1±0.5	6.1±0.4
14		6.2±0.4	5.3±0.3
15		5.9±0.6	5.4±0.3
16		7.2±0.9	5.5±0.2
17			5.9±0.3
18			5.1±0.4
19			5.5±0.3
20			5.5±0.3
21			6.3±0.3
22			6.1±0.3
23			6.1±0.3
24			6.1±0.4
25			5.6±0.3
26			5.7±0.4
27			6.0±0.4
28			5.7±0.4
29			6.0±0.4
30			5.7±0.3

*-reliably relative to the indicator in group 1

On the first day after the injury, a tendency to an increase in CO was revealed in all groups of patients to 6.1-6.5 liters per minute (tab. 3). In group 1, no significant changes in the mesor of the circadian rhythm of CO were observed in the dynamics. In group 2, a significant difference was found relative to the indicator in group 1 on days 3, 4, 6-9, 13%, 48%, 27%, 30%, 35%, 25% ($p < 0.05$, respectively). At the same time, in group 3, the indicator of the mesor of the circadian rhythm CO did not significantly differ from the indicators of group 1, maintaining a certain stability throughout the entire acute period (fig. 1).

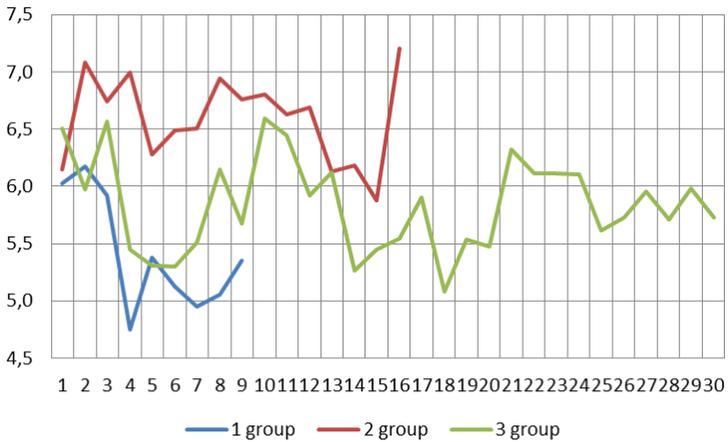


Figure 1. Dynamics of the mesor of the circadian rhythm CO

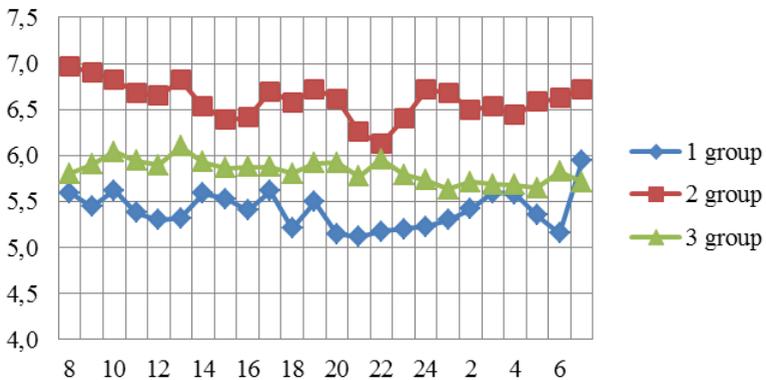


Figure 2. Average hourly circadian CO values

As can be seen from the data presented in fig. 2, regardless of the time of day (in the daytime and at night), significantly higher CO values were observed in children of the second group relative to the data in the first group and a tendency to increase relative to the hourly CO indicator in group 3 (fig. 2). The ultradian rhythm, which consisted of 5,5,3,5,6 hour periods of fluctuations, was most pronounced in the 2nd group of children with circadian rhythm acrophase -7 l/min in 7 hours and circadian rhythm bathyphase -6.1 l/min in 22 hours ($p > 0.05$) (tab. 4).

Table 4.
Average CO values in the circadian rhythm

	Group 1	Group 2	Group 3
8	5.6±0.6	7.0±0.6*	5.8±0.4
9	5.4±0.6	6.9±0.4*	5.9±0.4
10	5.6±0.7	6.8±0.3*	6.0±0.5
11	5.4±0.5	6.7±0.7*	5.9±0.5
12	5.3±0.8	6.6±0.6	5.9±0.4
13	5.3±0.7	6.8±0.5*	6.1±0.6
14	5.6±1.0	6.5±0.6	5.9±0.5
15	5.5±0.9	6.4±0.7	5.9±0.4
16	5.4±0.4	6.4±0.7	5.9±0.4
17	5.6±0.5	6.7±0.7	5.9±0.5
18	5.2±0.8	6.6±0.9	5.8±0.4
19	5.5±0.5	6.7±0.3*	5.9±0.5
20	5.1±0.6	6.6±0.7	5.9±0.5
21	5.1±0.5	6.3±0.6	5.8±0.4
22	5.2±0.3	6.1±0.7	6.0±0.6
23	5.2±0.5	6.4±0.5*	5.8±0.4
24	5.2±0.3	6.7±0.5*	5.7±0.6
1	5.3±0.6	6.7±0.4*	5.6±0.5
2	5.4±0.6	6.5±0.6	5.7±0.6
3	5.6±0.4	6.5±0.6	5.7±0.5
4	5.6±0.7	6.4±0.5	5.7±0.6
5	5.4±0.4	6.6±0.6*	5.7±0.5
6	5.2±0.5	6.6±0.6*	5.8±0.5
7	5.9±0.7	6.7±0.6	5.7±0.5

*-reliable relative to the indicator in group 1

Analysis of the results of hourly control (tab. 4) CO revealed a significant increase in CO in patients of group 2 at 8-11.13 hours by 25%, 25%, 24%, 24%, 28%, at 23-1 by 20%, 28%, 27%, 28%, 26%, at 5.6 hours by 23%, 26% ($p < 0.05$, respectively) relative to group 1. A more pronounced tendency towards the formation of a hyperdynamic type of blood circulation in patients of group 2, both in the morning and at night, was revealed than in the first and third groups of children.

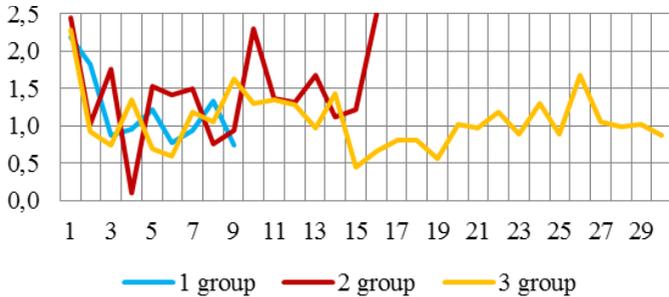


Figure 3. Dynamics of the amplitude of daily fluctuations in the circadian rhythm of CO

The change in the amplitude of daily fluctuations in CO was the most significant on day 1 in all subjects, amounting to 2.2-2.5 liters per minute, increasing again only in children of group 2 to 2.3 l/min on the 10th day and up to 2.5 liters per minute on the 16th day. While in groups 1 and 3, daily fluctuations occurred with an amplitude of 0.7-1.3 l/min in group 1 and 0.5-1.6 l/min in group 3.

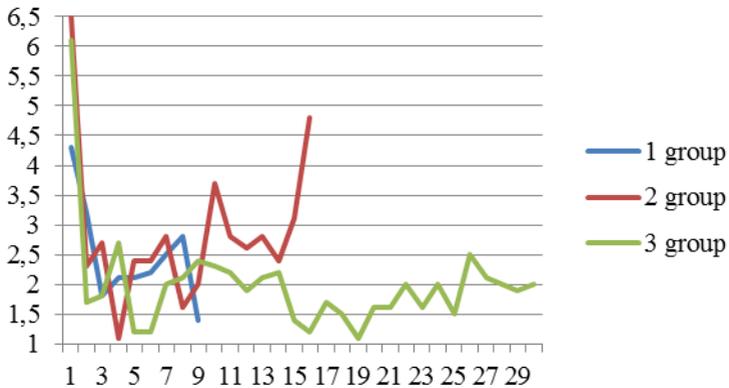


Figure 4. Maximum daily CO changes

It was revealed that CTBI was absent in group 2, and CTBI was absent in 1+3 groups in 8 children; SAH in 1+3 groups was detected in 7 patients, in group 2 only in 3 patients; IVH in 1+3 groups complicated STBI in 3 patients, while in group 2 IVH was not detected. From this it follows that group 2, with a total severity of injuries almost equal to that in group 3, differed in comparatively less traumatic damage to brain structures, when in 1+3 groups 18 severe structural brain injuries were revealed, and in group 2 the same traumatic factors were found in 6 times less. Comparatively more pronounced deviations in group 2, apparently, are the result of a more adequate mobilization of compensatory mechanisms implemented through hypersympathetic influences in conditions of relatively less damage to brain structures than in patients of group 3. Thus, SCTBI, cerebral ventricular hemorrhage, SAH, and dislocation syndrome had the most aggravating effect in children.

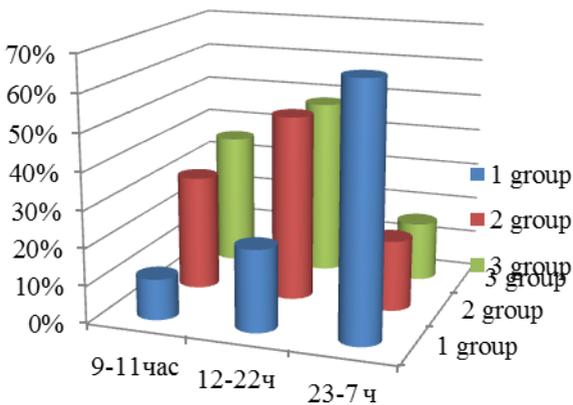


Figure 5. Duration and degree of CO circadian rhythm acrophase shifts

As shown in Fig. 5, the inversion of the circadian rhythm of CO was the most prolonged in group 1 during 67% of the duration of intensive therapy in the ICU. In groups 2 and 3, a more prolonged (50% and 48%) was a moderate shift in the peak of CO acrophase in the daytime.

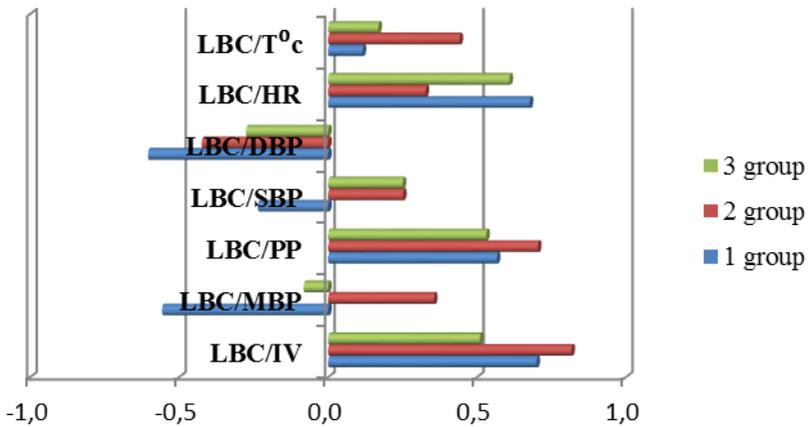


Figure 6. Correlation links of the minute volume of blood circulation

Direct strong correlation between CO and SV blood was observed in 1 (0.7) and 2 groups (0.8), CO and PBP (0.7) in group 2. A tendency towards a hyperdynamic variant of hemodynamics was also revealed in group 1 in the form of a negative correlation between CO and DBP (-0.6). A direct moderate relationship between CO and HR was noted in group 1 (0.7), that is, in the formation of hyperdynamic hemodynamics in patients of group 1, the sympathotonic effect on the activity of the sinus node took an active part (fig. 6).

Conclusion

The most aggravating effect on the condition of children was exerted by severe closed craniocerebral trauma, hemorrhage in the cerebral ventricles, subarachnoid hemorrhage, dislocation syndrome in 1.3 groups of children with SCTBI. The predominance of the hyperdynamic nature of blood circulation in injured children of group 2, more pronounced daily fluctuations, a large amplitude of the circadian rhythm of CO was revealed. Comparatively more pronounced deviations in group 2, apparently, are the result of a more powerful mobilization of compensatory mechanisms realized through hypersympathetic influences in conditions of relatively less damage to the brain structures.

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甘草酸在鼻内给药时可能的细胞毒性作用的体外评估
**IN VITRO ASSESSMENT OF THE POSSIBLE CYTOTOXIC EFFECTS
OF GLYCYRRHIZIC ACID AT INTRANASAL ADMINISTRATION**

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抽象的。众所周知，甘草酸具有抗炎和免疫调节作用，包括用于粘膜时。此外，目前有关于以甘草酸及其衍生物为基础的超分子复合物与用于给药的各种药物产生的数据。与上述有关，研究甘草酸的特性作为内服给药的基础具有科学意义。

关键词：甘草酸，鼻内给药，给药系统，细胞毒性，免疫活性细胞。

Abstract. *It is known that glycyrrhizic acid has anti-inflammatory and immunomodulatory effects, including when used on mucous membranes. In addition, there are currently data on the creation of supramolecular complexes based on glycyrrhizic acid and its derivatives with various drugs for drug delivery. In connection with the above, it is of scientific interest to study the properties of glycyrrhizic acid for use as a basis for drug delivery when administered internally.*

Keywords: *glycyrrhizic acid, intranasal administration, drug delivery system, cytotoxicity, immunocompetent cells.*

Introduction

Among the plants that humans use as a medicine, licorice attracts much attention, it is also licorice, it is also the roots and rhizomes of sweet licorice species *Glycyrrhiza glabra* L. and *Glycyrrhiza uralensis* Fisch. It was these licorice types, most common in Eurasia, that were used in ancient medical recipes. Doctors of Ancient China, Egypt, India, as well as Greece and Rome used licorice root to treat many diseases: eye diseases, diseases of the respiratory tract, stomach, and Tibetan doctors prescribed it as an antidote for snake bites [1].

Glycyrrhizic acid is a licorice root glycoside consisting of aglycone, a triter-

pene derivative of glycyrrhetic acid and a disaccharide fragment. In addition to glycoside derivatives of glycyrrhizic acid, licorice root contains about 20 glycosides of other minor triterpene aglycones, which together with glycyrrhizic acid are collectively referred to as “glycyrrhizin” [2].

Over the past 50 years, the biological and therapeutic properties of glycyrrhizic acid have been actively studied in Asia and Europe. From 2000 to 2021, PubMed posted just over 1,700 publications mentioning glycyrrhizic acid. Most of this work is devoted to antiviral, anticancer activity, and more articles appear where glycyrrhizic acid is used as a component of the delivery system. I, in turn, would like to highlight the topic of the anti-inflammatory activity of glycyrrhizic acid.

According to literary sources, glycyrrhizic acid, the main bioactive glycoside of licorice root, has a wide range of pharmacological properties, including anti-inflammatory action, and also promotes sputum discharge, due to which licorice-based drugs are successfully used to treat diseases such as bronchial asthma and allergic rhinitis [3-5]. Also, in the last decade, it was found that glycyrrhizic acid and its derivatives have anti-inflammatory and pronounced antiallergic effects, due to which the use of these substances in the complex therapy of immunopathologies (primarily allergies) becomes very relevant [6-11]. In addition, it is known that glycyrrhizic acid and its derivatives have the ability to form intermolecular complexes and micelles, including drug molecules for the purpose of targeted drug delivery [12].

Results and discussion

First of all, we investigated the effect of the delivery system itself, glycyrrhizic acid (GA), on toxicity in relation to various types of cells that can be important when administered internally, namely, cells of the nasal cavity and immunocompetent cells. For this, the effect on the cells of the RPMI 2650 line (nasal carcinoma of the nasal cavity, a standard cell line for creating a model for assessing the penetration of drugs through the nasal mucosa) was evaluated, the effect of HA on this cell line is being studied for the first time, as well as the primary culture of peripheral blood mononuclear cells (PBMC) from healthy donors and the mouse melanoma cell line B16. PBMC were isolated from heparinized venous blood of healthy donors by centrifugation in a density gradient of ficoll-urografin. The cells were cultured in RPMI-1640 nutrient medium containing 0.3% L-glutamine, 50 µg / ml gentamicin, 25 µg / ml thienam, and 10% inactivated FCS serum. To assess the viability, cells were cultured in the presence of various concentrations of HA for 72 h in a 96-well flat-bottom plate in the amount of 10 thousand / well for cell lines and 100 thousand / well for PBMC. DMSO was used as a negative control, which has a toxic effect on all species. cells. After 72 hours, 10 µl of WST-1 was added to each well, the results were evaluated spectrophotometrically at a wave-

length of 450 nm (reference 620 nm). Statistical processing of the study results was carried out by calculating the median (Me), 25th and 75th percentile (LQ, HQ), and presented as Me (LQ, HQ). Differences between the groups were assessed using the nonparametric Mann-Whitney U-test; the results were considered significant at $p < 0.05$.

As a result, it was found that GA reduces the viability of RPMI 2650 cells at a high concentration (500 mg / ml); in other concentrations (100 μg / ml and below), GA did not affect the viability of these cells (Table 1). It was shown that GA does not decrease the viability of PBMC in all studied concentrations. Moreover, an increase in the viability of PBMC was observed upon the addition of GA at a concentration of 10 $\mu\text{g}/\text{ml}$, which is possibly associated with the activation of cells and an increase in their proliferative activity in the presence of GA. It was also found that at a concentration of 100 $\mu\text{g}/\text{ml}$ and 1 $\mu\text{g}/\text{ml}$ there is a tendency to increase cell viability, however, the results obtained are not reliable. In the case of the B16 cell line, GA is able to increase the viability of these cells, apparently by enhancing the proliferation of these cells, only at a high concentration of 0.5 $\mu\text{g} / \text{ml}$ (Table 1). Consequently, GA has low toxicity for various types of cells, which is consistent with the literature data.

Table 1.

Effect of different concentrations of glycyrrhizic acid on the viability of various cell cultures, %

	PBMC	RPMI-2650	B16
0 $\mu\text{g}/\text{ml}$	100,0 (95,4-104,1)	100 (98,3-103,9)	97,2 (97,9-103,6)*
1 $\mu\text{g}/\text{ml}$	104,1 (99,3-115,1)#	94,1 (83,6-99,9)	94,1 (93,8-97,9)
10 $\mu\text{g}/\text{ml}$	106,1 (103,2-117,6)*	99,5 (96,2-105,7)	97,3 (91,0-101,9)
100 $\mu\text{g}/\text{m}$	108,4 (92,2-142,4)#	96,4 (67,8-100,2)	93,5 (91,5-96,6)
500 $\mu\text{g}/\text{ml}$	108,0 (96,6-133,2)	81,2 (79,9-93,3)*	117,5 (101,9-146,1)

Notes: * significant differences ($p < 0.05$) compared to control (concentration 0 $\mu\text{g} / \text{ml}$); # trend ($p < 0.07$) compared to control.

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Institutional Review Board Statement

The study was conducted according to the guidelines of the Declaration of Helsinki, and approved by the Institutional Local Ethical Committee of Research Institute of Fundamental and Clinical Immunology.

Informed Consent Statement

Informed consent was obtained from all subjects involved in the study.

Conflicts of Interest

The authors declare no conflict of interest.

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爱泼斯坦-巴尔病毒相关慢性扁桃体炎的诊治要点
**ASPECTS OF DIAGNOSIS AND TREATMENT OF CHRONIC
TONSILLITIS ASSOCIATED WITH EPSTEIN-BARR VIRUS**

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注解。 文章回顾了 Epstein-Barr 病毒在腭扁桃体慢性炎症发病机制中的作用。 特别注意疾病的临床表现及其诊断方法,包括血清学检测和可视化。 讨论了病毒再激活和复制的抑制剂: 药物、微量营养素、维生素和膳食补充剂。

关键词: 慢性扁桃体炎, 爱泼斯坦-巴尔病毒, EBV抗原, EBV中的微量营养素, 膳食补充剂

Annotation. *The article reviews the role of the Epstein-Barr virus in the pathogenesis of chronic inflammation of the palatine tonsils. Special attention is paid to the clinical picture of the disease and methods of its diagnosis, including serological testing and visualization. Inhibitors of reactivation and replication of the virus are discussed: medications, micronutrients, vitamins and dietary supplements.*

Keywords: *chronic tonsillitis, Epstein-Barr virus, EBV antigens, micronutrients in EBV, dietary supplement*

The problem of diagnosis and treatment of chronic tonsillitis (CT) remains relevant. This is due to the high prevalence of the disease among the population, the emergence of new methods of conservative and surgical treatment, a large arsenal of drugs recommended for chronic inflammation of the tonsils, the ongoing otorhinolaryngological discussion on the classification of chronic tonsillitis, the objectification of criteria for the diagnosis of the disease and the effectiveness of treatment. CT is an infectious and allergic disease of the whole organism with local manifestations in the form of a persistent inflammatory reaction of the palatine

tonsils, morphologically expressed by alteration, exudation and proliferation [2]. This definition reflects the etiological and pathogenetic relationship of chronic inflammation of the palatine tonsils with the development of pathological processes in other organs and systems, which is the result of a long-term interaction of an infectious agent located in the palatine tonsils and a macroorganism. The lymphoid tissue of the palatine tonsils is divided into three functional zones: lymphoid nodules, there are B-lymphocytes in the its germinal centers, interstitial diffuse lymphoid tissue containing T-cells, and supranuclear clusters of lymphocytes and monocytes [14,15].

Epstein-Barr virus (EBV) is a DNA-containing virus, he is one of the etiological factors of HT, causing the features of the clinical picture of the disease and its frequent relapses. 90% of the world's population are carriers of this virus [7]. In the palatine tonsils, EBV infects not only B-lymphocytes and lymphoepithelial cells, but also T-lymphocytes [6,9,10].

EBV affects the epithelium of the nasopharynx and oropharynx, small and large intestines and lymphoid tissue, which determines the features of the clinical picture of the disease. The main symptoms include respiratory phenomena (nasal congestion, tickling, sore throat, cough), loose stools, an increase in peripheral lymph nodes, an increase in body temperature. The clinical picture of chronic inflammation of the palatine tonsils associated with EBV is characterized by lability of symptoms: at the moment there is a sore throat, but during the day it gets better, the pain is completely self-relieved, then after a while the process repeats. Diarrhea is single, not accompanied by spasms, the nature of the stool is normalized independently during the day without the use of medications. EBV is characterized by an increase in the chin, submandibular, anterior and posterior cervical, parotid, occipital, supraclavicular, subclavian, axillary, inguinal lymph nodes and lymph nodes of the abdominal aorta. Body temperature rises to subfebrile values almost daily, gradually, closer to night, it can decrease independently and be accompanied by perspiration.

Evidence of the association palatine tonsils inflammation with the persistence of EBV is the detection of antibodies to immunogenic proteins in the blood serum: EA - early antigen, EBNA - Epstein-Barr nuclear antigen and VCA - viral capsid antigen. The type of antibodies detected makes it possible to differentiate the stage of the infectious process and, consequently, determine the optimal treatment tactics for each of them (Table 1) [10].

Table 1.

Stages of the infectious process caused by the Epstein-Barr virus

	VCA IgM	EA IgG	VCA IgG	EBNA IgG
EBV is absent	-	-	-	-
Early stage	+	-	-	-
Active stage, primary infection	+	±	+	-
Suffered from infection	-	±	+	+
Reactivation	±	+	+	+

Capsid antigen (VCA) indicates the presence of EBV in the body. When a person becomes ill for the first time, from the first day of infection to one month, immunoglobulins of class M to the capsid antigen (VCA IgM) are detected in the blood serum. From the second month of the disease, VCA IgM disappear forever, immunoglobulins of class G to the capsid antigen (VCA IgG) are formed, which persist for life and indicate that a person is a carrier of EBV. Early antigen (EA IgG) is positive from the first day of the disease, but no more than three months from the beginning of infection, from the fourth month it is not detected in the blood. It allows you to determine the prescription of the process, which determines the choice of treatment tactics. The nuclear antigen (EBNA IgG) indicates the activity of the process. If the presence of EBV in the patient has not been diagnosed earlier, it is advisable to determine all four indicators. Otherwise, it is sufficient to assess the presence of VCA IgG and EBNA IgG. Thus, a positive test result for VCA IgG with negative EBNA IgG indicates that a person is a carrier of EBV, but currently the infectious process is not active, treatment is not required. A positive test result for VCA IgG and EBNA IgG indicates an exacerbation of the infectious process and at a certain titer of EBNA IgG requires the appointment of treatment. With a positive result of the analysis for VCA IgG, it is advisable to perform an ultrasound examination of the peripheral lymph nodes in order to fix their size, exclude the inflammatory process in them.

The treatment regimen for the infectious process caused by EBV includes antiviral and antibacterial drugs from the macrolide group, probiotics and symptomatic therapy. There is no doubt that adequate nutrition is important in maintaining protective reactions at all stages of the immune response [5,13]. The lack of trace elements affects the innate and adaptive immunity, causing immunosuppression [1,3,4]. The main micronutrients necessary for maintain an immune response against EBV are zinc, magnesium, selenium, vitamin A, as well as a dietary supplement – curcumin.

Zinc plays a key role in regulating the function of innate and acquired immunity [5,11], it has a direct antiviral effect on EBV, maintains the integrity of

the membrane barrier [13,17], reduces oxidative stress [16]. Zinc orotate or zinc picolinate are two easily digestible forms of zinc. Magnesium is a cofactor of more than 100 detoxification reactions of the body. The replacement of magnesium deficiency is necessary for the activation of antiviral protection proteins against EBV, prevents magnesium losses caused by taking antiviral drugs and antibiotics [1]. Selenium is a cofactor of glutathione, a strong antioxidant, involved in reducing the viral load on the body [5]. An easily digestible form for the body is selenium methionine. However, selenium methionine is not able to enter the tissues in which EBV persists, therefore complex additives containing selenium methionine and selenium cysteine are needed. Selenium cysteine is able to transport selenium from selenium methionine into tissues. Vitamin A helps to maintain the integrity of the epithelium, regulates the number and functions of natural killers (NK), macrophages and neutrophils [5,18]. By suppressing the level of interferon (IFN)- γ expression and increasing the secretion of interleukin (IL) -5, vitamin A plays a regulatory role at the early stage of NK cell differentiation. In addition, it regulates the differentiation of dendritic cell precursors and promotes the secretion of proinflammatory cytokines IL-12 and IL-23 by dendritic cells, participates in the antimicrobial action of macrophages, playing a role in phagocytic and oxidative activity [8]. Curcumin exhibits antiviral activity against EBV replication by inhibiting the redox potential of human apurine/apirimidine endonuclease 1 (APE1), a key enzyme of the DNA repair mechanism [12].

Conclusion

Features of the clinical picture of chronic tonsillitis and its frequent relapses suggest that the disease occurs against the background of the persistence of EBV. Serological markers confirming the viral etiology of HT are antibodies to early, nuclear and capsid EBV antigens detected in blood serum. The combination of the detected antibodies makes it possible to differentiate the stage of the pathological process. Biochemical aspects of the cascade of pathogenetic reactions in CT cause the need to include vitamins and trace elements in the treatment protocol.

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文明病: 历史、生态、遗传

DISEASES OF CIVILIZATION: HISTORY, ECOLOGY, GENETICS

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抽象的。 文章研究与工业革命和工业化国家大多数人生活方式的变化(文明病)相关的疾病问题。 分析了改变生活方式的原因、与这些现象相关的不利因素、它们对人体的影响、新疾病出现的原因及其特点。 讨论了通过保持健康的生活方式来预防此类疾病的措施以及发达国家保护正常生态的措施。

关键词: 文明疾病, 影响自然的人为因素, 运动机能减退, 心血管疾病, 肿瘤疾病, 肥胖症, 糖尿病, 肺结核, 预防措施。

Abstract. *The article studies the problem of the diseases associated with the industrial revolution and changes in the lifestyle of most people in industrialized countries (diseases of civilization). The reasons for changing the way of life, the negative factors associated with these phenomena, their influence on the human body, the causes of the emergence of new diseases, and their characteristics are analyzed. Measures for the prevention of such diseases by maintaining a healthy lifestyle and measures to preserve a normal ecology in developed countries are discussed.*

Keywords: *diseases of civilization, anthropogenic factors of impact on nature, hypokinesia, cardiovascular diseases, oncological diseases, obesity, diabetes, tuberculosis, preventive measures.*

There are various theories about how health is maintained or destroyed person and what biological and social factors affect it. Currently, the most common theory of the emergence of new diseases as they develop social and industrial relations is the theory of "diseases of civilization", which has existed since the 50s XX century and becomes more and more relevant as it develops industrial and post-industrial society [1,2].

Diseases of civilization are mainly associated with the lag in adaptation mechanisms of a person to the unfavorable factors of the anthropogenically altered

environment in conditions of the rapid growth of scientific and technological progress. At the present stage of transition a highly developed civilization in the post-industrial space, people are faced with the real possibility of degradation and destruction of the environment and humanity itself since the transforming power of social production has become comparable in power with natural processes. Such the most powerful potential and real factors are the production of new super-powerful weapons, impact on near-earth space, deforestation, global pollution of land and oceans by plastic waste and industrial waste, massive use of herbicides, depletion of mineral resources, destruction of species diversity of wildlife, overproduction, and overconsumption of energy resources and global climate change. Against the background of growing environmental pollution environment, the danger of mutational and carcinogenic activity of xenobiotics is growing, the number of hereditary diseases, chromosomal and gene mutations leading to accumulation of genetic load in the population. The impact of teratogenic factors on the body of pregnant women leads to an increase in the number of newborns with congenital malformations.

People, intoxicated by their technological advances, seek to subjugate their natural processes, not realizing that many natural factors are still are not sufficiently studied, and the impact on them can lead to catastrophic cataclysms capable of destroying human civilization. Today, the world's population is still given a choice: either smart governance further social progress or the death of civilization. The resource intensity of the lifestyle of a modern industrial civilization exceeds the natural possibilities of our habitat. These resources are already being used up without the natural possibility of replenishment, at the expense of other less developed countries. This how lives about 13% of the world's population, which consumes about 70% of non-renewable resources and releases into the environment about the same proportion of polluting substances [3].

At the same time, the main characteristic of the post-industrial society, which currently exists in Western Europe and North America, is the fact that information becomes more important and more costly than land, material labor, capital, raw materials, and mass standardized production is transferred to the countries of the "third world" and is replaced by a system that is not based on manual, but mental work based on informatics and super technologies. Direct "human-to-human" interaction is replaced by an indirect "human-computer-human" interaction, which leads to the rupture of social ties, and social isolation subject, loss of emotional ties and understanding between people of different generations.

Nevertheless, there is no doubt that, along with the above negative trends, the progress of medicine has had a huge positive impact on the fate of humanity. Largely thanks to discoveries in medicine, the fate of every person have been greatly facilitated. This led to significant changes in demographic situations. The

diseases that gave rise to mass deadly epidemics (plague, smallpox, cholera) have been defeated. As a result of the discovery of new methods of therapy for various diseases, both the average and the maximum life expectancy of people have increased significantly. Methods of treating previously incurable diseases have been found.

However, the seemingly defeated old diseases are replaced by new ones, modified, more cruel and sophisticated, mimicking, seeking to bypass protective properties of the immune system. This group of diseases of civilization can be attributed to the pathology of the cardiovascular, nervous, immune, digestive, endocrine systems. Of these, cardiovascular, oncological, pulmonary diseases, diabetes mellitus top the list of causes of death, disability and temporary disability, chronic course of the pathological process.

According to the World Health Organization (WHO), seventy-five percent of all deaths in industrialized countries are diseases of civilization. First place is taken by cardiovascular diseases (atherosclerosis and its complications: strokes, heart attacks, as well as hypertension) [4].

Oncological diseases follow, which compete in some regions for causes of mortality with cardiovascular disease. Oncological diseases are very diverse. They can affect almost any organ and tissue of the body. Among the most common are breast, ovarian and uterine cancers in women; cancer lungs, stomach, prostate - in men. Despite colossal efforts to create new cancer treatments, progress in this area is very slow.

Further, among the diseases of civilization, there is a large group in terms of prevalence diseases that occupied a very modest place in the previous history of mankind. It is obesity, diabetes, diseases of the stomach and intestines (ulcers, gastritis, colitis, enteritis), allergic diseases, asthma, diseases of the spine and joints (osteochondrosis and osteoarthritis), venous insufficiency and varicose veins, and many others.

What are the main causes of diseases of civilization, which practically do not are found in traditional societies in Asia, Africa, Latin America? Diseases of civilization in the modern sense are diseases associated with a way of life modern man in conditions of usually urban life and the most typical Western civilization. Usually, these diseases are caused by unfavorable environmental environment, lack of physical activity, unhealthy diet, constant psychoemotional stress against the background of hypokinesia, and hence - abuse alcohol, smoking, and drugs.

Hypokinesia is associated with lack of movement due to lifestyle in cities, features of professional activity associated with a long-term static stay in confined spaces of offices and other confined spaces.

Binge eating. Modern man does not spend energy for obtaining food but receives her even delivery to your home or work, and food variety and abundance

is a strong temptation for chronic overeating. Constant overeating leads to weight gain - obesity, and obesity - to disease.

In many cases, overeating is associated with constant stress in which there is modern man due to excessive psycho-emotional stress in conditions industrial metropolis, unstable working conditions, and uncertainty about tomorrow in the context of recurring crises characteristic of capitalist public relations. Being in a state of chronic stress, a person "seizes" rich food, adding alcohol, tobacco, and psychoactive substances to "relieve stress". Hence - neuroses, psychosomatic disorders, and sometimes more serious psychiatric illness and addiction.

Since the beginning of the 20th century, the incidence of civilization diseases despite all the efforts of doctors began to grow exponentially. The present is characterized by the exceptionally rapid growth of social changes. At the same time adaptation and restructuring of the biological processes of the human body occur much slower. In the collision and contradiction of the first with the second, one of the causes of civilization diseases.

This discrepancy finds its specific clinical manifestation primarily in the neurosis of suppressed emotions, which is the basis of myocardial infarction, hypertension, stomach ulcers, diabetes mellitus, and neuropsychiatric disorders. The ever-increasing mechanization and automation of labor lead to physical inactivity. The share of physical labor in human activity was 98% a hundred years ago, and now - about 2%. Lack of constant physical fitness contributes to the development of cardiovascular disease, obesity [5].

About the prevalence of cancer among the population of industrialized countries statistics are extremely disappointing. Back at the beginning of the XX century such oncological diseases as sarcomas and leukemias were encountered in isolated cases. In 1913, German physician Adler counted 375 cases of lung cancer worldwide. But already in 1970, 50,000 cases were registered in the USSR, in 1985 in the USA - 125,000. In most cases, the leading etiological factor of this disease is smoking, as well as working in hazardous chemical industries. Among the factors causing oncogenesis, emit chemical (inorganic fertilizers, pesticides, asbestos, nickel, industrial emissions, and exhaust gases), physical (all types of ionizing and radioactive radiation, microwave, vibration), immunological (immune suppressants and immune modulators), genetic (exposure to xenobiotics, mutagens, and carcinogens) [6,7].

Modern civilization is characterized by a significant increase in the number of diseases, which are based on the vicious inclinations of a person arising from chronic stressful influences and the activities of international crime groupings.

These include smoking, alcoholism, substance abuse, gambling addiction, drug addiction, various sexually transmitted diseases, and associated AIDS and hepatitis.

Tuberculosis, over the centuries, has taken an uncountable number of human lives. In the XX century, against the background of successes in the production of new effective antibiotics, it seemed that tuberculosis had been defeated and the problem had been solved. However, at the end of the 20th century after a long period of relative calm, the incidence of tuberculosis is significantly increased, new resistant forms appeared, rapidly progressing and ending with a lethal outcome. In 1993, WHO declared tuberculosis a problem "Worldwide danger". Currently, a third of the world's population is infected with tuberculosis [8].

Another disease that is increasingly covering the civilized world is diabetes mellitus. According to the European Association for the Study of Diabetes (EASD), this disease can already be attributed to a non-infectious pandemic. For the last few years, more than 90 million people have joined the ranks of patients with diabetes mellitus. In the world today there are more than 250 million people with diabetes mellitus, with about half of the - people 35-55 years old.

More than 2.5 million people with diabetes are currently registered in Russia. According to experts, their actual number is 3-4 times higher. The treatment of diabetes and its complications leave up to 25% of the Russian health care budget; 90% of these funds are spent on the treatment of complications of diabetes. Complications of diabetes lead to the fact that concomitant of diabetes mortality from heart disease, and stroke in diabetic patients is 2-3 times higher than in the general population. Blindness among diabetic patients is 10 times more common, gangrene lower extremities - almost 20 times! [9,10].

The last and most difficult test, which undoubtedly can be attributed to diseases of civilization, there was a pandemic of the coronavirus COVID-19. This disease is many signs, it is no coincidence. The cause of this pandemic, as well as possible subsequent, in our opinion, lies in the overpopulation of some vast regions of the Earth, where there is an intense interaction of the genomes of humans and other living beings, which can lead to the emergence of new mutant forms of viruses and bacteria, which is specific for certain animal species can mutate and infect the human body. These new forms are the most aggressive and deadly because the human immune system is not prepared to repel such virus attacks and is practically defenseless against a new viral agent. Will pass a sufficiently long period until humanity can develop a collective immunity to a new viral agent, as well as the general efforts of doctors to create effective vaccines against each new infection. It will certainly cost enormous losses in the economy and human potential, but, unfortunately, such is the harsh price of the population for thoughtless waste of natural resources.

Protecting health and combating the most dangerous diseases is one of the global tasks of mankind since it is central to the preservation of life on Earth. Among factors shaping the health of the population, a decisive role is played not

only by a healthy lifestyle, environmental conditions, heredity, and level of health care but and the cultural and spiritual potential of society. The progress of civilization must be coupled with the spiritual improvement of people, with the rejection of the absolutization of material values and consumerism, the revival of harmony between man and nature in the spirit the best achievements of the historical-cultural heritage. In the imbalance of human relationships with nature lies the root cause of all diseases of civilization.

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COVID-19相关肺炎患者OCT血管造影数据分析
**ANALYSIS OF OCT-ANGIOGRAPHY DATA IN PATIENTS WHO
HAVE UNDERGONE COVID-19 ASSOCIATED PNEUMONIA**

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抽象的。本文介绍了我们自己使用 OCT 血管造影术对 COVID-19 相关肺炎患者出院 3 个月后玻璃体视网膜界面的研究结果。由于许多患者在恢复期注意到视力受损,因此有必要排除病毒的促视网膜作用以及血栓栓塞并发症。OCT 血管造影是一种安全且信息丰富的评估血流动力学紊乱的方法。

我们检查了 40 名抱怨视力下降的患者。同时,粘度计和检眼镜各项指标均保持在正常范围内。研究组患者的 OCT 血管造影分析未显示任何眼后段的急性病理。同时,玻璃体视网膜界面的变化与躯体多发病有关。

关键词: OCT-血管造影, 视网膜, COVID-19, 眼科

Abstract. *The article presents the results of our own study of the vitreoretinal interface using OCT-angiography in patients with COVID-19 associated pneumonia 3 months after discharge from the hospital. Since many patients note visual impairment during the period of convalescence, it is necessary to exclude the retinotropic effect of the virus, as well as thromboembolic complications. OCT-angiography is a safe and informative method for assessing hemodynamic disturbances.*

We examined 40 patients with complaints of decreased vision. At the same time, the indicators of visometry and ophthalmoscopy remained within the normal range. Analysis of OCT-angiography in the study group of patients did not reveal any acute pathology of the posterior segment of the eye. At the same time, changes in the vitreoretinal interface are associated with the presence of somatic polymorbidity.

Keywords: *OCT-angiography, retina, COVID-19, ophthalmology*

Relevance

A serious problem for scientific and practical health care is the long recovery period in many patients after COVID-19 associated pneumonia [4,7]. One of the common symptoms that worsen the quality of human life is decreased vision and hemodynamic disorders of the eyeball and its adnexa [5,6].

According to studies, SARS-CoV-2 causes COVID-19 disease by binding to angiotensin-converting enzyme-2 (ACE2). It is known that ACE2 receptors are located in the structures of the eye, in particular, in the conjunctiva, corneal epithelium, as well as in the vitreous body, in the retina [1,2]. Thus, the eye can potentially act as one of the target organs, and be damaged secondarily, as a result of vascular dysfunction, thromboembolic complications, and neurotropicity of the virus [3].

In this regard, it is necessary to control and monitor the organ of vision at various periods of the disease, including during the period of recovery.

OCT-angiography (OCTA) is a modern diagnostic method for non-invasive intravitreal examination of biological tissues.

OCTA provides high-resolution images of the vasculature of the retina and choroid without dye injection. This method is aimed at detecting vascular abnormalities in the layers of the retina, and also allows you to assess hemodynamic disturbances in occlusion of retinal vessels (the presence of ischemic zones, neo-vascularization or shunts).

Purpose of the study

Analyze OCT data, including OCT-angiography, in order to identify the features of the vitreoretinal interface of vascular anomalies in patients who have undergone COVID-19 associated pneumonia 3 months after discharge from the

hospital due to dyslipidemia.

Results of our own research

A survey of 40 patients with COVID-19 associated pneumonia was carried out 3 months after discharge from the hospital. The study included 20 men, median age 38 (18-62) years, 20 women, median age 50 years (20-64). Complaints of decreased vision after suffering from COVID-19 associated pneumonia, the indicators of visometry, tonometry, perimetry are within normal values. Assessment of concomitant pathology in the study group revealed the presence of dyslipidemia in 90% (36/40) patients, arterial hypertension (AH) in 87.5% (35/40) patients; metabolic syndrome and diabetes mellitus with the same frequency of occurrence in 16.7% (10/40) of patients.

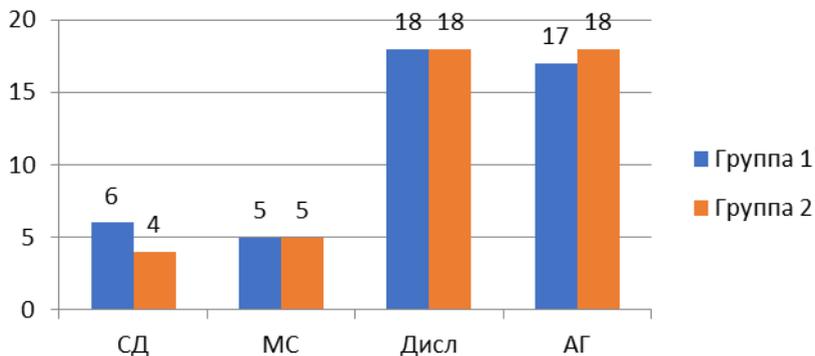


Figure 1. Assessment of comorbidities in the study groups

All underwent optical coherence tomography - angiography (Canon OCT-HS100, Software: RX Capture for OCT-HS100 Version 4.4.1.9).

In 30 patients, incomplete detachment of the posterior vitreous plate was revealed; in 35 - focal fibrosis of the macular region (hyperreflective site of fixation of the posterior hyaloid membrane in the fovea) (overweight, arterial hypertension, dyslipidemia); in 14 patients - corkscrew tortuosity of small venules - symptom of Gvst (with obesity and arterial hypertension); in 4 - wavelike deformation of the pigment epithelium (myopia, metabolic syndrome); in 5 - thinning of the neuroepithelium.

Clinical case

Patient K., born 1967 complained of blurred vision in both eyes, discomfort, feeling of a foreign body that arose 3 months ago during hospital treatment for COVID-19 associated pneumonia. She received antibacterial, antiviral, steroid, antiplatelet therapy, as well as antihypertensive and antihypertensive therapy.

The degree of lung damage was 70%, CT3. Examined by a cardiologist. Primary diagnosis: IHD; Arterial hypertension, stage II, degree 3, risk 4 (very high). Dyslipidemia. Diabetes mellitus type 2. Obesity II. Visus OU=0.6 sph +1.0=0.7.

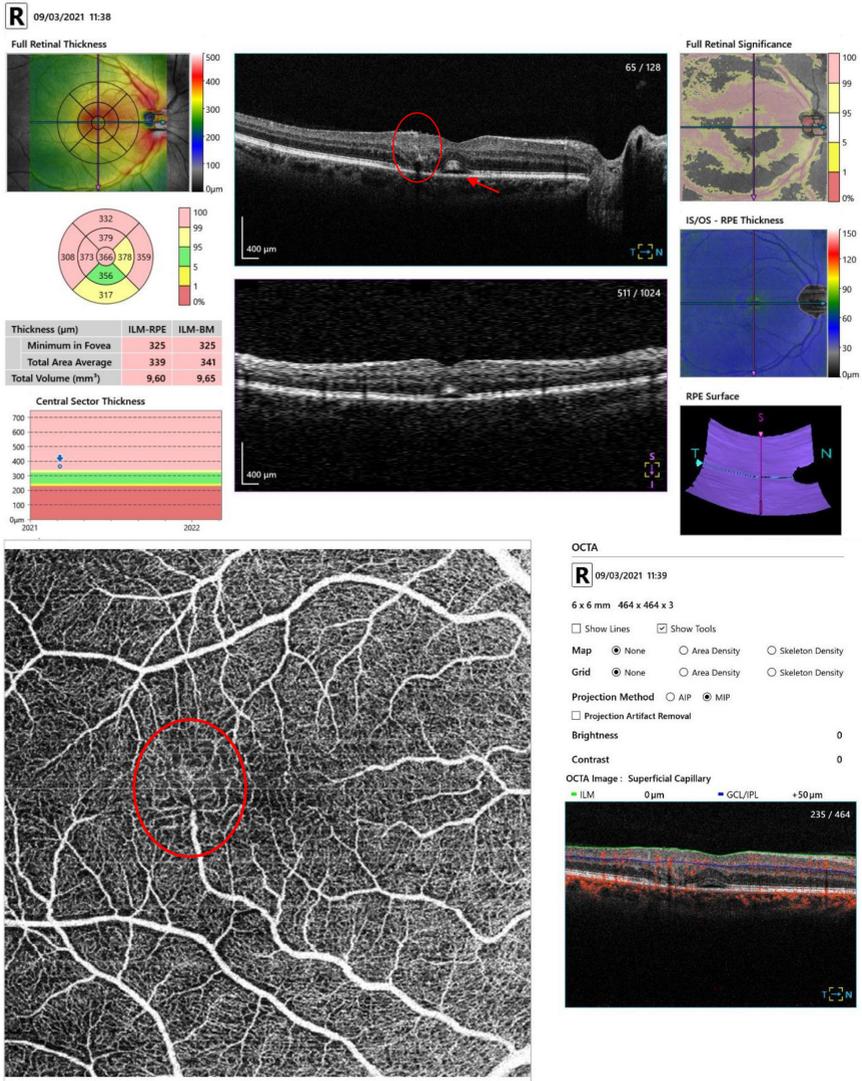


Figure 2. Structural OCT and OCT-angiography of the superficial capillary plexus of the right eye

Pneumotonometry OD/OS=16/13 mmHg. Schirmer's test OD/OS = 7/8 mm in 5 min. Objectively: the anterior segment of the eyes without pathology, phasclerosis. The fundus of the eye: OU-in the foveolar region, the macular reflex is smoothed, focal destruction of the pigment epithelium, neuroepithelium, dyspigmentation, other parts without pathology. According to OCT data: the foveolar contour is moderately deformed, the thickness of the retina is within OD/OS = 366/343 μm , respectively. Subfoveolar focal destruction of the pigment epithelium, slit-like detachment of the neuroepithelium (red arrow), parafoveolar layer of ganglion cells, plexiform layers. According to OCT-angiography: in the deep capillary plexus, pronounced hyperreflectivity and an increase in the caliber of vessels parafoveolar in the temporal sector (red circle). When comparing the maps of the superficial capillary plexus and deep capillary plexus, the formation of a vascular anastomosis is visualized.

Diagnosis: Angioretinopathy (diabetic?), Macular edema in both eyes (given the increase in thickness and the presence of subretinal fluid), Dry eye syndrome of moderate severity in both eyes.

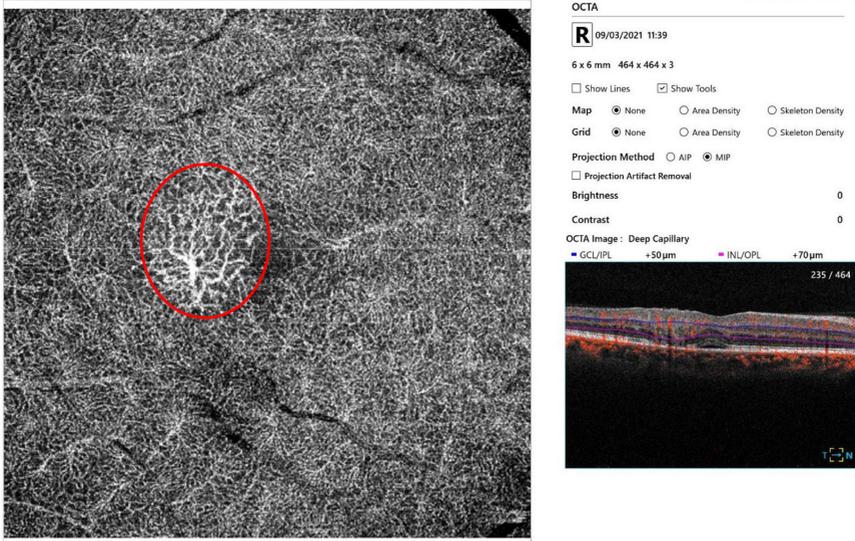


Figure 3. OCT-angiography of the deep capillary plexus of the right eye

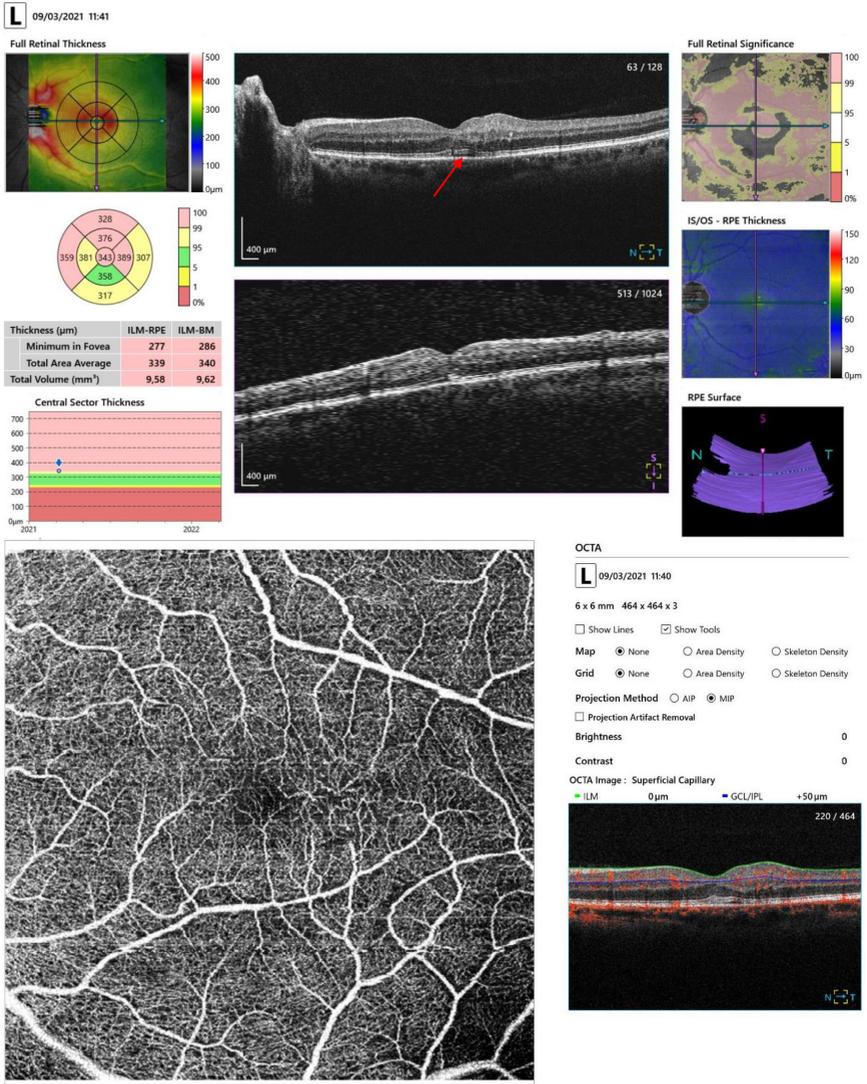


Figure 4. Structural OCT and OCT-angiography of the superficial capillary plexus of the left eye

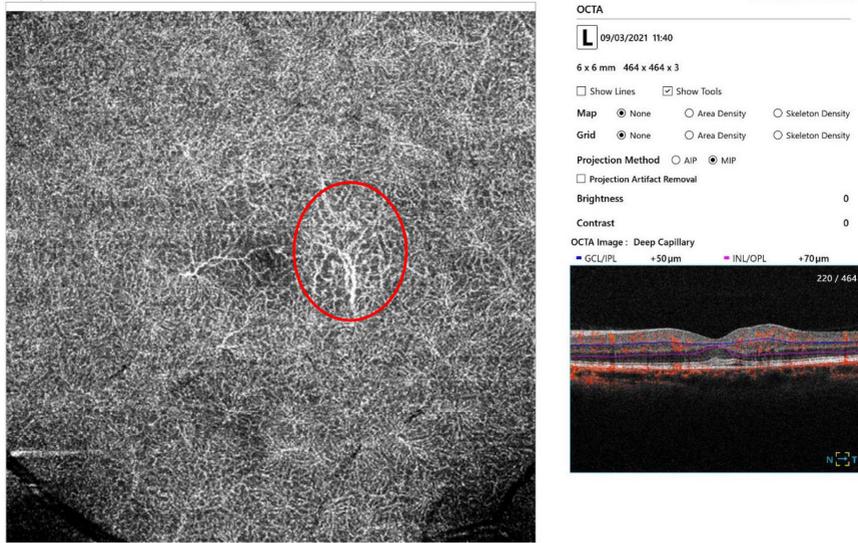


Figure 5. OCT-angiography of the deep capillary plexus of the left eye

Conclusions

Based on the data on possible damage to the posterior segment of the eye against the background of coronavirus infection [4] in patients with dyslipidemia, it is necessary to monitor the state of the retina and perform OCT-angiography during the period of convalescence. It is especially important to control patients with somatic polymorbidity to prevent the development of both acute conditions and exacerbation of chronic processes. To shorten the rehabilitation period in the absence of signs of an acute process, it is necessary to correct underlying diseases, including dry eye syndrome, improve hemodynamics, and prescribe symptomatic metabolic therapy [5].

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中性粒细胞弹性蛋白酶作为干眼症炎症的标志物
**NEUTROPHIL ELASTASE AS A MARKER OF INFLAMMATION
INFLAMMATION IN DRY EYE SYNDROME**

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抽象的。基于对于干眼症 (DES) 患者泪液 (TF) 中中性粒细胞弹性蛋白酶 (NE) 水平的评估, 研究 0.007% 对氨基苯甲酸 (PABA) 溶液对炎症过程的影响. 材料与 方法。对诊断为 DES 的 10 名患者 (20 只眼) 进行了检查。患者以滴眼液的形式接受 0.007% PABA 治疗 1 个月。TF 中 NE 含量采用酶联免疫吸附法测定。对照组 由几乎健康的志愿者组成 - 10 人 (20 只眼睛)。结果。与对照组 (0.22 ± 0.08 ng / ml) 相比, 患者显示出更高的 NE 含量 ($3,85 \pm 0,13$ ng / ml)。治疗开始 1 个月后, 所有患者双眼的这些指标均显著下降: 平均下降 58.7%。结论。PABA 0.007% 具有抗炎作用, 可抑制 DES 患者 TF 中 NF 的产生。

关键词: 干眼症, 中性粒细胞弹性蛋白酶, 对氨基苯甲酸, 炎症

Abstract. *To study the effect of a 0.007% solution of para-aminobenzoic acid (PABA) on the inflammatory process based on the assessment of the level of neutrophil elastase (NE) in the tear fluid (TF) of patients with dry eye syndrome (DES). Material and methods. 10 patients (20 eyes) diagnosed with DES were examined. Patients received 0.007% PABA in the form of eye drops for 1 month. The content of NE in the TF was determined by the method of enzyme-linked immunosorbent assay. The control group consisted of practically healthy volunteers - 10 people (20 eyes). Results. The patients showed a higher content of NE ($3,85 \pm 0,13$ ng / ml) compared to the control group (0.22 ± 0.08 ng / ml). After 1 month after the start of treatment, a significant decrease in these indicators was observed in all patients in both eyes: on average, by 58,7% . Conclusion. PABA 0.007% has an anti-inflammatory effect, suppressing the production of NF in TF in patients with DES.*

Keywords: *dry eye syndrome, neutrophil elastase, para-aminobenzoic acid, inflammation*

Dry eye syndrome (DES) is one of the most common abnormalities of the ante-

rior surface of the eyeball. According to the accepted definition (DEWSII 2017), DES is a multifactorial disease of the ocular surface, characterized by impaired tear film homeostasis and accompanied by ophthalmic symptoms, in the development of which an etiological role is played by impaired stability, hyperosmolarity of the tear film, inflammation and damage to the ocular surface, as well as neuro-sensory changes [1]

To assess inflammation as one of the leading pathogenetic links of DES [2], which develops according to the principle of an “inflammatory vicious circle” [3], various laboratory markers are used: acute phase proteins, cytokines, cell adhesion molecules, proteolytic enzymes, etc.

Neutrophil elastase (NE) is the main serine protease in humans and is found in the azurophilic granules of neutrophils. Released during inflammation as a result of the death or activation of neutrophils, this enzyme can cause serious damage to surrounding tissues. In case of inflammation or injury, when the permeability of the vascular wall is disturbed, the number of leukocytes in the moisture of the anterior chamber and the tear fluid (TF) increases significantly, respectively, the content of elastase also increases many times. In addition, it can be released from the cellular elements of the cornea and conjunctiva [4].

The content of elastase in the TF increases with such eye pathologies as trauma, uveitis, DES, including in patients with diabetes mellitus with DES [5]. With DES, due to insufficient activity of nucleases, extracellular DNA traps (primarily neutrophilic) accumulate in the precorneal tear film, the main component of which, as is known, is elastase. This contributes to the development of inflammation in the conjunctiva and cornea. Another factor contributing to the accumulation of extracellular DNA traps in DES is hyperosmolar stress [6].

The aim of this study is to evaluate the effect of a 0.007% solution of para-aminobenzoic acid (PABA) on the levels of NE in the TF of patients with DES.

Material and methods

The NE levels in the TF were determined in 10 patients (20 eyes) with DES. 0,007% PABA was administered in the form of 1 drop instillations 3 times a day for 30 days. As a control, biochemical studies of the TF of 10 apparently healthy individuals (20 eyes). The reflex tear of each eye was examined. Tears were taken on the 1st day of the examination and the next day after the end of the course of treatment.

Results

In all patients before treatment, a significant increase in the content of NE was recorded in the TF, compared with the control group of apparently healthy volunteers $3,85 \pm 0,13$ ng/ml and $0,22 \pm 0,08$ ng/ml, respectively, $p < 0.001$). By the end of the course of treatment, the patients showed a significant decrease in the content of NE ($2,26 \pm 0,29$ ng / ml, $p < 0.001$) compared with the initial value

On average, after treatment, the content of NE in the TF decreased by 59% ($p < 0.001$) compared to the initial level. This was observed in all patients and in both eyes, the individual variation ranged from 10 to 88% in comparison with the baseline data before treatment. It should be noted that in 40% of cases after treatment, the NE content was comparable to the control level, and in 60% of cases it remained above it.

Conclusion

The study of the local production of cytokines and other humoral factors in various pathologies of the organs of vision expands our understanding of the features of the pathogenesis of these diseases, and also allows the use of pathogenetically oriented therapy.

The results of the present study showed that in patients with DES in the TF, the content of NE increases, which is consistent with the literature data [7,8]. The use of 0.007% PABA solution in the form of eye drops for one month significantly reduces the content of the studied markers of inflammation, which indicates a subsiding of the inflammatory process. However, the indicators normalized only in 40% of cases. Thus, it can be recommended to increase the duration of the course of treatment by 0.007% PABA until all clinical and laboratory parameters are completely normalized.

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组织在紧急情况下提供心理和精神护理 (选项)

**ORGANIZATION OF PROVIDING PSYCHOLOGICAL AND
PSYCHIATRIC CARE IN EMERGENCIES (OPTION)**

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抽象的。目前,每年在世界范围内,不同性质的紧急事件数量都在增加,受影响的人数众多。需要综合分析行政辖区的医疗卫生能力,在组织向受各种性质、大规模突发事件影响的人群提供医疗服务时,要考虑卫生损失的规模和结构的形成。人的伤害。由于各种压力因素的影响,突发事件数量的增加导致社会上患有各种精神障碍的人数不断增加。

组织和提供医疗服务,包括对现阶段紧急情况下的民众提供精神和心理援助,是灾难医疗服务的一项复杂而紧迫的任务。向民众提供心理和精神方面的援助主要涉及实施准备措施,最终应尽量减少紧急情况造成的受害者人数和物质损失。

关键词: HAZMAT (危险材料)、紧急情况、风险区、潜在危险物品、卫生损失、心理和精神援助。

Abstract. *Currently, every year around the world, the number of emergencies of a different nature with a massive number of people affected is increasing. There is a need for a comprehensive analysis of the health care capabilities of administrative territories, taking into account the formation of the magnitude and structure of sanitary losses in organizing the provision of medical care to those affected in large-scale emergencies of various natures with massive injuries of people. The increase in the number of emergencies leads to a constant increase in the number of people in society with various mental disorders due to the impact of various stress factors.*

The organization and provision of medical care, including psychiatric and psychological assistance to the population in emergency situations at the present stage, is a complex and urgent task of the disaster medicine service. The provision of psychological and psychiatric assistance to the population primarily involves the implementation of preparatory measures, which ultimately should minimize the number of victims and material damage from emergencies.

Keywords: *HAZMAT (hazardous materials), emergencies, risk zones, potentially dangerous objects, sanitary losses, psychological and psychiatric assistance.*

To substantiate our option for organizing the provision of medical care in emergency situations, we used the model of medical care in case of possible accidents at the chemical industry facilities of the Republic of Tatarstan.

An analysis was made of the structure of sanitary losses in case of previous industrial accidents with various chemicals and literature data indicate that, on average, 60-75% of the total number of those affected have a mild degree of injury, 10-25% - average, in 4-10% - severe, mortality is 1-5%. However, at present, for individual accidents with various substances under specific conditions, the actual ratio of sanitary losses may differ from the average values.

Despite the fact that for predictive calculations, containers with HAZMAT were taken several times smaller (storage technology) in emergency situations with the participation of chlorine as a damaging factor, sanitary losses are quite large.

The amplitude of the victims with a severe degree of injury can be: Kazan 625; Almetyevsk 783; Bugulma 342; Zelenodolsk 420; Leninogorsk 195; Naberezhnye Chelny 793; Nizhnekamsk 727; Chistopol 430. Irrecoverable losses, respectively, may amount to 313, 392, 171, 210, 97, 396, 363, 215 affected. After providing emergency care and reaching the state of transportability, they need urgent (first of all) evacuation to the stage of qualified and specialized medical care, by ambulance, in a prone position, accompanied by a doctor.

The victims of moderate severity, in their mass, can reach 25% of the total number of victims and amount to the risk zones: Kazan 1562; Almetyevsk 1958; Bugulma 856; Zelenodolsk 1051; Leninogorsk 487; Naberezhnye Chelny 1982; Nizhnekamsk 1816; Chistopol 1075. The peculiarity of this group is that after the provision of emergency medical care, they, like the seriously injured, require immediate evacuation to the stage of qualified medical care, accompanied by medical personnel. [2,3,4]

The number of mild victims can reach 60%. This group of those affected by chlorine may be characterized by a contingent without symptoms of damage. However, the affected person should not fall out of sight of the medical personnel and is sent by any means of transport under the supervision of the clinic.

In this regard, an important problem is not only the organization of medical protection of the population in case of chemical disasters arising from technological accidents, destruction of chemical industry enterprises, or HAZMAT storage facilities, as well as in case of emergency situations in transport transporting HAZMAT, but also the organization of psychological and psychiatric assistance

to the affected population.[2, 3, 4]

Timely and full medical assistance in case of chemical accidents is possible only if the appropriate forces and means are prepared in advance on the basis of a preliminary assessment of the emergency hazard of production facilities, predicting the situation that develops in accidents, and calculating options for sanitary losses. [1]

In these accidents, it is possible to damage the medical institutions located in the risk zone. The surviving on-site medical personnel and treatment-and-prophylactic healthcare institutions in and near the outbreak are usually insufficient for this purpose. The possibilities of ambulance, as the most mobile form of healthcare, in large foci are also limited and quickly dwindling. To strengthen it, treatment and prophylactic institutions are forced to separate from their composition a part of the medical personnel, creating from them mobile highly mobile medical units of varying degrees of readiness to move to the disaster area (emergency medical teams, emergency specialized medical aid teams, medical teams, mobile hospitals, etc.).

The organization of the provision of medical care to the affected can, to a certain extent, be resolved through the use of sanatorium and resort, preventive institutions and health centers for the provision of medical care, treatment and rehabilitation of victims in chemical accidents and disasters, provided that the system is planned in advance and the organizational and functional restructuring of their work in the conditions of emergency situations (ES).

Rationale for the use of sanatorium, preventive institutions and health centers:

First of all - the impossibility of timely and sufficient bed capacity of medical institutions to accommodate the victims.

Secondly - impossibility of release. In real conditions, therapeutic hospitals are filled by 85-95% of seriously ill patients who cannot be discharged for outpatient treatment.

Thirdly - on the territory of risk zones or in the immediate vicinity there are institutions with a sufficient number of beds, equipment and equipment, all conditions for organizing meals, sanitary and hygienic provision, with timely developed planning, reorganization of their work in an emergency situation, as well as strengthening the appropriate forces and means (toxico-therapeutic teams).

Fourthly - some of the hospitals may end up in the HAZMAT contamination zone and be unable to receive the HAZMAT infected.[2,3,4]

We must not forget that in case of emergencies of various natures with a massive number of affected people, it is necessary to organize psychological and psychiatric assistance. An order of the Ministry of Health of the Russian Federation of October 24, 2002 N 325 "On psychological and psychiatric assistance in emergency situations" was issued, which approved the "Regulation on the organization

of psychological and psychiatric assistance to victims in emergency situations."

The provision of psychological and psychiatric assistance to the population primarily involves the implementation of preparatory measures, which ultimately should minimize the number of victims and material damage from emergencies. The number of people who applied for psychological and psychiatric help in ES is determined not by the true need for this type of help, but by the location of the psychiatrist's office. Therefore, it is necessary to carefully consider where the psychiatrist (psychotherapist) should conduct the appointment. We propose to use medical and recreational institutions not only as an additional bed fund for victims in emergency situations, but also for the provision of psychological and psychiatric assistance to those affected.

Approximately 10-15% of those affected require hospital treatment in neuropsychiatric hospitals and at least 50% in outpatient settings. The primary task in these cases is to identify victims with psychomotor agitation, ensure their safety and those around them, eliminate the atmosphere of confusion, and exclude the possibility of massive panic reactions.

Psychiatrists (psychotherapists) should also provide outpatient appointments. As practice shows, the number of people who applied for psychological and psychiatric help with ES is determined not by the true need for this type of assistance, but by the location of the psychiatrist's office. Therefore, it is necessary to carefully consider where the psychiatrist (psychotherapist) should conduct the appointment. In some cases, it is advisable to conduct a reception in the same building (and, if possible, in the same compartment) where the victims are being treated. [4]

The organization and provision of psychiatric and psychological assistance to the population in emergency situations at the present stage is a difficult and urgent task of the disaster medicine service, which requires the involvement of medical specialists to solve it and training in the appropriate skills for providing this type of assistance to the EMERCOM medical staff.[5]

Conclusion

In emergencies of various natures, we can use medical institutions as an additional bed fund to provide specialized assistance to victims. In this case, the issue is being resolved with the possible location of the department of psychological and psychiatric care, an office for psychological and psychiatric care, an advisory mobile team of psychological and psychiatric care. In addition, when carrying out medication measures in the psycho-psychiatric direction, it should be borne in mind that when drugs are administered to the affected HAZMAT (provoking factor), toxic pulmonary edema may develop and it is necessary to provide psychiatric care in the presence of a toxic-therapeutic team.

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通过研究孕妇的同型半胱氨酸水平来预防生殖风险
**PREVENTION OF REPRODUCTIVE RISKS BY STUDYING THE
LEVEL OF HOMOCYSTEINE IN PREGNANT WOMEN**

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抽象的。预防和识别生殖风险的推荐方法之一是监测孕妇血液中的同型半胱氨酸水平，包括有生殖丧失病史的孕妇，然后服用 B 族维生素和含叶酸的药物。

关键词：妊娠，同型半胱氨酸，高同型半胱氨酸血症，生殖风险。

Abstract. *One of the recommended ways to prevent and identify reproductive risks is to monitor the level of homocysteine in the blood of pregnant women, including those with a history of reproductive loss, followed by taking B vitamins and folate-containing drugs.*

Keywords: *pregnancy, homocysteine, hyperhomocysteinemia, reproductive risks.*

Relevance

In recent years, the evolution of the trend of studies of the level of homocysteine (HC) both in cardiological practice and in the field of embryology and obstetrics has been evident [2, 4]. Thanks to the development of clinical and laboratory research, the emergence of modern laboratory equipment and standardized analysis methods, on the one hand, and the interest of doctors of various specialties in hyperhomocysteinemia (HHC), on the other hand, the parameters of HC concentration in the blood as a metabolic factor have been determined. When HC exchange changes, HHC arises. Normally, HC is found in the body in low concentrations, being an intermediate metabolic product of methionine.

The main cause of HHC is a decrease in the activity of enzymes that provide HC metabolism as a result of genetic disorders and/or a decrease in the level of cofactor vitamins (folic acid, B6 and B12). In turn, it may be the result of a nutritional deficiency, the use of certain medications, or the result of a number of diseases. The clinical significance of an increase in HC levels is determined by a number of reasons. HHC occurs at a high frequency in the population, as it can be inherited or acquired. HHC is associated with thrombotic complications, neurologic symptoms, and reproductive disorders. [2]. It has been established that HHC has a negative effect on both the fetus and the course of pregnancy in general. It was found that folate deficiency and, as a consequence, HHC, due to thrombogenic and teratogenic effects, lead to complications of pregnancy and an adverse effect on embryogenesis. Embryonic cells and chorionic tissues in pregnant women, along with hematopoietic and epithelial cells, are highly sensitive to the negative effects of folate deficiency [1]. Among the main negative influences, there is a violation of the proliferation of chorionic villi and the formation of the placenta. In turn, a violation of the formation of the placenta leads to reproductive risks: the risk of termination of pregnancy, the formation of fetal malformations, placental disorders increases, the frequency of preeclampsia and placental abruption increases [1,3]. The formation of homocysteine and the prevention of negative effects caused by its excess are urgent issues and require medical and social justification.

Purpose of the study

To study the effect of HC levels in pregnant women on fetal development in health and disease.

Materials and methods

Was studied scientific work devoted to the study of 47 pregnant women, whose fetuses were observed various types of developmental anomalies [5]. The first group - comparison consisted of 39 women with normal fetal development. The second group - the main one - included 8 women in labor, whose fetuses had developmental abnormalities. The studied groups did not differ in age, gestational age, onset of menstruation and the presence of pathologies in the development of the genital organs. All examined women underwent analysis of blood plasma for the content of total HC by high-performance liquid chromatography with a fluorescence detector. A survey of pregnant women was carried out (questions of nutrition and vitamin therapy). The processing of the obtained statistical data was carried out using nonparametric statistics.

Results and discussion

Normally, the HC content in the blood is 5.46-16.2 $\mu\text{mol/l}$ for men, and 4.44-13.56 $\mu\text{mol/l}$ for women. Most often, HC in the cell is in conjunction with various proteins (up to 75% of the total HC) or is in its oxidized state. The aggregate of all

HC in plasma is called total homocysteine. [2] An increase in the level of HC in the blood - hyperhomocysteinemia corresponds to three stages: moderate (16-30 $\mu\text{mol/l}$), medium (31-100 $\mu\text{mol/l}$) and pronounced (more than 100 $\mu\text{mol/l}$). The causes of HHC are: increased rate of HC formation; decrease in the rate of HC remitting to methionine; the use of antiviral drugs; direct or indirect antagonists of enzymes or vitamins involved in HC metabolism (methionine synthetase and cystathionine β -synthetase are present in the tissues of the embryo already in the early stages of development); violation of transsulfonation processes; using a folic acid antagonist (metatrexate); large intake of methionine with food; mutation of the MTHFR gene; alcohol abuse, smoking, frequent drinking of coffee; renal failure, diabetes mellitus, diseases of the gastrointestinal tract and thyroid gland, leukemia, vitamin deficiency diseases [3,7]. Table 1 presents data on the level of HC in the blood plasma of pregnant women of both groups.

Table 1.

The level of homocysteine ($\mu\text{mol/l}$) in the blood plasma of pregnant women in the main group and the comparison group

Study groups	Number of observations	Homocysteine level ($\mu\text{mol/l}$) Me(25%-75%)
Hydrocephalus	8	48.55*/26.32-80.44
Neural tube defects	2	60.25*/48.55-71.89
Chromosomal pathology	6	71.06*/20.96-109.47
Skeletal dysplasias	5	25.24/15.7-52.17
CHD	6	38.31*/29.54-74.62
Abdominal wall pathology	8	25.36*/16.71-39.68
Other diseases	5	34.62/28.46-61.85
Comparison group	39	22.52/3.285-52.44

Note: * - reliability of differences in indicators in comparison with the data in the control group $P < 0,05$.

In pregnant women with severe fetal malformations (lesions of the central nervous system and heart, chromosomal abnormalities), a significant increase in the level of HC in the blood plasma was noted. In women in labor, whose fetuses had such abnormalities as skeletal dysplasias, abnormalities of the gastrointestinal tract, cystic fibrosis and other diseases, moderate HHC was established. Moderate HHC was also observed in 33% of pregnant women in the comparison group, which is most likely the result of women's misinformation and a probable lack of pregravid preparation. The study and analysis of questionnaires showed that women took folic acid on the eve of the planned pregnancy and in the first two

weeks only in 10% of cases. From 7-8 weeks of pregnancy, 39.4% of women took folic acid, which is not correct, because the laying of the neural tube and 4-chambered heart occurs at 4 weeks and lasts up to 8 weeks from the moment of conception, therefore, the appointment of folic acid loses its beneficial effect. There were also such patients who took folic acid for up to 12 weeks (54.1%), and some learned about the need to take folic acid after diagnosing malformations in their child. These indicators indicate that a change in the approach to informing pregnant women about the forthcoming pregnancy is required. This will help prevent the development of many anomalies in unborn babies and prevent their early mortality. It was found that none of the patients from the main group had known genetic risk factors, and the average age of the studied women was 25-28 years. Congenital anomalies in fetuses have been identified as a result of numerous ultrasound examinations, as well as with invasive diagnostic methods (with chromosomal abnormalities, in particular).

Currently, the relationship of HHC with the occurrence of fetal malformations is being studied in great detail. The main action of HC is associated with damage to the walls of blood vessels, their loosening. Cholesterol and calcium are deposited on the damaged wall, which form an atherosclerotic plaque, which inhibits the work of the blood anticoagulant system. This leads to the development and formation of blood clots, in particular, the formation of microthrombi leads to disruption of the uterine and placental circulation, which is one of the causes of infertility and miscarriage [4,8]. In addition, a lack of folic acid disrupts the process of HC remitting and leads to an increase in its level in blood plasma, which, according to a number of authors and in scientific studies, is the cause of neural tube defects and congenital heart anomalies in the fetus.

It is also known that HC and its derivatives disrupt the processes of apoptosis - planned cell death, which is the main mechanism for the formation of organs in the fetus, regulate the passage of calcium ions through membranes, suppressing the synthesis of antioxidant enzymes [5,6].

Conclusion

1. The data we studied confirm the important role of HC in the development of pathologies of the central nervous system and heart in the fetus. A significant increase in homocysteine levels is observed in chromosomal abnormalities (for example, in Down's syndrome), the possible cause of which may lie in a violation of DNA methylation, suppression of the activity of DNA methyltransferases and, as a consequence, modification of certain DNA regions. It is this mechanism that is key in explaining the influence of HC on the processes of occurrence of malformations. This allows us to classify HHC as a genetic risk factor for developing diseases.

2. Determination of the HC level should be a prerequisite for diagnosing a woman both before and in the first weeks of pregnancy.
3. Detection of a high HC level before pregnancy and in the first 2 weeks and timely preventive measures (taking B vitamins and folate-containing drugs) to lower its level in the blood plasma of women can play a very significant role in the prevention of reproductive risks.

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心血管系统病理学背景下代谢物对慢性卡他性牙龈炎综合治疗的影响
**THE INFLUENCE OF METABOLITES IN THE COMPLEX
THERAPY OF CHRONIC CATARRHAL GINGIVITIS AGAINST THE
BACKGROUND OF PATHOLOGY OF THE CARDIOVASCULAR
SYSTEM**

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抽象的。流行病学研究结果证实了口腔健康状况与心血管病理学发展之间存在关系。关于牙科治疗对心血管治疗结果影响的数据很少。研究表明，牙周病与内脏器官疾病之间存在显著的临床和发病关系。一个或几个在形态和功能上相互关联的身体系统活动的变化不可避免地影响口腔组织的形态功能状态的变化。血管疾病与慢性卡他性牙龈炎之间关系的核心是巨噬细胞的过度活跃表型，当与脂多糖接触时会导致抗炎细胞因子和炎症介质（IL-1-β、TNF-α、PGE 2）过度释放革兰氏阴性菌。同时，这些患者的牙周组织代谢发生了显著变化。

关键词：治疗，广泛性牙龈炎，代谢。

Abstract. *The existence of relationships between the state of oral health and the development of cardiovascular pathology has been confirmed by the results of epidemiological studies. There are few data on the effect of dental treatment on the outcome of cardiovascular therapy. Studies have shown significant clinical and pathogenetic relationships between periodontal disease and disease of internal organs. Changes in the activity of one or several morphologically and functionally interrelated body systems inevitably affect the change in the morphofunctional state of the tissues of the oral cavity. At the heart of the relationship between vascular diseases and chronic catarrhal gingivitis is the hyperactive phenotype of macrophages, which causes excessive release of anti-inflammatory cytokines and inflammatory mediators (IL-1-β, TNF-α, PGE 2) upon contact with lipopolysaccharides of Gram-negative bacteria. At the same time, significant changes in metabolism in the periodontal tissues were found in these patients.*

Keywords: *treatment, generalized gingivitis, metabolism.*

Introduction

The relevant objective of practical periodontology is to find ways of early detection and increase the effectiveness of the available treatment of inflammatory diseases of the tissues surrounding the tooth. Despite the growing interest of researchers, many issues remain controversial, in particular, the etiology, triggers, and pathogenesis of diseases.

Homeostasis of the oral cavity is largely determined by the structural-functional state of tissues and microorganisms of the oral cavity. Fundamental and applied research of the last decade in the field of dentistry has enhanced the understanding of the biochemical aspects of dental hard tissues, saliva, gingival fluid, metabolic characteristics of microorganisms and xenobiotics in health and disease [1].

Numerous factors, both local and general, contribute to the spread of periodontal disease [2]. An important argument affecting the severity of the course of chronic catarrhal gingivitis is the presence of somatic pathology, in particular, the patient's anamnesis of atherosclerosis and coronary heart disease. The relationship between somatic diseases and the state of the oral cavity organs is associated with metabolic disorders, hemodynamics, immunological and neuroregulatory disorders and shifts in microbiocenosis.

It is known that the inflammatory process in the human body is a nonspecific reaction. The monocytes adhesion to activated cells of the tunica intima should be considered as an early stage of inflammation characteristic of atherosclerosis, due to the overexpression of adhesion molecules of vascular cells on their surface. Endothelial adhesion molecules, specifically and firmly binding to blood monocytes and lymphocytes, are the basis for the subsequent differentiated migration of these cells under the influence of specific factors (MCP-1, tumor necrosis factor - $TNF-\alpha$) into the subendothelial space of coronary vessels [3]. In the initiation of the atherosclerosis process, the interaction of CD40 molecules with their ligand on platelets is of great importance, which leads to inflammatory activation of endothelial cells. It enhances the coagulating ability of blood [4] through an increase in the expression of tissue factor. As you know, the CD40 molecule is expressed not only on B-lymphocytes, but also on endothelial cells, macrophages, and its ligand CD154 (CD40L) on activated T cells, mast cells and basophils. Activation of CD40 and CD40L stimulates the expression by leukocytes of adhesion molecules, chemokines, cytokines involved in the process of atherogenesis, as well as the expression and release of matrix metalloproteinases [5]. The specific interaction of CD40 and CD40L was revealed in almost all cells, in all types of atherosclerotic lesions.

The complexity of the pathogenesis of claudication in general, as well as in

catarrhal gingivitis, requires further comprehensive study. It was found that in chronic gingivitis, the basal layer of epithelial cells proliferates unevenly in the form of finger-like outgrowths into the underlying connective tissue. The superficial layers of the epithelium undergo degenerative changes. In the presence of an active local reaction to irritation, the layers of the epithelium are thickening, sometimes by 4-5 times. Acanthosis is often observed. Polymorphonuclear leukocytes accumulate under the surface layers of the epithelium. There is a loosening of the vascular walls through which erythrocytes found in tissues pass. Erythrocytes die and form hemosiderin pigment. The cellular infiltration is observed in connective tissue, as a result of irritation. The tissue around the vessels is filled with extensive locules of granulocytes and lymphocytic elements, pushing the bundles of connective tissue fibers in different directions [6]. Circular collagen fibers of the gums are the most resistant to inflammation. They largely limit the spread of the inflammatory process deep into the tissues.

An urgent direction is the search for new, objective, fairly simple and affordable methods of treating periodontal diseases against the background of pathology of the cardiovascular system.

Levocarnitine is a co-factor of metabolic processes that maintain CoA activity. It has an anabolic effect, reduces basal metabolism, slows down the breakdown of protein and carbohydrate molecules. It also promotes the penetration of mitochondrial membranes and the breakdown of long-chain fatty acids with the formation of acetyl-CoA (it is necessary to ensure the activity of pyruvate carboxylase in the process of gluconeogenesis, the formation of ketone bodies, the synthesis of choline and its esters, oxidative phosphorylation and the formation of ATP). It has a fat-mobilizing effect due to the presence of three labile methyl groups. It includes a fatty acid metabolic shunt, the activity of which is not limited by oxygen (unlike aerobic glycolysis) competitively displacing glucose, therefore it is effective in acute tissue hypoxia.

Aims and objectives of the study: to determine the effectiveness of the therapeutic use of levocarnitine in patients with chronic catarrhal gingivitis against the background of pathology of the cardiovascular system according to the data of immediate and long-term results. To assess the state of local blood circulation and microcirculation in the area of the pathological process of the gums in patients with chronic catarrhal gingivitis under the influence of this drug.

Materials and research methods

To achieve this goal and solve the problems of the study, we examined 68 patients with chronic catarrhal gingivitis against the background of pathology of the cardiovascular system at the age from 46 to 62 years old, who did not have mineralized dental deposits.

All patients, depending on the method of treatment used, were divided into

2 groups comparable in terms of clinical and functional characteristics: the main group - 34 patients who were treated with levocarnitine (in the form of application of the drug solution) and the control group - 34 patients who received standard treatment using antiseptic drugs.

In addition to general clinical examination and calculation of generally accepted periodontal indices, all patients used special research methods to assess the microcirculatory process in the gum area. So, to objectify the symptom of gingival bleeding, the Muhlemann index was used. Local thermometry was used to assess the state of local blood flow, which was carried out in two anatomical and physiological zones (incisors and molars) on both jaws using a portable non-inertial TPM thermometer. For assessing the microvasculature in the area of the pathological process, the method of Laser Doppler flowmetry was used (apparatus LAKK-01, "Lazma" SPA, Russia), with the help of which the main indicators of capillary blood flow were determined. They are the level of capillary blood flow (M) in nominal units; vasomotor activity of microvessels (Kv) in % and intensity of microcirculation (?) in nominal units. The studies were carried out before and after the course of treatment.

Results

The values of the Muhlemann index before the start of treatment in both groups significantly differed from the norm, exceeding its value by 5 times (2.7 ± 0.11 - $p < 0.001$). They also indicated increased bleeding of the gums in the area of the pathological process, which also confirms the presence of a mild inflammatory process in the studied area.

When studying the results of local thermometry before the start of treatment, thermal asymmetry was revealed in both groups due to an increase in temperature in the area of gingival inflammation. In the overwhelming majority of patients (94.6%), there was an increase in the local temperature in the area of the incisors by 1.8°C compared to the norm during examination in the area of inflammation, and in the area of the molars by 2.2°C compared to the norm. This indicates not only about the presence of an inflammatory process in the studied area of the gums, but also about the violation of local blood circulation due to the presence of venous stasis, which is clinically reflected as edema and hyperemia in the area of the pathological process in the gums.

There was a significant decrease in the level of capillary blood flow (M) by 1.5 times against the background of a similar decrease in vasomotor activity of microvessels by 1.4 times when examining using laser Doppler flowmetry in the observed patients of both groups before the start of treatment. That indicates a significant disorder as in arteriolar, and in the venular links of microcirculation and indirectly indicates a drop in the level of perfusion in the tissues of the studied gingival region. All this was accompanied by a 1.67 times decrease in the intensity

of microcirculation, and, consequently, the overall efficiency of microcirculatory processes.

After 5 procedures of using levocarnitine applications in the overwhelming majority of observed patients with chronic catarrhal gingivitis, on average, in 89% of cases, signs of local inflammation of the gums were not determined. Only in a few patients edema and hyperemia of the gingival mucosa persisted, bleeding and soreness, which presented themselves in much less degree than the original state.

In patients of the control group, after 5 standard therapy procedures, on average, in 42%-46% of cases, objective presentations of chronic catarrhal gingivitis were still determined, although their severity was also less significant in the main group than in the outcome.

After the course of treatment, the outlined differences in the regression of the main symptoms in patients of the main and control groups were significantly leveled. This was expressed in the fact that in the main group, almost all signs of local inflammation were stopped, while in the control group, some signs remained in another 6-10% of cases.

The clinical results obtained in the patients of the main group remained for 1 year. None of the patients had complaints corresponding to chronic catarrhal gingivitis, and there were also no signs of a disease recurrence during an objective dental examination.

In the control group, after 3 months, 18%-38% of the observed patients had complaints, mainly pain and bleeding when eating solid food and brushing their teeth, as well as fetor ex ore.

The above-mentioned phenomena increased in the patients of the control group and were determined already in 35%-60% of cases in 6 months, in connection with which the patients were provided with symptomatic treatment.

Under the influence of the use of levocarnitine, the values of the Muhllemann index did not differ from the norm, not only after the course, but also during the entire observation period, which indicates a pronounced metabolic effect of this therapy.

In the control group, the values of this index after the course of treatment exceeded the norm by 16% and after 3, 6 and 12 months by 22%, 28% and 32%, respectively.

When studying the local temperature in the process of using parmidin therapy, there was complete normalization in the studied areas (incisors and molars) after 5 procedures, which persisted during the observation period (after the course, as well as in the long-term period - after 3, 6 and 12 months after treatment). It indicates effective relief of local inflammation in the studied area of the gums, as well as indirectly indicate the restoration of violated local blood circulation in the observed patients.

In the patients of the control group, although there was a significant decrease in the local temperature values in the studied areas. They did not reach the normal values and had an upward trend in 3 months, reaching the initial values by 12 months.

The study of the effect of levocarnitine on the state of microcirculation in the area of the inflammatory process of the gums in patients with chronic catarrhal gingivitis against the background of pathology of the cardiovascular system revealed a pronounced vasoprotective and antihypoxic effect. It presented in an increase in the level of capillary blood flow and the intensity of microcirculation to the values of the physiological norm (level of capillary blood flow) (increased to 20.5 ± 1.6 $p < 0.001$, vasomotor activity of microvessels (Kv) increased to 19.0 ± 1.3 $p < 0.001$, the intensity of microcirculation increased to 5.1 ± 0.2 $p < 0.001$).

In the control group, no significant dynamics of microcirculation indices was observed (the level of capillary blood flow (M) reached values of 12.1 ± 1.3 $p < 0.001$, vasomotor activity of microvessels (Kv) 13.2 ± 1.4 $p < 0.001$, the intensity of microcirculation was $3, 5 \pm 0.2$ $p < 0.001$).

Discussion and conclusion

Comparative evaluation of the results of studying the gingival Muhlemann index in patients with chronic catarrhal gingivitis against the background of pathology of the cardiovascular system under the influence of metabolic and standard therapy confirmed the higher result of the proposed therapy. When evaluating the indicators, the results objectively confirmed the high anti-inflammatory effect of therapy with levocarnitine, which was observed when assessing the clinical presentations of local inflammation in the studied patients.

The results of the study of local thermometry indicators in the observed patients confirmed the relief of local inflammation in the studied areas of the gums under the influence of levocarnitine, which is not observed in the control group.

The combined comparative evaluation of the regression of clinical symptoms and the dynamics of the results of special research methods made it possible to establish the high efficiency of the proposed method of treatment in comparison with the control based on the data of direct results.

Thus, metabolic therapy is a highly effective and pathogenetically justified treatment method for chronic catarrhal gingivitis.

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钙通道阻滞剂——药物治疗高血压的一线药物

**CALCIUM CHANNEL BLOCKERS - FIRST LINE DRUGS FOR THE
MEDICINAL TREATMENT OF ARTERIAL HYPERTENSION**

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抽象的。用于高血压药物治疗的钙通道阻滞剂在 2004 年、2015-2016 年的俄罗斯联邦药物使用联邦指南中得到广泛介绍。2004、2015-2016 年处方体系中钙拮抗剂清单的比较特征表明，这些版本每年都会发生变化。发现钙通道阻滞剂在 2004 年和 2015-2016 年的处方系统中有 10 个商品名，有 20 个商品名。钙通道阻滞剂研究药物清单的确定特征反映了临床实践中在高血压药物治疗中引入药物的方法的动态实施，这确保了医疗质量和患者满意度的提高。

关键词：钙通道阻滞剂，高血压药物治疗，联邦指南。

Abstract. *Calcium channel blockers used for the medicinal treatment of hypertension are widely presented in the Federal Guidelines for the Use of Medicines of the Russian Federation for 2004, 2015–2016. Comparative characteristics of the list of calcium antagonists included in the 2004, 2015–2016 formulary system showed that changes are made to these editions every year. It was found that calcium channel blockers are presented under ten trade names in 2004 in the formulary system and in 2015–2016 - under twenty trade names. The identified features of the list of studied drugs for calcium channel blockers reflect the dynamic implementation in clinical practice of approaches to the introduction of drugs in the medicinal treatment of hypertension, which ensures an increase in the quality of medical care and patient satisfaction.*

Keywords: *calcium channel blockers, medicinal treatment of hypertension, Federal guidelines.*

Every year on May 17, at the initiative of the International Society of Hypertension and the World Hypertension League, World Hypertension Day is officially celebrated.

Currently, the term "arterial hypertension" (AH) means a syndrome of in-

creased blood pressure (BP) in case of hypertension and symptomatic AH. It should be noted that there is practically no semantic difference in terms of "hypertony" and "hypertension". As follows from the etymology, hyper is from the Greek "over, extra" - a prefix indicating an excess of the norm; tensio - from lat. "voltage"; tonos - from the Greek "voltage". Thus, the terms "hypertony" and "hypertension", in fact, mean the same thing: "overvoltage" [1, p. 16].

Hypertension (synonyms - essential arterial hypertension, primary arterial hypertension) is a disease of the cardiovascular system that develops because of primary dysfunction of the higher vasoregulative centers and the subsequent activation of neurohormonal (hypothalamic) and renal mechanisms. In this case, an increase in blood pressure is not due to the body's natural reactions to one or another physiological situation, but is a consequence of an imbalance in the systems that regulate blood pressure.

In the modern world, the AH prevalence is 30–45% among the adult population [3, p. 6–9]. According to international publications, the total number of people with hypertension in the world in 2000 was 972 million. (303 million in developed and 669 million in developing countries), or 26.6% of men and 26.1% of women. It is predicted that the number of patients with this disease will be 1.6 billion by 2025 [4, p. 217-223].

The insidiousness of the disease is that it can proceed unnoticed by the patient himself. Various symptoms indicated the arterial hypertension above 130/90 Mmhg: a person is suffered from headaches, irritability, dizziness, his/her memory is impaired, his/her working capacity decreases. However, in the initial stages of the disease, these symptoms may disappear after rest, and the patient does not consult a doctor for years. Over time, hypertension progresses, symptoms become permanent and are accompanied by damage to target organs in the later stages: kidneys, heart, central nervous system [2, p. 33].

There are two indicators of blood pressure: systolic blood pressure (SBP), also called "upper" - reflects the pressure in the arteries, which is created by the contraction of the heart and the release of blood into the arterial part of the vascular system. There is also a diastolic blood pressure (DBP), also called "lower" - reflects the pressure in the arteries at the time of relaxation of the heart, during which it is filled before the next contraction.

Most often, hypertension is diagnosed out of time, respectively, and the treatment of the disease occurs at later stages. Therefore, timely diagnosis, prevention and treatment of hypertension are the most important task of health care, since they can significantly prevent the most serious consequences - heart failure, myocardial infarction, pulmonary edema, cerebral edema associated with a high risk of death, annually claiming about 18 million lives [7, p.30-33].

Treatment of hypertension must necessarily be comprehensive, individually

selected and aimed at normalizing blood pressure and constantly maintaining it at an optimal level [5, p.261-263]. For this, several main classes of drugs are used: diuretics, β -adrenoceptor blocking agent (BAB), angiotensin-converting enzyme inhibitors (ACE inhibitors), calcium antagonists (AC) [8, pp. 254–284].

At the same time, there is no doubt that, based on the safety profile and proven efficacy, the drugs of choice for hypertension are calcium antagonists - a group of drugs whose main property is the ability to reversibly inhibit calcium flow through the so-called slow calcium channels [8, pp. 254–284].

Calcium channel blockers (calcium antagonists) drugs of this group inhibit the penetration of calcium ions into the muscle cells of the heart and blood vessels through slow L-type calcium channels. They dilate the coronary arteries and peripheral arteries and arterioles and have a pronounced vasodilator effect by reducing the concentration of Ca^{2+} ions in cardiomyocytes and vascular smooth muscle cells [6, p.36-39].

The aim of the work is to carry out a comparative characterization of calcium channel antagonists used in the medicinal treatment of hypertension and included in the Federal Guidelines for the Use of Medicines of the Russian Federation for 2004, 2015–2016.

Materials and methods

Comparative characteristics of the list of calcium channel blockers included in the Federal Guidelines for the Use of Medicines of the Russian Federation for 2004, 2015–2016 were performed.

Results and its discussion

An assessment of the list of calcium channel antagonists for the pharmacotherapy of arterial hypertension showed (Table 1, 2) that in the 2004 Federal Guidelines, calcium channel blockers are presented under the following trade names: finoptin (40 and 80 mg-coated tablets, manufactured by Finland), isoptin (solution for internal administration 5 mg/2 ml, manufacturer - Germany). There are also isoptin (40 and 80 mg-coated tablets, manufacturer - Germany), cardilopin (tablets at 2.5; 5 and 10 mg, manufacturer - Hungary), amlodipine (5 and 10 mg tablets, manufacturer - India), cordafen (10 mg coated tablets, manufacturer - Poland). In addition, the list includes fenigidin (10 mg tablets, manufacturer - Russia), osmo-adalat (30 and 60 mg-controlled release coated tablets, manufacturer - Germany), cardil (60 mg film-coated tablets, manufacturer - Finland), diltiazem lannacher (sustained-action film-coated tablets 90 and 180 mg, manufacturer - Australia), diazem (60 mg film-coated tablets, manufacturer - Cyprus). Ten trade names and eight manufacturing countries are presented in the list of calcium channel blockers included in the Federal Guidelines for the Use of Medicines for 2004.

In the course of this study, it was shown that the formulary for 2015–2016 includes: verapamil-ratiopharm (coated tablets 40; 80 and 120 mg, manufacturer

- Germany), verohalide ER240 (sustained-action tablets, 240 mg, manufacturer - Czech Republic), vero-amlodipine (tablets at 5 and 10 mg, manufacturer - Russia), Norvasc (tablets at 5 and 10 mg, manufacturer - Belgium), normodipine (tablets at 5 and 10 mg, manufacturer - Hungary). There are also veronifedipine (coated tablets 10 mg, manufacturer - Russia), nifedicap (10 mg capsules, manufacturer - Russia), cordaflex (coated tablets 10 mg, manufacturer - Hungary), cordinfar UNO (sustained-action tablets, film-coated 40 mg, manufacturer - Germany), cordipin (10 mg film-coated tablets, manufacturer - Slovenia). It includes thiakem (60 mg tablets, manufacturer - France), lomir (2.5 mg tablets, manufacturer - Italy), lacidil (coated tablets at 244 mg, manufacturer - Spain), nimotop (solution for infusion (bottle) 10 mg, manufacturer - Germany), plendil (sustained-action film-coated tablets at 2.5; 5 and 10 mg, manufacturer - Sweden), auronal (coated tablets 2.5 mg, manufacturer - Hungary). Excluded from the list: isoptin (solution for internal administration 5 mg/2 ml, manufacturer - Germany), amlodipine (tablets at 5 and 10 mg, manufacturer - India), cordafen (coated tablets 10 mg, manufacturer - Poland), phenigidin (tablets 10 mg, manufacturer - Russia), osmo-adalat (controlled release film-coated tablets, 30 and 60 mg, manufacturer - Germany), diltiazem lannacher (sustained-action film-coated tablets, 90 and 180 mg, manufacturer - Australia). In the list of calcium channel blockers, based on the recommendations of the Federal Guidelines for the Use of Medicines for 2015-2016, the list of trade names has been expanded, drugs in new dosages have been added, and the list of manufacturing countries has increased to 10.

Table 1.

List of calcium channel blockers included in the Federal Drug Guidelines, 2004

Actual substance	Trade name	Presentation and dosage	Manufacturing countries
Verapamil	Finoptin	Film-coated tablets 40 and 80 mg	Finland
	Isoptin	Solution for internal administration 5 mg/2 ml	Germany
		Film-coated tablets 40 and 80 mg	Germany
Amlodipine	Cardilopin	Tablets at 2.5; 5 and 10 mg	Hungary
	Amlodipine	5 and 10 mg-tablets	India
Nifedipine	Kordafen	10 mg-film-coated tablets	Poland
	Phenigidin	10 mg-tablets	Russia
	Osmo-Adalat	Controlled-release coated tablets 30 and 60 mg	Germany

Diltiazem	Cardil	60 mg film-coated tablets	Finland
	Diltiazem	Sustained-action film-coated tablets 90 and 180 mg	Australia
	Lannacher	60 mg-coated tablets	Cyprus

Table 2.

Comparative characteristics of calcium channel blockers based on the recommendations of the Federal guidelines for the use of medicines for 2015-2016

Actual substance	Trade name	Presentation and dosage	Manufacturing countries
Verapamil	Finoptin	Film-coated tablets 40 and 80 mg	Finland
	Verapamil-ratiopharm	Film-coated tablets 40; 80 and 120 mg	Germany
	Verogalide ER240	Sustained-action tablets, 240 mg	Czech
Amlodipine	Vero-amlodipine	5 and 10 mg-tablets	Russia
	Norvask	5 and 10 mg-tablets	Belgium
	Normodipin	5 and 10 mg-tablets	Hungary
	Cardilopin	Tablets at 2.5; 5 and 10 mg	Hungary
Nifedipine	Vero-nifedipine	10 mg film-coated tablets	Russia
	Nifedicap	Capsules 10 mg	Russia
	Cordaflex	Coated tablets 10 mg	Hungary
	Cordinfar UNO	Sustained-action film-coated tablets 40 mg	Germany
	Cordipin	Film-coated tablets 10 mg	Slovenia
Diltiazem	Tiakem	60 mg-tablets	France
	Diazem	60 mg-tablets	Cyprus
	Cardil	60 mg-coated tablets	Finland
Isradipin	Lomir	2.5 mg-tablets	Italy
Lacidipine	Lacidil	244 mg-coated tablets	Spain
Nimodipine	Nimotope	30 mg-coated tablets	Germany
		Solution for infusion (bottle)	
Felodipine	Plendil	10 mg	Sweden
	Auronal	Sustained-action film-coated tablets 2.5; 5 and 10 mg	Hungary

The availability of calcium channel blockers under INN in the Federal Guidelines simplifies the process of focusing for pharmaceutical and medical professionals, drug supply specialists, and consumers and provides the right to choose the manufacturing country.

Conclusion. Thus, the performed comparative characteristics of calcium channel blockers included in the Federal Guidelines for the Use of Medicines of the Russian Federation for 2004, 2015–2016 for the medicinal treatment of hypertension revealed that additions and changes are made to the list of drugs annually. The analyzed formulary notes the inclusion of new trade names of drugs of domestic and foreign production, an increase in the number of countries producing drugs from the group of calcium antagonists. In the 2004 Federal Guidelines for the Use of Medicines, ten trade names of calcium channel blockers from eight manufacturing countries are presented. In 2015–2016 twenty trade names and ten manufacturing countries of these drugs, and the dosage range has also been expanded.

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小麦粉特性对饼干品质的影响
**INFLUENCE OF WHEAT FLOUR PROPERTIES ON BISCUIT
QUALITY**

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抽象的。该研究的目的是研究不同研磨级别的最高等级小麦粉的特性对饼干质量的影响,以减少次品并确保产品始终如一的高品质。已经确定了面粉厂根据我们的建议生产的优质小麦烘焙面粉和优质饼干小麦粉的颗粒的粒度组成、个体物理化学和流变学特性。结果发现,对于颗粒含量小于80微米的烘焙面粉,约占颗粒总数的71%,淀粉破坏程度为28.3%,因此面粉的WAQ降低到55设备的单位。饼干粉的特点是粒度组成较大,因此粒径在 160 微米到 100 微米之间的颗粒占颗粒总质量的 60%,而小于 80 微米的颗粒仅占 20%。同时,饼干粉中淀粉的破坏程度是该装置的 15.8 单位,并注意到的相当高的 WAQ - 60 单位的装置。比较的是使用面包店和饼干粉制作的饼干。在几乎相同的产品水分含量 $\approx 25\%$ 的情况下,与由烘焙面粉制成的饼干相比,由饼干粉制成的饼干具有更发达的孔隙率和更高的比容。使用具有适合生产饼干的优化粒度组成的面粉,可以在不使用化学改良剂的情况下以最少的废料获得高质量的成品。

关键词: 饼干半成品, 产品质量, 优质小麦粉, 粒度组成, 淀粉破坏程度。

Abstract. *The aim of the research was to study the influence of the properties of wheat flour of the highest grade of different grinding on the quality of the biscuit, in order to reduce rejects and ensure a consistently high quality of products. The granulometric composition of particles, individual physicochemical and rheological properties of high-quality wheat bakery flour and high-quality biscuit wheat flour, produced by a flour mill according to our recommendations, have been determined. It was found that for bakery flour, with a particle content of less than 80 microns, about 71% of the total number of particles, the degree of starch*

destruction is 28.3% and, as a result, the WAQ of flour is reduced to 55 units of the device. Biscuit flour is distinguished by a larger granulometric composition, so particles ranging in size from 160 microns to 100 microns make up 60% of the total mass of particles, and particles less than 80 microns make up only 20%. At the same time, the degree of destruction of starch in biscuit flour is 15.8 units of the device and a rather high WAQ is noted - 60 units of the device. Compared were biscuits made using bakery and biscuit flour. With practically the same moisture content of the products $\approx 25\%$, a biscuit made from biscuit flour has a more developed porosity and an increased specific volume in comparison with a biscuit made from bakery flour. The use of flour with an optimized granulometric composition adapted for the production of biscuit will make it possible to obtain high-quality finished products with a minimum amount of scrap, without the use of chemical improvers.

Keywords: *biscuit semi-finished product, product quality, premium wheat flour, granulometric composition, degree of starch destruction.*

In Russia, flour confectionery products (FCP) is traditionally in great demand among the population [1]. Wheat flour, mainly of the highest grade, is used as the main recipe component in FCP.

Until now, manufacturers of sweet products use the main raw materials produced taking into account the requirements of the baking industry (GOST 26574-85. Wheat baking flour), which is practically not adapted to the needs of a wide range of FCP, which leads to a decrease in quality stability, loss of marketable products, increase in rejects and necessitates the use of various, including chemical, improvers.

As you know, FCPs are distinguished by a wide variety of rheological properties and quality characteristics, which dictates the need to develop requirements for the main raw materials for each specific product. Such requirements should contain a set of ratios of individual, largely interdependent, indicators of flour quality, reasonably allowing to achieve high quality products. It is possible to form such a set by studying the influence of a certain indicator of flour on biscuits.

Biscuits – one of the most popular types of baked goods in the world. Biscuit-based products occupy a special place in the huge assortment of FCP [2], these are cakes, pastries, rolls, etc.

The purpose of our research was to study the influence of the properties of the highest grade wheat flour on the quality of the biscuit, in order to reduce rejects and ensure a consistently high quality of products.

It is known that wheat flour is a crushed grain of wheat with a complex composition containing starch and a protein-proteinase complex that forms gluten, which determines its unique properties.

The most important parameter of the quality of flour is its water absorption qualities (WAQ), regardless of the type of products, which affect the entire technological process [3].

Water absorption during kneading and molding of dough is largely influenced by the state of proteins and their physical connection with starch. If, when grinding wheat grain, the amount of intact starch granules in the surrounding protein network is 90%, and the amount of destroyed starch is 10%, then the flour will have a high water-absorbing capacity [4].

Therefore, an important indicator directly related to WAQ is the degree of starch degradation. The stability and predictability of the rheology of the dough depends on the degree of destruction of the starch granules and the surrounding protein network; porosity and volume of the product.

In turn, the degree of destruction of starch directly depends on the granulometric composition of the flour.

The physicochemical and rheological properties of wheat bakery flour of the highest grade, obtained from a flour mill in one of the regions of Russia, produced in accordance with GOST 26574-85, were studied.

Further, tab. 1 shows data on the percentage distribution of particles of premium wheat flour, on sieves with different mesh sizes.

Table 1.
Granulometric composition of wheat bakery flour

Index	Sieve size, microns								
	240	200	180	160	140	120	100	80	≥ 80
Remainder, % on a sieve, descent	0.01	0.2	0.3	1.2	1.1	1.4	10.2	14.3	71.29

Analyzing the data in Table 1, it can be noted that the most representative fraction of particles in bakery flour is a fraction with a size of less than 80 microns, it is 71.29% of the total number of particles. Fraction with a particle size of less than 100 microns and more than 80 microns is in the aggregate - 24.5%. Fractions of particles with a size less than 240 microns and more than 160 microns constitute an insignificant amount in the total mass of particles.

It can be assumed that the established particle size distribution leads to significant destruction of starch grains in flour.

The quality of wheat flour was assessed using generally known methods (ash content, moisture content, protein content). WAQ (viscosity) was assessed - on a Farinograph device, per unit of the device, (the farinogram shows the viscosity characteristics and gives an indirect understanding of water absorption (viscosity)

and the tendency to liquefy the dough, as well as the degree of starch destruction - on the SDmatic damaged starch analyzer.

Table 2 shows the physicochemical and rheological properties of wheat flour (GOST).

Table 2.
Characterization of the physicochemical and rheological properties of bakery flour

Indicators	Bread flour (GOST)	
	Result	Norm
Ash content, %	0.50	no higher than 0.55
Protein, %	12.0	10-14
Degree of degradation of starch, units pr.	28.3	16.0-19.0
Humidity, %	12.2	no higher than 14.5
WAQ (viscosity) units pr.	55	no lower than 58

The results obtained showed that the test sample of flour, according to some indicators, does not meet the established standards, so the degree of destruction of starch is 28.3 units pr. at a rate of 16.0-19.0 and, as a consequence, a low WAQ (55 units pr.).

For further research, we used wheat flour, prepared by a flour mill in accordance with our proposals, obtained on the basis of a series of experiments, desirable for the production of biscuits (biscuit flour).

Table 3 shows the percentage distribution of particles of premium wheat flour with an optimized particle size distribution, preferred for biscuit production.

Table 3.
Granulometric composition of wheat flour optimized for biscuit production

Indicator	Sieve size, μm								
	240	200	180	160	140	120	100	80	≥ 80
Remainder, % on a sieve, descent	1.0	1.0	1.0	1.2	20	20	20	15.8	20

The results of tab. 3 showed that the newly produced wheat flour sample contains larger particles than the baker's one. So, the most representative is the fraction with a particle size of less than 160 microns and more than 100 microns. The yield from a sieve with a mesh size of 80 microns was 20%, in comparison with \approx 71% for bakery flour.

Table 4 shows the characteristics of the physicochemical and rheological properties of biscuit flour.

Table 4.
Characteristics of the physicochemical and rheological properties of biscuit flour

Indicators	Biscuit flour
Ash content,%	0.51
Protein,%	9.6
Degree of degradation of starch, units pr.	15.8
Humidity,%	12.1
WAQ (viscosity - farinograph) units pr.	60

Analyzing the data in tab. 4, a significant decrease in the degree of starch degradation was noted in biscuit flour - 15.8 units pr (28.3 units in bakery flour), an increase in WAQ, which was 60 units pr. (versus 55 units pr. in bread flour).

Bakery and biscuit flour were used in the production of biscuits. The biscuit dough was prepared in the main way without heating [5], using the traditional recipe № 1 (main) [6]. The following quality indicators were determined in biscuits: moisture, specific volume, porosity.

The moisture content of the finished biscuit semi-finished products was determined by drying the prepared samples in a drying cabinet using an accelerated method. The specific volume of finished products was calculated by dividing their volume by weight in grams, the porosity of baked products was determined by the standard method using a Zhuravlev device. The data obtained are presented in tab. 5.

Table 5.
Comparative characteristics of biscuits

Indicator	Biscuit properties	
	on bread flour	on biscuit flour
Humidity, %	25.5	25.3
Specific volume, m3/kg	4.2	5.1
Porosity, %	80.5	88.6

The data in tab. 5 allow us to conclude that, with practically the same moisture content, biscuits, the consumer advantages of products made with biscuit flour, namely the specific volume and porosity, significantly exceed those of biscuits

made with baking flour. The use of wheat biscuit flour with an optimized granulometric composition will make it possible to obtain high-quality finished products with a minimum amount of scrap without the introduction of chemical improvers.

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智力生产元本体论

METAONTOLOGY OF INTELLECTUAL PRODUCTION

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注解。随着工业数字化，物联网与知识互联网的融合正在发生。本文介绍了智力生产的创造技术。

关键词：知识库，智能系统，机械工程产品，机械工程技术，信息模型，设计方法。

***Annotation.** With the digitalization of industry, the integration of the Internet of things and the Internet of knowledge is taking place. This article describes the technology for creating of intellectual production.*

***Keywords:** knowledge bases, intelligent systems, mechanical engineering products, mechanical engineering technology, information models, design methods.*

Intelligent Manufacturing

The existing theory of a manufacturing firm is a deterministic model, while the external environment and most fairly large firms are stochastic systems, and in accordance with the cybernetic law of the required diversity, such a model can only be useful for analysis individual static situations, since a firm that does not have the required level of diversity and stochastic properties is not able to survive in the real conditions of a market economy. Such an ontological model of a knowledge-based economy brings it to the plane of an innovative economy with a single form of value increment (value acquisition) in the form of new technical results.

It follows from this that the production itself should belong to the category of flexible production systems. In accordance with GOST 26228-90, a flexible production system (FPS) is a computer-controlled set of technological equipment consisting of various combinations of flexible production modules and (or) flexible production cells, an automated system for technological preparation of production and a system for ensuring functioning, which has the property of an

automated changeover when changing the program of production of products, the varieties of which are limited by the technological capabilities of the equipment. This formulation gives the industrial characterization of the flexible production system depicted below. The figure shows a diagram of the metaontology of intelligent industries. Metaontology contains general concepts and relationships that do not depend on the subject area. It follows that production itself should be classified as flexible production systems. In accordance with GOST 26228-90, a flexible production system (FPS) is a computer-controlled set of technological equipment consisting of various combinations of flexible production modules and (or) flexible production cells, an automated system for technological preparation of production and a system for ensuring functioning, which has the property of an automated changeover when changing the program of production of products, the varieties of which are limited by the technological capabilities of the equipment. This formulation gives the industrial characterization of a flexible production system. In the transition to post-industrial technologies, all components of the life cycle of enterprises and products should be included here.

The knowledge bank consists of the following interrelated components: source systems, data systems, generating systems, structured and metasystems. These components describe different epistemological levels, i.e. levels of knowledge regarding the phenomena under consideration. Epistemology is a philosophical and methodological discipline that studies knowledge as such, its structure, structure, functioning and development [1].

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The presentation of materials is given in accordance with the above metaontology, which determines its structure. The discipline consists of two parts, the first of which contains materials on the content of the knowledge bank of intellectual production, and the second on the description of flexible production. Thus, the book presents a metatheory that analyzes the methods and properties of the subject theory of intellectual production.

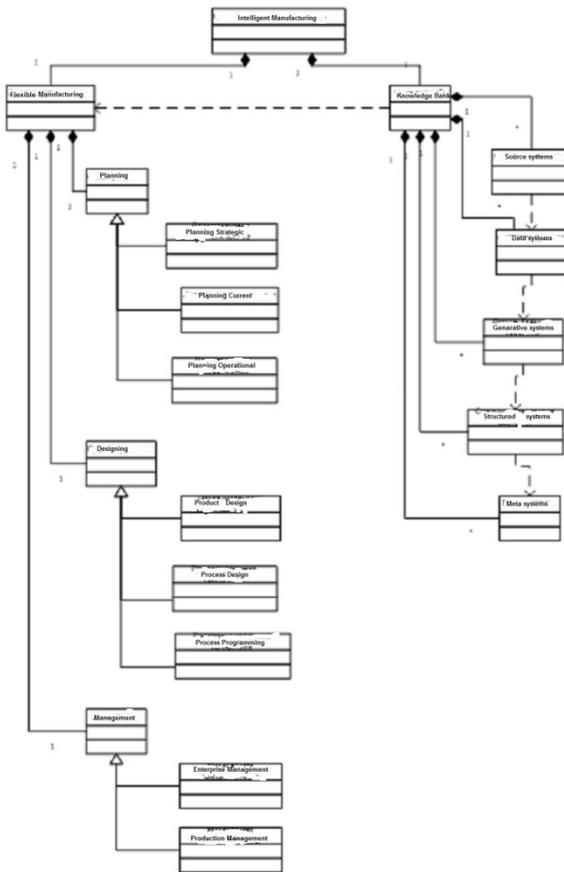


Figure 1. Conceptual model of intelligent manufacturing

An ontology is defined as [1, 2, 3, 4]

$$O = \langle X, R, F \rangle$$

Where

- **X** - a finite set of concepts (concepts) of the subject area
- **R** is a finite set of relationships between concepts
- **F** is a finite set of interpretation functions defined on concepts and / or relationships.

When $R = 0$ and $F = 0$, the ontology is transformed into a simple dictionary.

The model of an ontological system allows one to describe the relationship

between ontologies of different levels. Knowledge levels are studied in epistemology [1].

The basis for the hierarchical classification of systems in systemology is the hierarchy of their epistemological levels. The lowest level in this hierarchy, denoted level 0, is the system discerned by the researcher as such. At this level, the system is defined through a set of properties (variables), a set of potential states (values) of these properties, and an operational way of describing the meaning of these states in terms of the values of the corresponding attributes of a given system. For systems defined at this level, the term source system is used to indicate that it is, at least potentially, a source of empirical data.

At a higher level, all the knowledge of the lower-lying systems is used and, in addition, additional knowledge that is inaccessible to the lower levels. After the original system is supplemented with data, i.e. the actual states of the main variables for a certain set of parameters, consider the new (original system with data) as defined at the epistemological level 1. Systems of this level are called data systems.

Higher epistemological levels contain knowledge about the relationships of the variables under consideration, through which data can be generated under appropriate initial and boundary conditions. These characteristics of relations are usually contained in the normative technical documentation, sometimes their source is practical engineering experience.

Level 2, as applied to design automation tasks, is the level of the knowledge base for generating the values of variables that determine the properties of products and technological processes. Here, functional connections of the main variables invariant to the parameters are set, which include the variables determined by the corresponding initial system and, possibly, some additional ones. Each additional variable is determined by a specific transformation rule on a set of parameters, applicable either to the main variable of the original system, or to a hypothetical (unobservable) one entered by the user (the compiler of the model). This variable is called internal. Each rule for transforming the knowledge base at this level is usually an unambiguous function that assigns to each element of the set of variables, considered in this rule as an output, a single value from the set of admissible ones.

Since the task of generating properties is to implement a process in which the states of the main variables can be generated by a set of parameters for any initial or boundary conditions, level 2 systems are called generative systems. When designing, at level 2, there are knowledge bases associated with the calculation of structures, in the design of technological processes - knowledge bases for choosing blanks, forming a set of transitions, calculating processing modes, time norms, etc.

At epistemological levels 4 and higher, systems consist of a set of systems

defined at a lower level and some meta characteristic (rules, relations, procedures) describing changes in systems of a lower level. Such systems are called meta systems. Meta systems are required to have the same source system and be defined at level 1, 2, or 3.

The considered classification of epistemological levels is closely related to the main scientific disciplines of computer science: mathematical linguistics, database theory, theory of artificial intelligence, computational geometry and computer graphics. Observations of all properties of the system must be uniquely determined by the bases of the system, i.e. each element of the base set identifies one and only one manifestation of any of the properties.

The system of an entity is a set of properties, each of which is associated with many of its manifestations, and many bases, each of which is associated with many of its elements. Formally, the entity system can be represented as

$$O = (\{(a_i, A_i) \mid i \in N_n\}, \{(b_j, B_j) \mid j \in N_m\}),$$

where O is the entity system; a_i and A_i - respectively a property and a variety of its manifestations; b_j , B_j - base and set of its elements

$$N_n = \{1, 2, \dots, n\} \text{ и } N_m = \{1, 2, \dots, m\}.$$

The "original system" is so named because it is the source of interpretations of abstract data, which are either given by an engineer or output from CAD.

The digital revolution should radically change this scheme and enable a non-programming carrier of knowledge to enter it into a computer without intermediaries. This became possible using the expert programming methodology [5]. In this methodology, knowledge is described in the language of business prose, which is as close as possible to the literary language, but formalized so much that it is possible to automatically generate software tools corresponding to the source texts.

Modules of engineering knowledge (MK), which are elementary generating systems, are combined into structured generating systems, the models of which they are. Semantic networks are the model of structured generative systems. The semantic network MK is an acyclic directed graph. Acyclicity is necessary for the semantic network to fulfill its functional purpose – to ensure the determination of the values of the output variables for the given input ones. Due to the presence of cycles in the network, the ability to find the values of all or part of the sought variables is blocked.

Conclusion

The theoretical provisions and basic methods of creating intelligent industries have been developed, which are considered as the integration of the Internet of things and the Internet of knowledge. A conceptual model of such industries has been built.

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基于芯片功能控制测试的接口板设计自动化
**AUTOMATION OF INTERFACE BOARDS DESIGN BASED ON THE
CHIP FUNCTIONAL CONTROL TESTS**

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抽象的。实现被测超大规模集成（VLSI）和测试设备之间连接的接口板的开发是一个费力的“手动”过程，涉及 VLSI 生产的专家需要大量的手工劳动。本文首次介绍了自动解决接口板设计中最耗时的两个问题的算法。第一个任务是为接口板的开发准备初始数据。它的解决方案可以根据测试向量中包含的信息并考虑测试设备的特性，使生成接口板电路的过程自动化成为可能。为了解决第二个问题（确保差分对拓扑的平面性），使用了匈牙利算法。它基于该工作标准中建议的用于模拟接口板的一组差分对的图形的二元肋条的最大交集。这两项任务都是在 VLSI 功能测试软件和硬件复杂功能测试工作室的框架内实施的。

关键词：VLSI，测试解决方案，接口板，差分对，匈牙利算法，网表

Abstract. *The development of interface boards that implement the connection between the tested very large-scale integration (VLSI) and the test equipment is a laborious "manual" procedure of intense manual labor of specialists involved in the production of VLSI. This article is the first to present algorithms for the automatic solution of the two most time-consuming problems of designing interface boards. The first task is related to the preparation of the initial data for the development of the interface board. Its solution made it possible to automate the procedure for generating the electrical circuit of the interface board based on the information contained in the test vectors and considering the features of the test equipment. To solve the second problem (ensuring the planarity of the topology of differential pairs), the Hungarian algorithm was used. It is based on the suggested in this work criterion for the maximum intersection of binary ribs of a graph that simulates a set of differential pairs of an interface board. Both*

tasks had been implemented within the framework of the VLSI functional testing software and hardware complex Functional Test Studio.

Keywords: *VLSI, test solution, interface boards, differential pairs, hungarian algorithm, netlist*

Introduction

The development of integrated technologies is constantly increasing the cost of testing VLSI [1]. A complexity data processing of the VLSI functional control [2, 12], is also constantly growing and is accompanied by an increase in the number of random defects in their manufacture [3,16]. A decrease in technological standards during the designing of VLSI leads to an increase in the sensitivity of their elements, as well as to an increase in the influence of external factors on the operation of VLSI [4, 13]. As a result, the operational reliability of microcircuits decreases due to the appearance of latent defects in the material of integrated structures, with which now existing methods of technical control don't "cope" [17,18]. An additional the context of the constant tightening of topological design standards and the growth of VLSI integration, the requirements for the accuracy of electrical measurements and the quality of the obtained results of test control of integrated circuits are only increasing. Although high-purity materials, precision technological and the latest test equipment are used in modern integrated production, the efficiency of VLSI production testing largely depends on the quality of the electrical equipment. The most critical part of it, which implements the connection between the tested VLS and test equipment, is the interface board, which is shown in Figure 1 [5].

The design of the interface board changes every time a new series of VLSI comes into production. However, the following two tasks in the development of this board (according to the route shown in the figure) are still being solved in manual mode: (1) development of the interface board electrical circuit [6] and (2) ensuring that there are no crossings of the board wires connecting the tested microcircuits to the equipment. [7, 8]. The quality of interface board design largely determines the effectiveness of the entire test solution, by which specialists understand a set of functional tests and technical data for developing an interface board [9, 14]. Currently, there is no software in the industry that provides a continuous development cycle for interface boards, and developers are forced to resort to manual methods for their design according to the scheme shown in Figure 2 (at enterprise, blocks 1–6, which shown on a blue background, are performed in manual mode) [10].

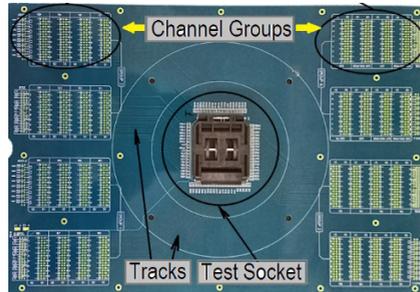


Figure 1. The interface board on a metal frame

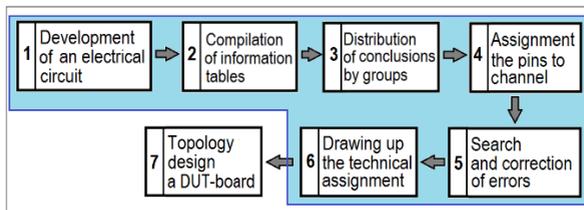


Figure 2. A interface board basic design stages

Currently, there is no software in the industry that provides a continuous development cycle for interface boards, and developers are forced to resort to manual methods for their design according to the scheme shown in Figure 2 (at enterprise, blocks 1÷6, which shown on a blue background, are performed in manual mode) [10].

The interface board design process begins with a general analysis of the technical specifications for the microcircuit; followed by the stage of compiling information tables in the Microsoft Excel environment, including a sheet with a list of outputs in the format shown in Figure 3, sheets with microcircuit configuration options, channel assignment options, and others. The last one here is an Excel sheet with a visual representation of the conclusions of the tested microcircuit, the upper part of which is shown in Figure 4 [11].

	1	2	3	4
1	№	Name	Type	Description
2	A1	NAN1	Input	Data 1
3	A2	NAN2	Input	Data 2
4	A3	NAN3	Input	Data 3
5	W0	N_WE	Output	NC
6	A0	NC	NC	NC

Figure 3. List and description of pins

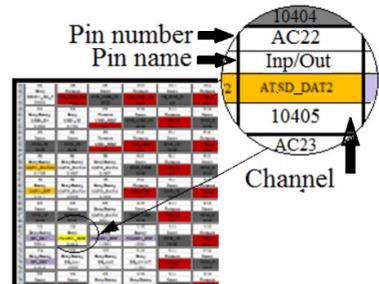


Figure 4. Visual representation of a chip pins

The visual representation of the VLSI pins, shown here, allows the designer to evaluate the type and method of connecting the pins of the microcircuit under test to the logic analyzer using the assigned colors (scan pins, differential pair pins, etc.). At the next stage, the developer determines the number of pins with different connections to the tester and distributes them into groups. That procedure is a poorly convergent, very time-consuming iterative process, which becomes many times more complicated if the pins of differential pairs fall into the group. The method proposed further in the article allows solving this problem in an automatic mode. The following procedure for assigning leads to the tester's channels is even more time consuming, since with a large size of the problem being solved (more than 1000 pins) it requires increased concentration of attention due to the limitation of the resource of the highways near the socket.

Automation creation of dut-board electrical diagram

In this work, we solve the problem of automating the design stage of the interface board schematic diagram and the stage of assigning VLSI pins onto the tester channels. Full automation of these two stages allows in parallel to automate all the "manual" stages of interface board design, shown in blocks 1 to 6 in Figure 2, since in this case the subjective factor will be eliminated from the process development. To implement the project, the domestic software and hardware complex Functional Test Studio (FT Studio) and the STeel language, the author of which is K.K. Smirnov.

FT Studio is an environment for the development of programs for the functional control and management of test and measurement equipment, in which any test can be described as an algorithm. Additionally, this complex has software that allows you to import and export programs from various test equipment. During the development of the FT Studio complex, the authors noticed the following circumstance. All data related to the design of an interface board is set by the de-

veloper already at the stage of compiling tests, including information about the test equipment, channel characteristics and the rules for their connection providing the correct testing. It directly follows from this that the development of a schematic diagram of a interface board (block 1 in Figure 2) can be replaced by automatic conversions of test vectors into lists of circuits and radioelements in the format of a design CAD system available at the enterprise. With this approach, there is no need to prepare a list of differential pairs, which can also be automatically obtained during the specified conversion in any predefined format.

In the simplest case of test development, the test engineer in language STeeL the purpose of the pins, function blocks and switching circuits to be tested. When designing more complex tests, the developer can use additional tools of the STeeL language, which allow, for example, to describe digital signal processing algorithms, create dynamic test tables, perform complex calculations directly in the algorithm and, depending on the result, generate the necessary signals on the pins to be tested.

The current version of FT Studio implements the following series of "standard" algorithms for generating tests using attributes: (1) multiple duplication and channel switching (2) automatic assignment of channel numbers and (3) Setting up various test configurations. The choice of these attributes and their inclusion in the "standard" category is dictated by the fact that testing algorithms implemented with their help are present in most tests being developed. Let's look at the implementation of the first of the above list of attributes - multiple duplication channel.

An example of duplication have shown using Figure 5. Here on the right is a part of an algorithm developed in STeeL for testing one VLSI instance, in which the "Duplication" attribute is specified. As a result of compiling this algorithm, 3 copies of this signal will be created, as shown in Figure 5 on the down. This example actually demonstrates the principle of automatic conversion of a testing algorithm described by test vectors in the STeeL language into a part of the circuit diagram of an interface board that implements parallel testing of 3 chips. At the stage of developing the algorithm, the developer works with one TDO signal, and the compiler, meeting the "Duplication" attribute for specific equipment, for example, Burn-In testing equipment, will replicate, leaving only one of signal copy. Other attributes "work" in a similar way, including user attributes, if they are placed in the original test in accordance with the rules of the STeeL language. The initial test table generated by the user regardless of its format (ASCII, AVC, WGL, STIL, STeeL, BSEL or in the format of the user himself) is represented in the STeeL language as object suitable for reuse. For the convenience of the user, FT Studio implements a visual representation of the logical models of the device under test, as shown in Figure 6.

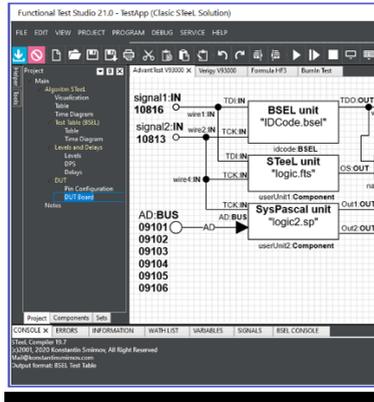


Figure 5. Channel mirroring example

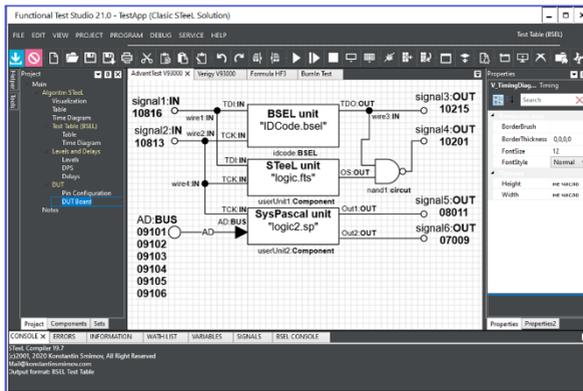


Figure 6. Test built developed by the user

The component-oriented property of the STeel language allows you to implement the project structure according to the diagram in Figure 7. The same property allows you to describe the testing algorithm in so that the electrical equipment, a model of tested VLSI and the functional tests had been presented in a single project in one language. In this case, the project can use built-in or user-developed components that describe the models of IP blocks of the VLSI under test, electrical circuits, test algorithms, pin assignment algorithms and test tables from other CAD systems, as shown above in Figure 6.

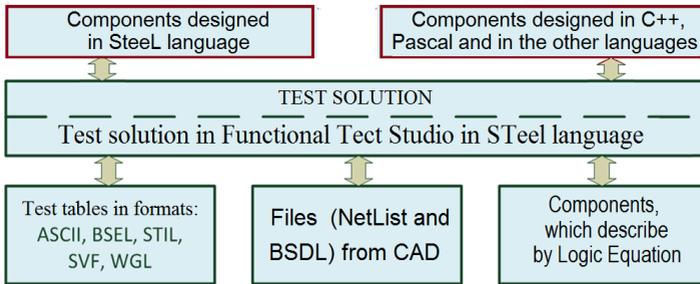


Figure 7. Project structure in the FT Studio environment

Optimizing the Tester Channel Structure

Modern "systems-on-a-chip" provides simultaneous support of a dozen interfaces [19], which imposes restrictions on the preparation of initial information about the number of equipment channels in automatic mode. To obtain this information, SSteel uses the DUTboard component, which connects new hardware to the system. Having received data on each of the channels of all testing devices of the system, the DUTboard component proceeds to the procedure for sequentially assigning channels to VLSI contacts. In this process, two non-overlapping lists of "assigned" and "free" channel numbers are created and constantly updated. Each assigned pair of contacts of the form "tester channel - VLSI output", hereinafter referred to as "coordination", is automatically included in the list of "assigned" and removed from the list of "free" channels.

As a result, a list of matching is dynamically generated, shown on the left in Figure 8, which is then rebuilt so that no two lines of this list intersect on the plane, as shown in Figure 8 on the right. The destination shown here was obtained using the Hungarian algorithm [20].

To explain the essence of the optimization criterion proposed below, with which the solution shown here have been achieved, consider the topology of the interface board shown in Figure 9.

The section of the board highlighted here by a big circle contains a typical fragment of the V-shaped topology of the differential pairs, the intersection of which is unacceptable. Here the set $\{T\}$ of pins is connected to the pin set $\{P + S\}$ by binary disjoint ribs. We have a typical model the matching's which formed by pairs of pins, one of which belongs to the set $\{T\}$, and the other to the set $\{P + S\}$. Formally, the problem can be posed as follows: find a map of the vertices set of the graph $\{T\}$ onto the vertices set $\{P + S\}$ such that the set of binary ribs formed by the vertices of all possible matching do not intersect on the printed board. Let's call this the minimum matching's.

The demonstration have been carried out on a model problem using Figure 10

with total number of vertices of the set $\{T\}$ to 6. We have distributed the vertices over the sets as follows: $\{T\} = \{A, B, C, D, E, F\}$; $\{P\} = \{a, b, c\}$; $\{S\} = \{d, e, f\}$.

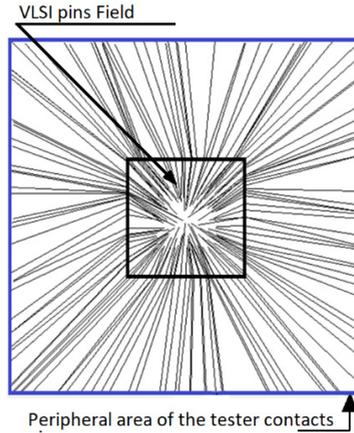


Figure 8. Solving by criterion "no intersections"

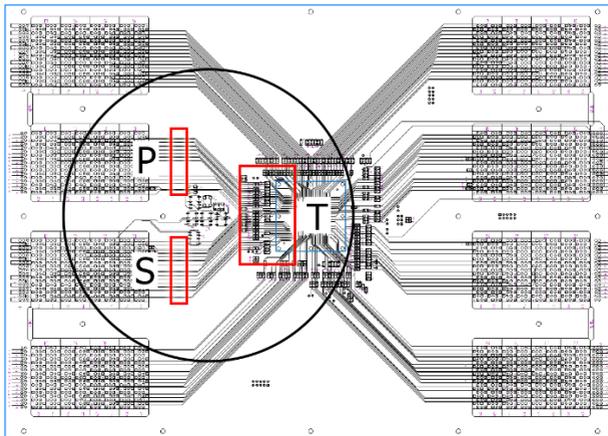


Figure 9. V-shaped branching of differential pairs

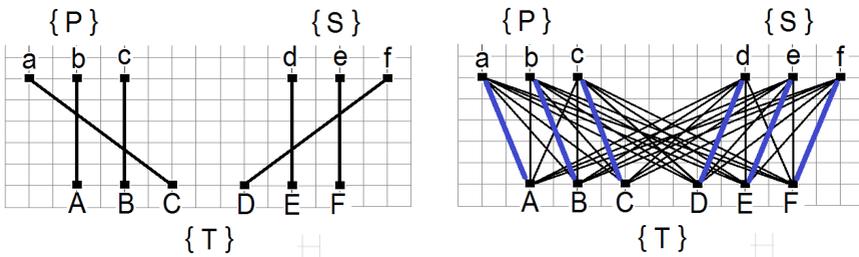


Figure 10. To the solution of problem of the graph ribs intersections minimizing

The problem posed is NP-complete and is solved if the number of intersections of the rib connecting the vertices i and j with the rest of the vertices of the graph writes at the intersection of the row i and column j of the cost matrix. The graph of intersections of all ribs of the current task is given on the right in Figure 10, and the cost matrix corresponding to this graph is shown in Table I. The final solution to this task is given in Table II. The graphical solution corresponding to this table is shown in Figure 10 on the right by blue ribs.

The Cost Matrix of Ribs Assignments for Bipartite Graph in Figure 10 (The Right)

	a	b	c	d	e	f
A	0	5	10	15	20	25
B	5	8	11	14	17	20
C	10	11	12	13	14	15
D	15	14	13	12	11	10
E	20	17	14	11	8	5
F	25	20	15	10	5	0

Result of Solving The Assignment Task
(Marked with "Asterisks")

	a	b	c	d	e	f
A	0*	0	2	7	15	25
B	2	0*	0	3	9	17
C	6	2	0*	3	5	11
D	11	5	3	0*	2	6
E	17	9	3	0	0*	2
F	25	15	7	2	0	0*

Conclusion

A critical analysis of the current state of the problem of designing interface boards for testing VLSI is given. The analysis showed that the "manual" methods of developing the electrical circuit of the board, as well as the "manual" assignment of the VLSI contacts to the channels of the test equipment, significantly slow down the entire process of developing the chips.

Methods for solving these problems in an automatic mode based on the FT-Studio hardware and software complex for testing microcircuits are proposed. The solution is based on the idea of developing the electrical circuit of the interface board based on the information contained in the test vectors themselves. As a result, the end-to-end development cycle of the interface board was implemented, from which the subjective factor was completely excluded.

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根据确保信号完整性的标准在电路板上放置放射性元素的算法
**ALGORITHM OF PLACING RADIOELEMENTS ON THE BOARD
ACCORDING TO THE CRITERION OF ENSURING THE INTEGRITY
OF THE SIGNALS**

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抽象的。今天使用的设计 CAD 系统没有设计程序来在自动放置元件的阶段最小化导体的电长度。这些系统提供的交互式工具大大减慢了设计速度。文章中提出的解决这个问题的方法使用二分法，但与其经典实现相反，为了最小化给定信号电路的电气长度，这项工作使用了元素相互拉动的标准。该标准与元件之间连接的电气长度成反比。在一个具体的例子中，显示了应用所提出的标准来自动解决控制关键信号电路长度问题的基本可能性和有效性，这是确保信号完整性的必要条件。

关键词：信号完整性，印刷电路板，自动元件放置，蛮力法，二分法，吸引准则

Abstract. *The design CAD-systems used today do not have design procedures to minimize the electrical length of conductors at the stage of automatic placement of elements. The interactive tools provided by these systems significantly slow down the designing. The method proposed in the article for solving this problem uses the dichotomous division procedure, but, in contrast to its classical implementations, to minimize the electrical length of the given signal circuits, this work uses the criterion of the elements pulling to each other. This criterion is inversely proportional to the electrical length of the connections between the elements. On a specific example, the fundamental possibility and effectiveness of the application of the proposed criterion for the automatic solution of the problem of controlling the length of critical signal circuits is shown, which is a necessary condition for ensuring the integrity of signals.*

Keywords: *signal integrity, printed circuit boards, automatic element placement, brute force method, dichotomous division, attraction criterion*

Introduction

Signal integrity issues in PCB design come to the fore when signal frequency exceed a hundred megahertz. Such signals can be significantly distorted due to crosstalk and reflection that occur in electrically short and electrically long lines, respectively. Since the reflection interference can be eliminated by matching the impedance of the communication line with the load, the length of the communication line in this case does not play a significant role in ensuring the integrity of the signal. The amplitudes of the crosstalk obey the following expression [1]:

$$U_{II} = \frac{C_{B3} \times \Delta U \times R_{BBLX}}{\tau_{\Phi_{min}}} \mp \frac{M \times \Delta I}{\tau_{\Phi_{min}}}, \tag{1}$$

where: C_{B3} – mutual capacitance value between adjacent conductors, M – value mutual induction between adjacent conductors, $\Delta U, \Delta I$ – range of voltage and current changing of the signal source, R_{BBLX} – signal source output impedance, $\tau_{\Phi_{min}}$ – minimum rise time of the transmitted signal.

The values of the mutual capacitance and mutual induction between adjacent conductors are directly proportional to the length of their mutual segment:

$$C_{B3} = C_0 \times l_{B3}, \quad M = M_0 \times l_{B3}, \tag{2}$$

here: C_0 – the value of the mutual capacitance between adjacent conductors per unit length, M_0 – value of mutual induction between adjacent conductors per unit length; l_{B3} – parallel segment length

The signal integrity condition is met if:

$$U_{II} \leq U_{Ioon} \tag{3}$$

From (1) it follows that the value of the crosstalk is proportional to the value of l_{B3} , therefore, to ensure signal integrity, it is necessary that:

$$l_{B3} \leq l_{B3don} \tag{4}$$

This is especially true for signals carrying the function of synchronization or gating [1]. In what follows, such chains will be referred to as "main". The length of the signal conductors on the printed circuit board can be effectively controlled in automatic mode by rearranging the elements, placing in proximity those elements that take part in the transmission of the main signals. Usually, this problem is solved by the criterion of the minimum total length of links and is known in the literature [2] as the “quadratic assignment problem”. Its exact solution is possible only using the brute force method, which is inapplicable to solving the problem of minimizing the electrical length of conductors to ensure the integrity of signals for the following reasons.

First, the exact solution of this problem using the brute force method is unattainable in terms of time costs even with $n > 10$ elements on PCB, since it belongs to NP-complete problems of factorial complexity. These problems are usually

solved by approximate methods [3-5] and give only approximate results. "Fast" algorithms for sequential optimization are also not suitable for solving this problem since their low efficiency has been proven [6]. Secondly, the solution obtained using the brute force method allows minimizing the total length of all conductors "on average". In other words, in the process of exhaustive search, it is likely that the main chains can turn out to be long.

The development of an algorithm according by describing in [7] will allow minimizing the length of the main connections on PCB by using the priority's mechanism. However, since in [7] the formal side of this issue is not discussed of the problem, an algorithmic solution to this task is presented below.

The proposed method

The essence of the proposed algorithm is to implement a step-by-step procedure for combining elements on PCB into strongly connected groups (sectors), so that the presence of elements from other groups is prohibited within each game group, even if there are free positions in them.

Let's consider how the algorithm works on a model problem. Let the vertices $\{x_1, \dots, x_9\}$ of the graph $G(X, R)$, shown on the left in Figure 1, be located at the nodes of the lattice with a unit step in the positions $\{P_1, \dots, P_9\}$ shown in Figure 1. The matrix of connections of the graph vertices $G(X, R)$ is shown in Table 1, and the Manhattan distance matrix is shown in Table 2. This placement was obtained after its optimization using the fractal aggregation algorithm proposed in [8]. Its efficiency was estimated by the value of the total bond length L_{Σ} , as a component-wise product of the indicated matrices: $L_{\Sigma} = (3 \times 2) + (8 \times 1) + (2 \times 4) + \dots + (1 \times 1) = 58$ conventional units.

Let's select the three longest chains in this last optimized placing and mark them in red color. Suppose that to ensure the integrity of the signals in the placement at the positions shown on the right in Figure 1, it is necessary to minimize the length of these circuits. "Red" (main) chains are represented in the graph $G(X, R)$ by edges, the total length of which in the Manhattan geometry is $(3 \times 2) + \dots + (4 \times 2) + (2 \times 3) = 20$ conventional units

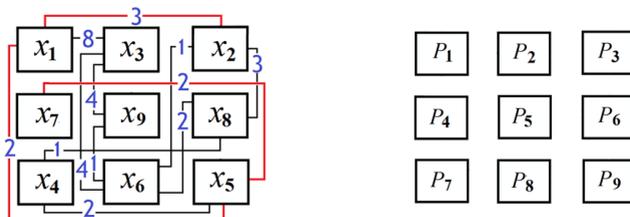


Figure 1. Placement of vertices by the method of aggregation of fractals without considering the signal integrity criterion

Table 1.

Matrix of connections

	x_1	x_2	x_3	x_4	x_5	x_6	x_7	x_8	x_9
x_1		3	8		2				
x_2						1		3	
x_3						4			4
x_4					2			1	
x_5							2		
x_6								2	1
x_7									
x_8									
x_9									

Symmetrically

Table 1.

Distance matrix

	1	3	2	7	9	8	4	6	5
1	0	2	1	2	4	3	1	3	2
3		0	1	4	2	3	3	1	2
2			0	3	3	2	2	2	1
7				0	2	1	1	3	2
9					0	1	3	1	2
8						0	2	2	1
4							0	2	1
6								0	1
5									0

Symmetrically

To assess the degree of attraction of elements on PCB to each other, we take into consideration the "Attractions Matrix". As the initial data for its construction, we will use the bipartite graph $G(X,Z,R)$, which we obtain from the monocotyledonous one as a result of the transformation: $G(X,R) \rightarrow G(X,Z,R)$. To this end,

we will consider the edges of the graph $G(X, R)$ on the left in Figure 2. The edges connecting the elements, we replace by the edges Z_1, Z_2 and Z_3 of the bipartite graph (see Fi. 2 in center). We will define the attraction of vertices x_1 and x_2 to each other only by the chain Z_1 , as the value inverse of the number of elements in the chain Z_1 , that is, $t_{z_1}(x_1) = t_{z_1}(x_2) = 0,5$.

To pass to the general case, we use the definition of the quantifier Γ_{z_j} as the set of vertices X incident to the vertex Z_j of bipartite graph. Then "the attraction of a vertex to other vertices belonging to the quantifier of generality Γ_{z_j} " will be equal to:

$$t_j(x_i) = \frac{1}{|\Gamma_j|} : \forall x_i \in \Gamma_j \tag{1}$$

We will define the total attraction between any pair of tops as the sum of the attractions by all chains, which them connected. Now, let us further unite the vertices Z_1, Z_2 and Z_3 into one with a new index (A) and we denote her as $Z_A (1,5)$, as shown in Figure 2 on the right.

Using the introduced terms, we define the "Attractions Matrix" by the element located at the intersection of its i -th row and j -th column. For the graph shown on the right in Figure 2, the Attractions Matrix, according to the introduced definition, will take the form shown in Table 3.

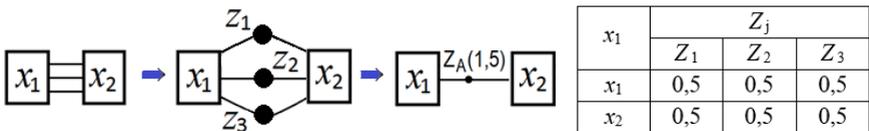


Figure 2. Converting a monocyledonous graph to a bipartite graph

We represent this matrix in an abbreviated form, for which we first calculate by formula (1) the attraction of the vertices (x_1, x_2) to each other along the chain

$$Z_1: t_{z_1}(x_1) = t_{z_1}(x_2) = \frac{1}{|(x_1, x_2)|} = 0,5 .$$

Thus, the total attraction of the vertex x_1 to the vertex x_2 as well as the vertex x_2 to the vertex x_1 is equal to 1,5 and the result of the transformation $G(X, R) \rightarrow G(X, Z, R)$ for the current x_2 example will take the form, shown on the right in Fig. 2, where the multi-edges Z_1, Z_2 and Z_3 are replaced by one edge Z_A by introducing the index A .

The algorithm for calculating the total attraction of the vertex (x_2) to the vertex (x_1) in the *Sum* cell at the first iteration of the first division stage consists of next steps:

1. Set 0 in cell *Sum*.
2. Go by along the line x_2 from left to right until a nonzero element. If such an element is found, go to step 3. When you reach column *MI*, go to step 5.
3. Go through the column in which a nonzero element is found, skipping zero elements. If a nonzero element is found (for example, in row *X*), then go to step 4.
4. If a nonzero element is not found until the end of the column scan, go to step 2.
4. If in column *MI* of row *X* there is a number with the number of the current iteration *N*, then perform the operation: $Sum := Sum + T \frac{N}{|N|}$ and go to step 2. Otherwise, just go to step 2.
5. Finish the calculation and read the result from the *Sum* cell.

Numerical calculation of the attraction of a vertex (x_2) to a vertex (x_1) in the *Sum* cell at the 1st iteration ($N = 1$) includes the following stages (in parentheses we will indicate the numbers of the algorithm steps):

Numerical calculation of the attraction value of a vertex (x_2) to a vertex (x_1) at the 1-st iteration ($N = 1$) includes the following stages (in parentheses - the numbers of the algorithm steps):

- {1} Set 0 in cell *Sum* → {2}.
- {2} Go by along the line x_2 from left to right up to $A = 1,5$ → {3}.
- {3} Go by down column *A* up to line x_8 with $A = 1,5$ element and → {4}.
- {4} Column *MI* in line x_8 has no number the current iteration (1st), therefore → {2}.
- {2} Go further by line x_2 up to column $E = 0,5$ → {3}.
- {3} Go by down column *E* up to line x_6 , with $E = 0,5$ element and → {4}.
- {4} Column *MI* in line x_6 has no number the current iteration (1st), therefore → {2}.
- {2} Go further by line x_2 up to column $P = 40$ → {3}.
- {3} Go by up column *P* up to line x_1 with $P = 40$ element and → {4}.
- {4} Column at line x_1 has the current iteration number (as -1), therefore we

calculate: $Sum := 0 + 40 \frac{-1}{|-1|} = 0 + 40 \times -1 = -40$ and → {2}.

- {2} Go by along the line x_2 up to column *MI* and finish calculate: $Sum = -40$;

The results of similar calculations with a nonzero sum for other vertices: ($x_3 = -5,5$) and ($x_5 = -41$) show that the maximum thrust to the vertex *a* at the 1-st iteration of the 1-st stage of division is at the vertex (x_5), therefore at the 2-nd iteration in the *MI* column we write number $N = -2$ in line (x_5) and go to the 2-nd iteration of calculating the total thrust of all (except x_1 and x_3) vertices to vertices x_1

and x_5 . We get the following nonzero results: $(x_2 = -40)$, $(x_3 = -5,5)$ and $(x_7 = -41)$. Similar calculations at the other 4 iterations determine the following order of including the vertices in the left sector.

Further calculations are carried out in a similar way. As a result, the length of the main chains was brought to the minimum possible (up to 7 cu), and the total length - up to 52 cu, that is, the optimum obtained by the search method [8] has reduced yet 10%. For comparison, Fig. 4 on the right shows a solution in which no restrictions on the length of the chains are imposed. As we can see, although the total length of the conductors has decreased significantly (to 45 cu), the length of the critical circuits has doubled.

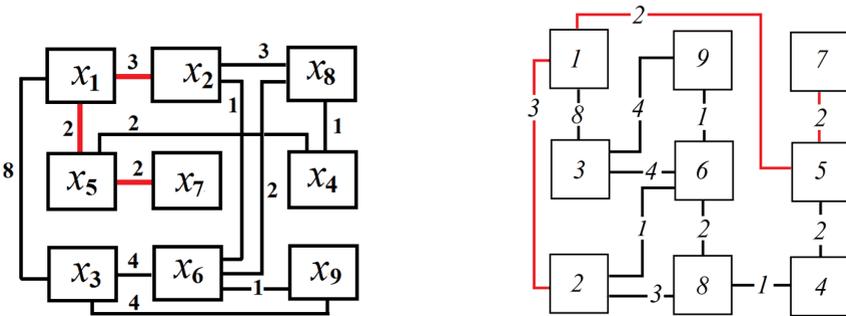


Figure 4. Placement of vertices by the dichotomy method according to the criterion of minimum the length of main chains (on the left) and according to the criterion of attraction (on the right)

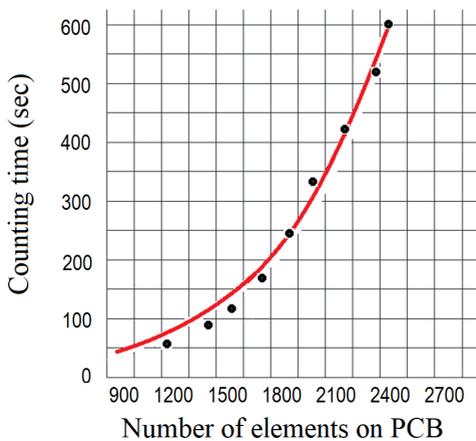


Figure 6. Dependence of placement time on the number of elements on PCB

Figure 6 shows a graph obtained from the results of a machine experiment and representing the dependence of the counting time on the number of elements involved in the placement. It can be rigorously shown that the dependence shown in Figure 6 is approximated by an exact parabola, that is, the computational complexity of the solution is proportional to the square of the number of placed elements. The algorithm has high performance because it does not use search procedures in its work.

Conclusion

An algorithm for placing elements on a printed circuit board according to the criterion of ensuring the integrity of signals on given signal circuits is proposed and a description of its operation is given on a specific example. The criterion underlying the operation of the algorithm provides "minimization-on-average" of the total length of the given "critical" electrical nets. The results of comparison of the proposed algorithm with a hybrid fractal aggregation algorithm working in tandem with a genetic algorithm are presented. This algorithm and most of the known search and search algorithms for automatic placement of elements on the board minimize, in contrast to the algorithm proposed above, the total length of all connections, which is obviously inapplicable to the solution of the problem posed in the article. The comparison, which was carried out on the same model example, showed that the proposed algorithm allows one to obtain a better quality placement in terms of reducing the "average" length of the electrical nets.

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哈萨克斯坦交通部门数字化的主要方向

**THE MAIN DIRECTIONS OF DIGITALIZATION OF THE
TRANSPORTATION SECTOR IN KAZAKHSTAN**

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抽象的。 本文讨论了哈萨克斯坦交通活动数字化的问题。 作者提供了表征运输基础设施和物流链数字化的数据。 分析了通过数字技术改善和协调该行业发展的可能性。

关键词: 运输活动信息化、运输服务、运输、运输、运输和物流系统。

Abstract. *The article discusses the issues of digitalization of transport activities in Kazakhstan. The authors present data characterizing the digitalization of transport infrastructure and logistics chains. The possibilities of improving and coordinating the development of this industry through digital technologies are analyzed.*

Keywords: *informatization of transport activities, transport services, transport, transportation, transport and logistics system.*

Currently, the growing relevance of the digitalization of the economy of Kazakhstan allows for further economic growth and competitiveness of the country throughout the world. The potential need for digitalization is high. The main in-

strument in achieving this goal is the "Digital Kazakhstan" state program. Digitalization can become the engine of the national economy and the generator of permanent jobs. Digitalization will become the engine for the development and adaptation of new technologies in the economy of Kazakhstan, which provide job creation.

In 2019, as part of the implementation of measures of the "Digital Kazakhstan" state program, 8 thousand jobs were created.

The total economic effect due to the program in 2018 and 2019 exceeded 600 billion tenge. Significant progress has been achieved in the implementation of digital technologies in the provision of public services, education, health care, finance, transport and the mining and metallurgical sector.

Further integration of digital technologies is critical for Kazakhstan's entry into the list of the 30 most competitive economies in the world and improving the well-being of Kazakhstanis.

In terms of digitalization of transport and logistics, the "Intelligent Transport System" project is being implemented, which collects and processes data on roads, vehicles, travels on toll roads, passengers on intercity buses, as well as on booked tickets.

One of the components of an intelligent transport system is a charge system, as well as a system for collecting and transmitting traffic information to road users.

To date, a charge system has been launched on the Almaty-Kapshagay (42 km), Almaty-Khorgos (295 km) and Astana-Temirtau (134 km) sections with a total length of 471 km.

24 special automated measuring devices have been implemented for automation transport control. Since September 2019, 82 violations of weight parameters have been identified and therefore, fees and fines in the amount of 8.6 million tenge were collected.

As part of the digitalization of industry, a project is being implemented to create model digital factories that will demonstrate the effectiveness and reversibility of digitalization, identify barriers and develop tools for state support. The implementation of 51 projects has begun, of which 16 projects have been completed.

The transport industry is one of the areas of economic activity mostly influenced by digitalization processes. This effect can be divided into obvious, superficial changes in this area and changes in the transport infrastructure itself. In the first case, we are talking about the implementation into the transport industry of technologies tested in other industries: "big data", intellectualization processes [2].

Thus, intelligent transport systems (ITS) are the main trend in the technological development of the industry. In the second case, the digitalization of the transport industry means a change in the technical and economic foundations of production. Currently, the process of digitalization of the transport industry has four main directions [3]:

- 1) digitalization of transport infrastructure and logistics chains (including storage facilities and service centers);
- 2) robotization of production processes;
- 3) large-scale automation, including management processes;
- 4) implementation of autopilot systems.

Let's consider these processes in more detail.

1) digitalization of transport infrastructure means that every stage in the supply chain, as well as the vehicle, must be involved in the digital sphere, that is, it must be individually identified on the Internet and also controlled by software. This allows you to manage the entire traffic flow in real time, reduce costs, non-core expenses, and predict the transport industry. An example of such digitalization is equipping all sea containers with chips, tracking the movement of each container;

2) robotization of production processes in the transportation sector is already proceeding at a very fast pace. However, labor-intensive storage facilities (especially packaging and equipment of cargo), maintenance of vehicles still require extensive involvement of manual labor;

3) automation of control processes takes place for a long time. In fact, the transport industry became one of the first industries where management processes began to be automated. The speed of modern traffic flows is such that a person really cannot make competent, well-thought-out decisions without the risk of a critical error;

4) the technological implementation of autopilot systems has been going on for a long time: first of all, it concerns civil aircraft, autopilot for sea cargo transportation. Law restricts the massive implementation of these technologies in many countries. Therefore, now there are only experimental projects in public transport (for example, unmanned buses). Research results and their discussion.

Digitalization has long been defined as a process of technological development in the transport industry. In fact, we can say that the penetration of digital technologies into the transport industry began with the advent of electronic computing. During this period, many different projects were implemented, both at the initiative of governments and private companies [4].

The areas of application of information and navigation technologies are differentiated according to various groups of tasks solved in the road complex [4]:

- automatic identification of the places of road traffic accidents;
- protection and control over the condition of transported goods and ensuring the safety of road users;
- management of public transport (buses, trolleybuses, trams, housing and communal services, transport for the delivery of food and industrial goods to the population, fire service, ambulance);
- management of technological transport during the construction and repair of

highways;

control, identification and management of transport in quarry and terminal transportation;

control, identification and management of transportation of bulky, high-tonnage and environmentally hazardous cargo;

transport management of departmental and commercial organizations (intra-city and suburban transportation);

transport management of mainline and intermodal (land-sea, land-river, etc.) carriers.

The requirements of consumers for the accuracy of vehicle detection depend on the purpose of certain technologies for monitoring and controlling transport processes:

the requirements for the accuracy of the location of detection of vehicles with an error of at least 30 m in solving many problems related to ensuring traffic safety and organizing the transportation of passengers and goods in the process of economic activity (maximum error) currently meet the needs of the automobile and road industry;

the highest requirements are the requirements for the accuracy of locating when solving special tasks (tracking environmentally hazardous goods, protecting against theft and searching for stolen funds, etc.).

Requirements for the size of the working area of consumers are established based on the analysis of the territorial and spatial conditions for the implementation of tasks using information and navigation technologies:

the territory of the state, the territory of the neighbouring countries and beyond, when organizing domestic and interstate transportation;

global region - when organizing intermodal transport, including the carriage of goods by river and sea transport.

The use of digital technologies in the field of transport allows solving the problems of traffic management, monitoring and managing the operation of all types of transport (personal, public, freight), informing citizens and enterprises about the organization of transport services in the region, the country.

One of the priority state tasks is the creation of a developed transport infrastructure to ensure the availability, safety and quality of transport services through the implementation of intelligent transport systems. Nowadays, the tasks of providing Broad Band WL for transport infrastructure enterprises (bus stations, ports, railway stations, airports) and the implementation of an intelligent transport system are being completed. This system is a complex of interconnected automated systems that solve the problems of traffic management, monitoring and control of the operation of all types of transport (private, public, cargo), informing citizens and enterprises about the organization of transport services on the territory of the

region, the country. Intelligent transport systems are focused on fixing three main problems: safety, mobility, environmental protection.

One of the most important components of any “smart city” is “Smart Transport” and geolocation, an online cartographic service. Geolocation helps to track the movement of urban transport online, determining the location of a specific bus, trolleybus or taxi. The problems of launching projects for digitalization and technological re-equipment and the development of digital infrastructure are relevant in this direction.

The object of our research: intelligent systems in the process of transportation.

Subject of research: the process of integrating an intelligent transport system into the optimization of passenger transportation in the city of Karaganda.

The active construction work of new residential complexes on the territory of the city of Karaganda, the long distance from the city districts from each other and unused sections of streets on the city route network make the city route transport inaccessible to some passengers. The organization of the new route will lower the tension on certain sections of the urban road system and increase the efficiency of organizing passenger transportation in the city.

The purpose of the thesis research: processing of cartographic data of the "Smart Transport" system for the optimization and management of passenger traffic by public transport in Karaganda.

Objectives:

- 1) analysis of the capabilities of intelligent transport systems in the management of the transportation process
- 2) consider the conditions and capabilities of intelligent transport systems in optimizing the urban road system;
- 3) analysis of the possibilities of the cartographic service in transport management and entering data on the routes of public transport of the city of Karaganda into the network geographic information system Yandex - "People's Map";
- 4) evaluation of the effectiveness of the proposed direction.

The theoretical novelty of our research: data coverage through a cartographic service of territories that were not previously involved in the urban road system, that is, road sections on which the movement of passenger transport is not currently organized.

Practical significance: the implementation of the solution proposed in the work will have a positive effect on the development of the urban road system of Karaganda. It reduces the passenger load on some road sections. Moreover, in the future it will give an impetus to the organization of new routes for passenger transport by organizing previously absent public transport stops.

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在合成洗涤剂技术中实施综合职业安全系统
**IMPLEMENTATION OF AN INTEGRATED OCCUPATIONAL SAFETY
SYSTEM IN THE TECHNOLOGY OF SYNTHETIC DETERGENTS**

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抽象的。合成洗涤剂的生产属于化学工业，大多数工人在危险的工作条件下工作，这需要引入综合职业安全体系并制定降低职业风险水平的措施。考虑了综合职业安全系统的主要功能。

关键词：职业安全、合成洗涤剂、表面活性剂、伤害、事故、安全技术。

Abstract. *The production of synthetic detergents belongs to the chemical industry, and most workers are employed in hazardous working conditions, which requires the introduction of an integrated occupational safety system and the development of measures to reduce the level of occupational risks. The main functions of the integrated occupational safety system are considered.*

Keywords: *occupational safety, synthetic detergents, surfactants, injuries, accidents, safe technology.*

Synthetic detergents include highly effective detergents containing 10-40% of surfactants, various functional additives (complexing agents, bleaches, pH regulators, structuring agents, antiresorbents) to increase the detergent ability of agents [1,2]. The priority direction in the development of SD technology is to ensure their environmental safety, which is due to the tightening of environmental standards and an increase in consumer demand for organic products. All surfactants used in the production of SD should be low-toxic with a degree of complete biodegradation of at least 70%. In this case, anionic surfactants are actively used, containing di- and trioxides of sulfur, sulfuric acid, alkylbenzenes, hydroxides of alkali metals, etc., which have a negative effect on the human body and the environment [5, 6].

Of all the components that make up SD, polyphosphates, which are used to bind ions that cause water hardness, are the most polluting. The products of hydrolysis of polyphosphates - monophosphates - accumulate in wastewater. They do not pose an immediate threat to humans, but they are considered dangerous for aquatic ecosystems, as they cause eutrophication of water bodies. SD are also strong deoxygenators, actively destroying oxygen dissolved in water. Degradation products from detergents can be toxic. Phosphates, which disrupt the ecosystem of water bodies, pose a particular threat. The impact of strong anionic surfactants contributes to the disruption of protein, fat and carbohydrate metabolism, a decrease in immunity, damage to the brain, liver, lungs, and deterioration of the barrier function of the skin.

There are three main directions for reducing the toxicity of synthetic detergents:

- replacement of water softening phosphates with zeolites;
- the introduction of legal restrictions and the construction of new factories;
- complete replacement of phosphate powders, development of formulations and production of fundamentally new third-generation washing powders, which would be superior to washing powders based on zeolites in terms of consumer properties, hygienic and environmental indicators [3].

The production of synthetic detergents belongs to the chemical industry, and most workers are employed in hazardous working conditions, which requires the organization of an effective labor protection management system at the enterprise with constant monitoring of the actual indicators of harmful factors and the development of measures to reduce the level of occupational risks.

In Russian practice, the identification of hazardous and harmful production factors is carried out at workplaces by the method of conducting a special assessment of working conditions, which was legislatively enshrined on January 1, 2014 with the entry into force of the Federal Law of December 28, 2013 № 426-FZ "On special assessment of working conditions" and Federal Law № 421-FZ of December 28, 2013 "On Amendments to Certain Legislative Acts of the Russian Federation in Connection with the Adoption of the Federal Law "On Special Assessment of Working Conditions". Together with the results of the previously valid certification (more than 15 million jobs), the total number of jobs for which there is reliable information on working conditions is almost 26 million jobs (54% of the total number of jobs). The largest share of jobs with optimal and acceptable working conditions was noted in such types of activities as financial (95.6%); wholesale and retail trade, repair of motor vehicles and motorcycles (92.1%); activities in the field of culture, sports, organization of leisure and entertainment (90.9%); activities of hotels and catering establishments (89.5%); activity on operations with real estate (88.4%); professional, scientific and technical activities (87.6%); activities

in the field of information and communication (86.1%), administrative and related activities (85.8%) [4].

The largest share of jobs classified as classes 3 and 4 (harmful and hazardous working conditions) was observed in the following types of economic activities: activities in the field of health care and social services (45.1%); agriculture, hunting and forestry, fish farming and fishing (34%); water supply, sewerage, waste collection and disposal, activities to eliminate pollution (33.5%); manufacturing industries (33.3%); mining (27.9%); provision of electricity, gas and steam; air conditioning (27.7%); construction (28.2%).

As a rule, the technical foundations for managing the safety of working conditions are quite typical and consist in the identification (recognition) of hazardous and harmful production factors, risk assessment, including their analysis and management. The introduction of a hazard identification procedure makes it possible to identify real hazards that threaten health damage in the workplace, for taking preventive measures, taking into account the results of a preliminary risk assessment, which makes it possible to exclude or reduce the degree of possible harm and the scale of negative consequences.

The main approach, which allows to solve comprehensively occupational safety problems, is to create and implement an integrated occupational safety system (IOSS) at each enterprise. IOSS functions are shown in Fig. 1.

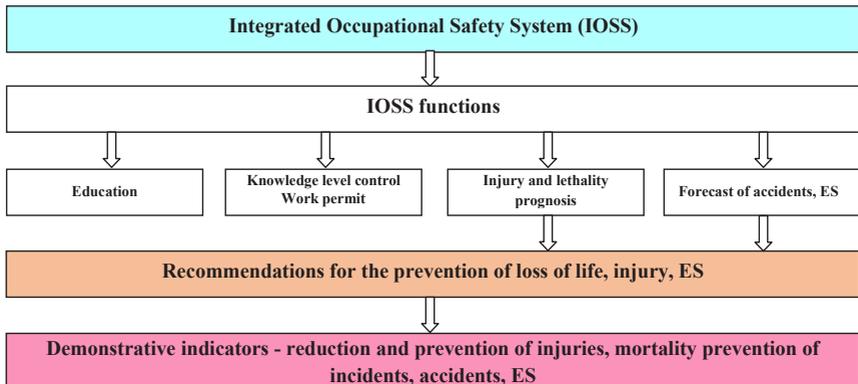


Figure 1. The main functions of the integrated occupational safety system

The integrated system of occupational safety allows for a set of measures, the implementation of which leads to a decrease in injury and mortality rates [3].

The functions of IOSS include the main elements - personnel training, control of the level of knowledge in the field of occupational safety, admission to work of

working personnel, prediction of mortality and injury rates at a given enterprise, prediction of accidents and emergencies.

An important element of IOSS is the forecast of injuries, mortality, accidents and emergencies at enterprises and hazardous production facilities (HPF).

Implementation of the IOSS functions should be based on modular technologies. The module for training and control of the level of knowledge, admission to work is carried out using standard test tasks, implemented using special computer shells.

The module for assessing injuries, mortality, and the risk of getting an occupational disease is considered in relation to the workplace. To assess the occupational risk of injury, occupational disease, mortality, it is planned to use the fundamental Weber-Fechner law and the results of the following measures: production control carried out in accordance with SP 1.1.1058-01; state sanitary and epidemiological supervision; sanitary and epidemiological assessment of production equipment and industrial products; special assessment of workplaces for working conditions; certification in the "System of voluntary certification of organizations, specialists and technological processes in the field of labor protection".

The accident prediction module is implemented on the basis of mathematical models of accidents, ES. For example, an accident and ES are considered as a model of an "aging system" or "rare events" based on the Poisson distribution [4].

Thus, the increase in the growth rate of the household chemicals market contributes to the tightening of requirements for the indicators of integrated safety of both the final product itself and the production technology. An urgent task in the field of labor protection is the development of an integrated occupational safety system, which allows to reduce the level of injuries and mortality, to predict the occurrence of accidents and emergencies, to control the level of knowledge of safety requirements among workers.

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西西伯利亚地区水库和水道冰情研究
**STUDY OF THE ICE REGIME OF RESERVOIRS AND
WATERCOURSES ON THE TERRITORY OF WESTERN SIBERIA**

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抽象的。本文介绍了对新西伯利亚州 Om 和 Karasuk 河以及新西伯利亚水库冰雪覆盖厚度形成的实地考察研究的方法和结果。对观测期间冰雪厚度增加的强度得出了结论。

关键词：冰情，冰盖形成，冰雪厚度。

Abstract. *The article presents the methodology and results of field expedition studies on the formation of ice and snow cover thicknesses on the Om and Karasuk rivers of the Novosibirsk Oblast and on the Novosibirsk reservoir. Conclusions are drawn about the intensity of the increase in ice and snow thicknesses over the observation period.*

Keywords: *ice regime, formation of ice cover, thickness of snow on ice.*

Introduction

Ice formed on rivers and reservoirs in winter has always been of interest to researchers. This is due to the solution of many engineering problems. For example, for the use of ice crossings. And also - to ensure the prevention of hazardous hydrological phenomena. Congestion and jamming are dangerous natural phenomena, during which there is a maximum rise in the level above the household level. Congestion leads to emergency situations and can damage national economic facilities. These problems are discussed not only in Russia, but also in the world [1, 2]. Based on the above, it becomes necessary to carry out a set of measures aimed at the unhindered passage of ice. These measures can be of a technological nature or include constructive solutions [3, 4]. There is a need to develop and improve the structural elements of hydroelectric systems that provide breakage of ice fields,

aimed at reducing the size of ice floes and successful passage of ice. The solution of problems associated with the passage of ice requires taking into account its physical and strength characteristics.

All dangerous phenomena must be predicted, which will mitigate their negative impact on the water sector. Forecasting of hydrological processes is based on both the creation of physical and mathematical models and experimental studies [5]. The latter make it possible to obtain information on the conditions of formation of the ice cover, as an integral part of the entire hydrological cycle. Field studies also provide an idea of the temporal variability of the phenomenon under study.

As is known, the formation of the ice cover is influenced by meteorological factors and the hydrodynamic regime of streams and reservoirs. The meteorological factors include: air temperature, humidity, wind, thickness of snow cover, etc. [6].

The aim of this work is to establish a relationship between the thickness of the snow and ice cover.

To achieve this goal, it is required to solve the following tasks:

- analyze the relationship between the formation of the thickness of the snow cover and the thickness of the ice;
- to carry out a complex of field studies on water bodies in winter.

The methods of carrying out full-scale field measurements were used:

- ice thickness;
- snow cover thickness;
- air temperature.

Field work was carried out on the Karasuk and Om rivers of the Novosibirsk Oblast and the Novosibirsk reservoir. The methodology and results of the work performed are presented at international conferences and are reflected in articles [7, 8, 9]. The thickness of ice and snow was measured in two characteristic sections (near the coast and in the middle). This makes it possible to assess the influence of the speed regime of the watercourse. The studies were carried out in 2017–2021.

References

The results of the completed field studies are presented below. The graph of changes in the thickness of ice and snow in the Novosibirsk reservoir for the winter period 2021–2021 is shown in fig. 1. Here are the measurements made on the Om river.



Figure 1. The graph of the increase in the thickness of the ice and snow cover on the Novosibirsk reservoir and the Om river

Table 1 shows the results of field studies to measure the thickness of ice and snow cover on the Om river.

Table 1.

Results of field studies to measure the thickness of ice and snow cover on the Om river in 2020–2021

Date	14.12. 2020	19.12. 2020	22.12. 2020	26.12. 2020	29.12. 2020	04.01. 2021	10.01. 2021
Temperature, C ⁰	-12	-9	-19	-36	-14	-10	-16
Ice thickness, cm (Om river)	34	43	58	62	56	64	66
Snow thickness, cm (Om river)	8	4	14	15	20	24	15

Figure 2 shows the relationship between the thickness of snow cover and ice at two studied sites: the Novosibirsk reservoir and the Om river.

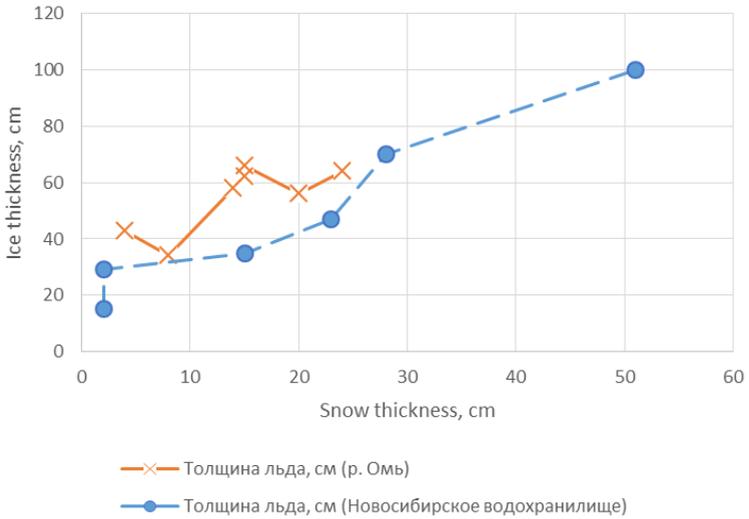


Figure 2. Experimental relationship between the studied parameters: thickness of ice and snow cover

Figure 3 shows the results of measurements on the Karasuk river and the Om river.

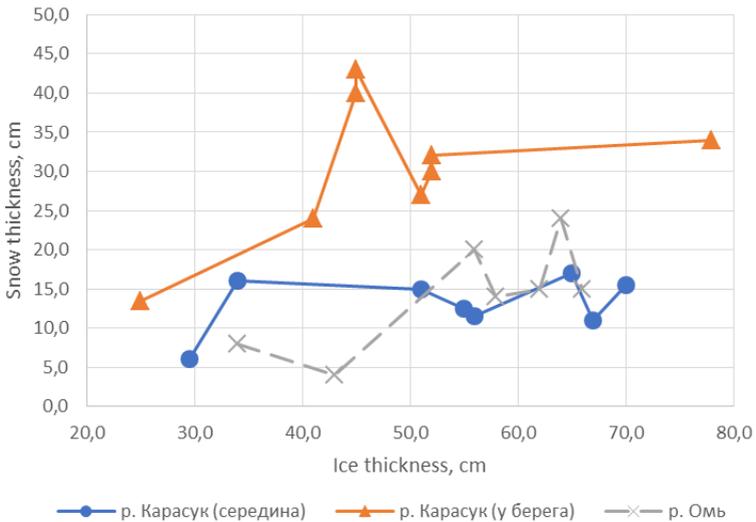


Figure 3. Relationship between snow cover thickness and ice thickness on the Om and Karasuk rivers

Discussions

The studies carried out show a relationship between the thickness of snow cover and ice both on the rivers and on the reservoir. At the same time, the influence of the flow hydraulics - its speed mode - is clearly traced. The ratio of the change in snow thickness to the change in ice thickness over the observation period for the objects under study is:

- Karasuk river: by the coast $\Delta h_c / \Delta h_n = 0,56$;
- Novosibirsk reservoir $\Delta h_c / \Delta h_n = 0,57$;
- Karasuk river: in the middle $\Delta h_c / \Delta h_n = 0,18$.

These two sites are located in more similar geographic and climatic conditions. Analysis of measurements of the thickness of ice and snow cover shows that they are approximately proportional to each other. So, for the period of expeditionary research at the Novosibirsk reservoir, the ratio of the thickness of snow and ice is $h_c/h_n = 0,43$; for the coastal zone, the river Karasuk $h_c/h_n = 0,52 \div 0,57$. These characteristics for the middle currents of the studied rivers are: on the river Karasuk $h_c/h_n = 0,22 \div 0,29$; on the river Om $h_c/h_n = 0,22 \div 0,35$.

The conditions for the formation of the ice cover and its subsequent interaction with the snow falling with different intensities are very complicated. The snow-gazing cover is in a state close to ultimate equilibrium. Under changing meteorological conditions, this balance is often violated [10].

As noted above, the study of the formation of the ice cover, its physical and static characteristics are an integral part of the initial data for the compilation of hydrological forecasts. So, adequate inclusion of experimentally established regularities is the main task of mathematical modeling of the hydrological process [5].

Conclusions

Analysis of the results of the completed field work allows us to draw the following conclusions:

1. The ratio of the thickness of the snow and ice cover shows that the thickness of the snow follows the thickness of the ice.
2. The thickness of ice and snow is approximately proportional.
3. The ratio of the thickness of the snow and ice cover is:
 - in the Novosibirsk reservoir – 0,43;
 - in the coastal zone of the Karasuk river – 0,52 ÷ 0,57;
 - in the middle course of the Karasuk river – 0,22 ÷ 0,29;
 - on the Om river – 0,22 ÷ 0,35.
4. The intensity of the increase in ice thickness during the study period is:
 - in the Novosibirsk reservoir – 0,92 cm/day;
 - on the Om river – 0,92 cm/day;
 - on the river Karasuk – 0,68 cm/day

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各类建筑系统中柱的标准分类和结构功能

STANDARD CLASSIFICATION AND STRUCTURAL FUNCTIONS OF COLUMNS IN VARIOUS TYPES OF BUILDING SYSTEMS

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抽象的。在本文中，将讨论建筑物中使用的多种柱子，它们的分类取决于载荷类型、横截面形状或用于构造柱子的材料。此外，柱故障的种类、柱必须设计的最佳尺寸以及柱在建筑物中的位置都将得到澄清。

关键词：柱，组合柱，轴向荷载，分析，长细比，预应力混凝土柱，破坏模式，结构。

Abstract. *In this article will be discussed many varieties of columns used in buildings, their categorization that depending on the type of loading, cross-section shape, or materials used to construct the column. Furthermore, the sorts of column failures, the best dimensions in which the column must be designed, and the column's position in a building will all are clarified.*

Keywords: *Columns, composite column, axial load, analysis, slenderness ratio, prestressed concrete column, failure mode, constructions.*

Introduction

One of the most significant structural elements and constructions is the column. Columns are vertical parts that are designed to bear axial compressive stresses. Columns, on the other hand, are known as compression rods because compression forces dominate their behavior. The load is transferred from the structure to the foundation through this component. Beams, floors, and columns are cast as a single piece in reinforced concrete constructions. Bending of the columns can create tensile forces in a portion of the cross-section. [1]

Depending on the load, length, column connections, frame trusses, and other factors, numerous types of columns can be used. In the following are the different types of columns used in construction:(See Fig.1)

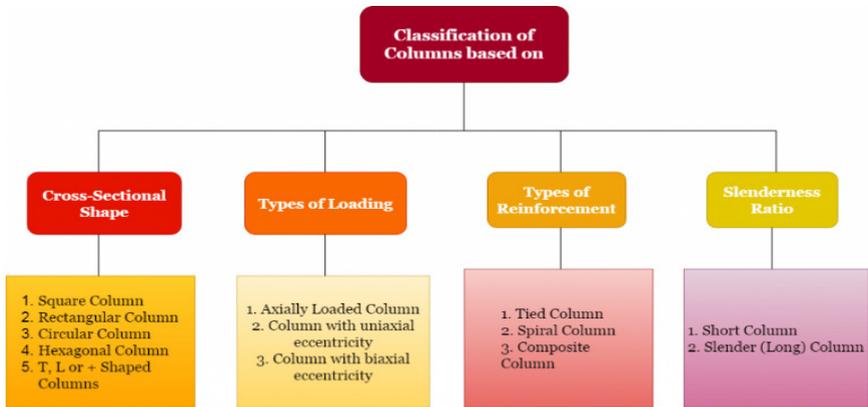


Figure 1. Classification of Columns

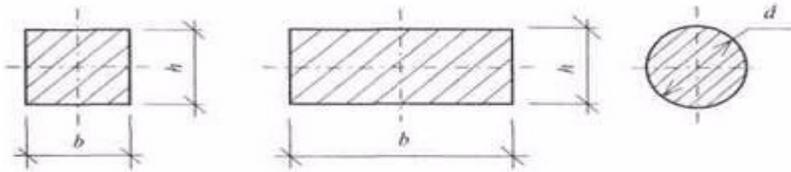


Figure 2. Type of column cross-sections

2- Classification of the column by load. (See fig.3)

- Columns with axial load

If vertical compressive loads act along the center axis of the column, it is called an axially loaded column. This type of column without bending is practically not found.

- Columns with eccentric loading: uniaxial

If the loads act at a distance "e" from the center of gravity of the cross section of the column, the column is called an eccentrically loaded column. In the case of a uniaxial eccentrically loaded column, this distance "e" can be along the x-axis or along the y-axis. These eccentric loads are bending moments in the x and y axes.

- Columns with eccentric loading: biaxial

In this type of column, loads are applied at any point in the cross section, but not along the axes. Loads because bending moments along the x and y axes simultaneously. [2]

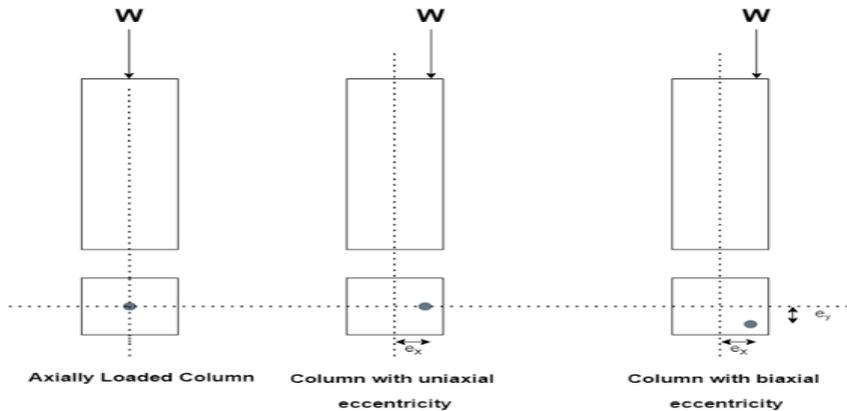


Figure 3. Classification of Columns based on Types of Loading

3- Classification based on column links. (See fig.4)

- Tied column

In a tied column, the longitudinal bars are interconnected by smaller bars. These smaller stripes are evenly spaced up the column. Steel tie bars in the column restrain the main longitudinal bars. More than 95 percent of all columns in buildings in non-seismic regions are connected columns.

- Spiral column

Spiral columns contain spirals to hold the main longitudinal reinforcement. The spiral is a spring type reinforcing rods. The main rods are arranged in a circle, and the ties are replaced with spirals. Spiral columns are used when high strength and / or high ductility is required. Because the helix resists lateral expansion of the column rods under high axial loads. The main rods are arranged in a circle, and the ties are replaced with spirals. Spiral columns are more commonly used in seismic regions. [3]

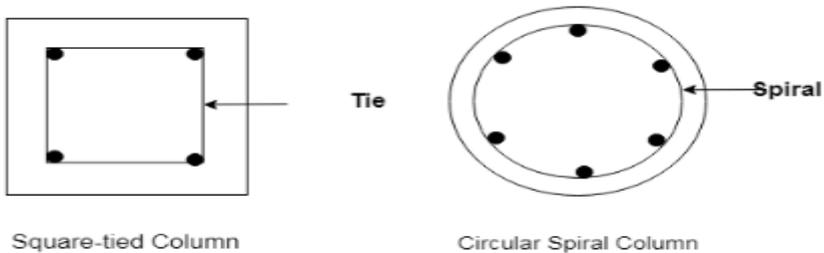


Figure 4. Classification of Columns Based on Types of Reinforcement

4- Column classification based on flexibility. (See fig.5)

- Short reinforced column

The slenderness ratio (the ratio of the effective length to the smallest transverse dimension) in a short reinforced column is less than 12. Short columns fail due to crushing or deformation of the steel rods. The loads that a short column can withstand depend on the size of the cross-section and the strength of the materials. Short columns offer some flexibility.

- Long reinforced column

Long columns have a slenderness ratio greater than 12. This column type is also known as a thin column. As the flexibility increases, the bending deformation increases. A long column fails due to the buckling effect, which reduces the load-bearing capacity. [4]

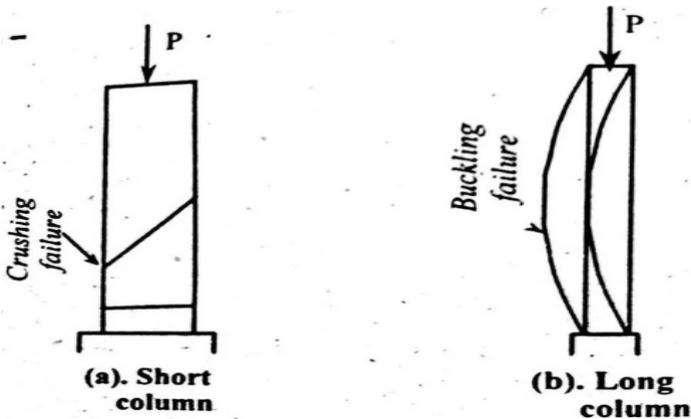


Figure 5. Column classification based on flexibility

5- Column classification by cross-sectional shape

- Geometric shape

Column sections can be rectangular, round, square, octagonal, hexagonal as required. Typically, columns can be square or rectangular, while spiral columns are circular. Round columns are used when high heights are required, for example in piles, bridge supports. Round columns provide a sleek and aesthetic finish. In contrast, rectangular columns are found in residential and office buildings. They are easy and cheaper to cast. [5]

- L - shaped

This type of column is not popular. The L-shaped column can be used as a cor-

ner column in a framing structure. This column design can be a good replacement to resist both axial compression and biaxial bending of corners.

- V-shaped

In a trapezoidal structure, this type of column can be used. V-shaped columns require comparatively more materials.

- T-shaped

T-columns can be used in bridge supports depending on design requirements.

6-Column classification according to building materials

- Reinforced concrete column

Reinforced concrete columns are the most common columns for frame construction. This type of column consists of concrete in the form of a matrix. The steel rod is cast in concrete. The concrete carries the compressive load and the reinforcement resists the tensile load. Reinforcement materials can be steel, polymers, or alternative composites. For a strong, plastic and durable structure, the reinforcement must have certain properties, such as thermal compatibility, high tensile stress resistance, good adhesion to concrete, anti-corrosion action, etc.

- Composite column.(See fig.6)

Composite columns are constructed using various combinations of structural steel and concrete. The interaction and holistic behavior of concrete and structural steel elements makes the composite column very stiff, more ductile, and cost-effective, therefore a structurally effective element in the construction of buildings and bridges. This type of column is also highly fire and corrosion resistant.



Figure 6. Type of composite column

- Steel, timber, brick column.

The steel columns are entirely made of steel. These columns are used in aircraft warehouses, closed shipyards, etc.

Wooden columns are made of timber. They provide an aesthetic appearance, creating a sense of spaciousness and openness. Wooden columns are intended for the construction of houses, reception rooms and repair rooms.

Brick columns are found in masonry structures. They can be reinforced with

concrete to increase strength, or they can be unreinforced. Brick columns can be round, rectangular, square, or elliptical in cross section. [6,7]

Some other column types

- Prestressed concrete column

Prestressed columns can be used as an expansion of reinforced concrete columns when bending moments are applied to the columns due to wind and earth forces, eccentric loads, or frame action. Prestressing converts a cracked area into a non-cracked area and resists significant bending. This type can be useful when the column is a tall thin column and a prefabricated column. [8]

- Greek and Roman column

Classical Greek and Roman architecture used four main columnar styles for their buildings and temples. These four types of columns were Doric, Ionic, Corinthian, and Tuscan. These columns look straight and uniform from a distance. But at close quarters, they may tilt or tilt slightly to the left or right.

Column Failure Mode

- Concrete or steel reinforcing compression failure.
- Buckling.
- Failure due to a combination of compression and buckling.
- Short and stocky columns are more prone to fail due to compression failure.
- Buckling is more likely with a long, narrow column.

Column Dimensions

Certainly, the columns have different dimensions that depend largely on the amount of load that will be column transferred from structures element to the foundation and the location of the column in the building that consists of several floors, as shown in Table 1. [9]

Table 1.

The relationship between the number of floors and the dimensions of the column

multi-storey building	Number of Storey	Size of column (mm)
10 storey building	1 to 10	700 x 700
20 storey building	1 to 7	750 x 750
	8 to 14	600 x 600
	15 to 20	450 x 450
30 storey building	1 to 10	800 x 800
	11 to 20	650 x 650
	21 to 30	470 x 470

Conclusion

Columns are vertical supporting structures. Reinforced concrete columns are used to strengthen one-story, industrial, residential, multi-story buildings. The columns take the load from the overlying elements and transfer it to the elements of structures located below. The reinforced concrete column designed to perform support functions at various building structures. With its help, beams, crossbars, trays and arches are strengthened. The columns are either prefabricated in the factory in prefab buildings, using cement M200 or M300 to construct it, or by casting on the work site.

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北极小冰川的实际情况（以普托拉纳高原为例）
**ACTUAL CONDITIONS OF THE ARCTIC SMALL GLACIERS (ON
THE EXAMPLE OF THE PUTORANA PLATEAU)**

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抽象的。北极地区的冰川作用主要以小型冰川作用为代表，面积达数万平方公里。在北极、亚北极地区，小冰川主要分布在乌拉尔、普托拉纳高原、拜兰加山脉、维尔霍扬斯克山脊北部、楚科奇高地等，绝对高度为400~1400米。它们位于气候雪线以下，它们的存在主要由山地气候因素决定。在1970年代初期，前苏联领土内的所有此类地区都编制了完整的冰川目录，其中包含有关已识别冰川对象的主要形态特征的信息。诚然，目录的内容主要基于对航拍照片的分析，只有一小部分冰川被路线研究覆盖（顺便说一下，只是偶尔的）。因此，毫无疑问，也无法进行任何详细的冰川学表征。正是在这种背景下，我们应该考虑由密歇根州立大学地理学院的实地团队于2002年8月、2003年、2004年、2019年在普托拉纳高原进行的冰川探险 [Kovalenko, 2011]。

关键词：小冰川，北极，亚北极，气候变化，冰川退化，森林火灾。

Abstract. *Glaciation of the Arctic territories is mainly represented by small forms of glaciation and covers an area of several tens of thousands of km². In the Arctic, Subarctic, small glaciers are mainly distributed in the Urals, the Putorana plateau, in the Byrranga mountains, in the northern part of the Verkhoyansk ridge, on the Chukotka highlands, etc., located at absolute heights from 400 to 1400 m. They are located below the climatic snow line, and their existence is determined mainly by oroclimatic factors. For all such areas within the territory of the former USSR, in the early 1970s, complete catalogs of glaciers were compiled, containing information on the main morphological characteristics of the identified*

glaciological objects. True, the content of the catalogs was based mainly on the analysis of aerial photographs, and only a small part of the glaciers was covered by route studies (by the way, only occasional ones). Therefore, there was no question and could not go about any detailed glaciological characterization. It is in this context that we should consider glaciological expeditions conducted by the field team of the Faculty of Geography of MSU on the Putorana plateau in August 2002, 2003, 2004, 2019 [Kovalenko, 2011].

Keywords: *small glaciers, Arctic, Subarctic, climate change, degradation of glaciers, forest fires.*

The main goal of the research undertaken in this work is to identify the modern regime and dynamic features of small forms of glaciation and to study the specifics of evolution against the background of current climatic changes. In this context, one should consider the meaning of the glaciological expeditions conducted by the Faculty of Geography of Moscow State University to the glaciers of the Lama Mountains of the Putorana Plateau in August 2002, 2003, 2004 and 2019. Almost all available literature was also analyzed, as well as primary sources containing the results of glaciological studies in the region of past years. The collection materials of the expeditions of the GIAS USSR and the MC RGS, carried out in particular in 1972 under the leadership of V.S. Koryakin and in 1993-2003 under the leadership of V.A. Sarana.

The glaciers of the Putorana plateau are scattered over a vast territory. The Lama Mountains became the testing ground for field research data, where three glacial centers were studied on the northern ledge, which abruptly drops off to the water area of lake Lama, with the Prives glaciers (№ 30 according to the USSR Glacier Catalog [1981]), Marlborough (№ 31) and the Strudoms snowfield lying in a deep square (fig. 1).



Figure 1. Fragment of a satellite image (Yandex): from left to right - perennial Strudoms snowfield, Prives and Marlborough glaciers

In the first two carats, classical crust-side-slope glaciers were observed (fig. 2), lying in the upper parts of the plateau ledges, in narrow strips along the leeward slopes. It is possible that these small forms of glaciation are the legacy of some previous, more ancient, stage of the Quaternary glaciation. They are characterized by small sizes: about 150 m long and about 250 m wide. Small (possibly moraine) hills are located within the enclosing kars.



Figure 2. Prives glaciers (right) and Marlborough (photo by V.V. Popovnin, 2004)

A feature of the morphology of the studied glaciers is the significant steepness of their surface (the average angle of inclination is 26°). The confinement of the Prives and Marlborough glaciers to the northern part of the Lama Mountains suggests that such an exposure is due to the prevailing direction of snow-carrying air

currents, as well as a favorable orientation relative to the sun's rays, which makes it possible to protect snow and ice from intense melting in summer. The surface of the Prives and Marlborough glaciers is complicated by longitudinal melting furrows, which become more pronounced as the slope of the surface increases. Many streams flow out from under the glaciers, and at the edge of the glaciers, swampiness and pronounced thixotropy of soils are often observed. Grain vegetation is widespread in Ulaïd languages [Kovalenko, 2005].

Materials and methods

Three expedition seasons 2002-2004 glaciological studies of two reference objects (Prives and Marlborough) on the northern ledge of the Lama Mountains, which were classified as glaciers, were continued at the end of the 2019 ablation period.

- snow profiling;
- densimetry in pits;
- measurement of the configuration of each object according to the data of digital photography (ground-based and from UAVs), including the results of decoding space images;
- calculation of the mass balance of glaciers № 30 and № 31

Our studies and the calculation of the mass balance of glaciers on the Putorana plateau are unique, since some basic balance characteristics of the two small glaciers, Prives and Malborod, for 2001/02, 2002/03 and 2018/19 balance years, were calculated for the first time for this region using direct regime measurements. True, due to the fact that the beginning of field studies could not be timed to the beginning of the ablation period, the most significant flaw in the design scheme was the lack of direct data on the maximum seasonal snow reserves at the studied objects. During the summer expeditionary work, data were obtained on the current water content in the layer of seasonal snow accumulation and the final water content of the firn residue (obtained during snow surveying in the middle and at the end of the ablation season) and density values (measured in pits). In such a situation, a non-standard indirect method was used to calculate the maximum winter snow storage.

Results

Based on the results of expeditions in 2002, 2003 and 2019, carried out on the snow-ice-firn formations of the Putorana plateau, the conditions of external mass transfer of glaciers were characterized, maps of the restored maximum snow content in their seasonal accumulation layer and maps of the water content of the firn residue for 2001/02, 2002/03. For the 2018/19 season, the values of the water content of the firn residue were obtained and the maximum seasonal accumulation was restored by the phytoindication method (2800 mm of water equivalent for the Prives glacier and 2500 mm for the Marlborough glacier).

The intensity of mass transfer processes on the Putorana plateau is much less than, for example, in the Caucasus. It characterizes its total glacier exchange, or the sum of the modules of the components of the mass balance equation. For the Djankuat recharge area, it is, on average, 4700 mm of water equivalent in long-term terms, in contrast to 3797 and 3470 mm of water equivalent on the Prives and Marlborough glaciers, respectively. Hence it follows that on Putorana it is almost a third less than in the Caucasus.

It is curious that the mass balance of the feeding areas of the studied Putorana glaciers is even comparable to the representative Djankuat glacier. The fact that at low values of the flow-rate, the mass balance is approximately comparable to the Caucasus, where accumulation and ablation are significantly higher, could indirectly indicate that the glaciation of the plateau is in a much more favorable budgetary state, if there were grounds to refute the counterargument that it can only be a reflection of the positive balance sheet anomaly of 2001/02 and 2002/03.

However, the most pronounced anomaly was the balance year 2018/19.

To assess the recent changes in the area of the Prives glaciers (fig. 3) and Marlborough (fig. 4), the Landsat 1973 and 2003 satellite images (with an error of $\pm 0.016-0.018 \text{ km}^2$) and Sentinel-2 with a spatial resolution of 10 m were decoded for August 2016 and 2019 (with an error of $\pm 0.008-0.009 \text{ km}^2$). It cannot be said that small forms of glaciation on the plateau are rapidly decreasing in area. If this were the case, then over a long period of time the situation would be similar to the glacier of Moscow State University in the Urals, which completely disappeared by 2019 [Nosenko et al., 2020]. Here, the contours of small forms from year to year can either sharply contract or expand sharply in their individual sectors. The area losses of both studied glaciers are approximately the same (0.060 km^2 each), although in percentage terms, the Marlborough area loss was slightly higher - 41% versus 37%. In other words, the Prives glacier, which is initially larger than its neighbor, is shrinking at a slower pace.

Nevertheless, compared with perennial snowfields (fig. 5), the configuration and sizes of small glaciers are still much more stable (fig. 6), and their fluctuations from year to year can be caused not so much by fluctuations in climatic conditions, but by errors in interpretation. In general, the outlines of small forms of glaciation have changed insignificantly over 17 years (fig. 3-4).

The period from 2016 to 2019 was generally favorable for the Gain and Marlboroughs, as they both increased by about 10%. In 2019, their area even increased due to abnormally low ablation (against the background of average accumulation values), caused, in particular, by a high degree of atmospheric smoke in the north of Krasnoyarsk Krai in the summer of 2019 due to forest fires in the surrounding taiga massifs. The degree of attenuation of the transparency of the atmosphere was so high that it was possible to look at the solar disk with the naked eye for

an average of 1-2 days during the expedition season. Apparently, the increasing intensity of forest fires in Yakutia, Krasnoyarsk Krai and adjacent territories in recent years partially explains the relative improvement in the balance conditions of glaciation of the plateau by a decrease in the expenditure component due to a cardinal weakening of direct solar radiation by an almost constantly hanging haze. It is not excluded, however, that an increased contribution to the accumulation of 2018/19 winter precipitation is also possible, including due to the greater deflationary transfer of snow to the quarries.



Figure 3. Prives glacier changes (№30): a -2002; b - 2019

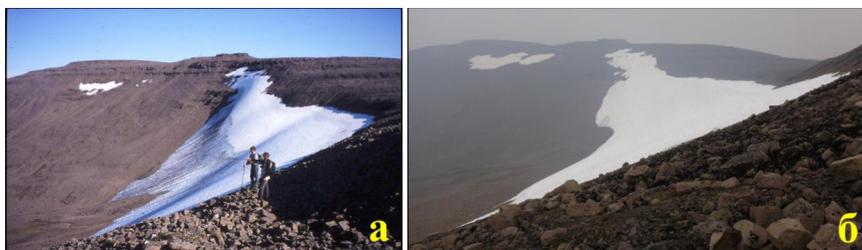


Figure.4. Marlboro glacier changes (№31): a -2002; b - 2019

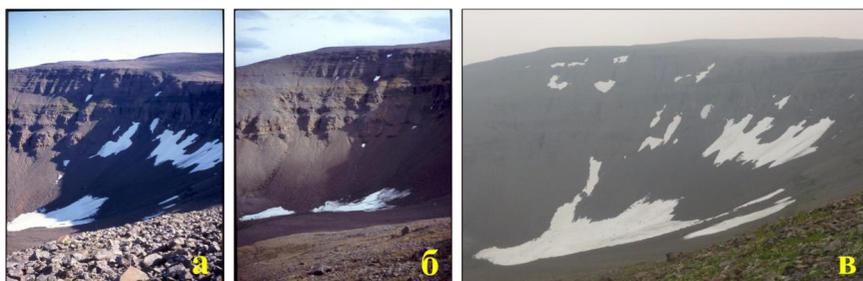


Figure.5. Change of Strudoms perennial snowfield : a -2002; b - 2003; c – 2019

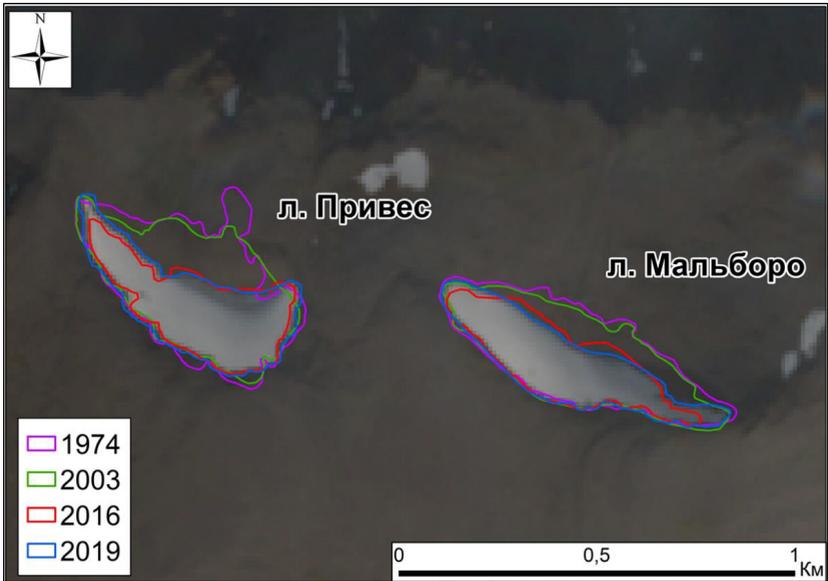


Figure 6. Changes in the areas of small glaciers

Table 1. Changes in the areas (km², in orthogonal projection) of the Putorana small glaciers

Year	Prives	Marlboro
1973	0.160	0.150
2003	0.148	0.136
2016	0.083	0.082
2019	0.100	0.089
1973-2019	-0.060 (-37%)	-0.061 (-41%)
2016-2019	+0.013 (+20%)	+0.007(+9%)

Conclusion

The small glaciers of the Putorana plateau are relatively stable, despite a clear increase in the average annual temperature and a decrease in the average annual precipitation in this region: seasonal trends in meteorological determinants are becoming much more important. During the research period, an increase in the amount of winter precipitation was recorded and a certain drying in summer, while the summer seasons became somewhat cooler. As a result, glaciers receive more

nourishment and lose less mass during the ablation period. In addition, the preservation of glaciers is favored by the presence of permafrost in the bedrock.

For the first time, an attempt was made to calculate the mass balance of small glaciers on the Putorana plateau.

The somewhat unexpected favorable state of all 3 objects in 2019, manifested in the positive anomaly of their areas and water content of the firn residue according to areal snow surveys, is discordant with the earlier conclusion about the persistent dominance of the tendencies towards deglaciation of the Putorana glaciers. Probably, the noted favorable budgetary situation is associated with a decrease in ablation caused by a decrease in the intensity of the insolation radiation flux due to rare forest fires in Siberia this year.

The response of glaciers to global changes in the glaciopause is most rapid in areas of small glaciation, such as the Putorana plateau. Moreover, it is in such areas that it is easier to organize and carry out work on measuring the components of the water-ice balance of glacial basins. Therefore, remote sensing studies carried out on the Putorana plateau are of both theoretical and methodological interest. They should be continued in the field with the establishment of regular water and heat balance monitoring at least at one representative Putorana site, and at the optimum at two or three.

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景观建筑领域透视实践型培训的任务与原则
**TASKS AND PRINCIPLES OF PERSPECTIVE PRACTICE-ORIENTED
TRAINING IN THE FIELD OF LANDSCAPE ARCHITECTURE**

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抽象的。文章介绍了在改造、景观美化、对象景观美化、自治市范围内进行的设计工作的方向，考虑了景观设计的基本原则和方法，给出了设计解决方案的例子。解释了在工作执行过程中形成的设计项目文档的类型和组成，以及设计的阶段和结果。通过景观建筑领域的实践导向培训来掌握所呈现的材料。

关键词：建筑、景观、外部环境、改造、园林绿化、园艺、设计、人才培养、设计成果。

Abstract. *The article presents the directions of design work carried out during renovation, landscaping, landscaping of objects, territories of municipalities, considers the basic principles and methods of landscape design, gives examples of design solutions. The types and composition of design project documentation, formed during the execution of work, as well as the stages and results of design are explained. The mastery of the presented materials is provided with practice-oriented training in the field of landscape architecture.*

Keywords: *architecture, landscape, external environment, renovation, landscaping, gardening, design, personnel training, design results.*

Architectural and design design focused on improvement, prospective renovation, landscaping, functional development of territories, objects of the external environment, is carried out as a set of research, development and artistic creativity aimed at creating compositions of natural and artificial elements, using, in particular, the following components:

vegetation, relief, water bodies, small architectural forms, decorative sculpture, visual communications, decorative coating.

Typical measures for complex landscaping, using landscape design technologies, include:

pre-project inspection of objects; architectural design and technical design; reconstruction and plastic organization of relief; construction and installation work on the territory; planting trees, shrubs and flowers; installation of fences, recreation facilities; architectural lighting of streets, quarters; placement of small architectural forms, design objects. planar solution of the terrain relief. Accordingly, the tasks of personnel training in the field of landscape architecture are: methods and means of design design, development of design and working technical documentation for landscape architecture objects; execution of works in the field of creation of design sketch and technical projects of objects of landscape gardening and construction.

Typical examples of solving practical problems of landscape design are presented in publications prepared based on the results of renovation and improvement of facilities in the city district of Togliatti, Samara region, Russian Federation [1, 2, 3].

1. General principles of organizing a comfortable space of the external environment

1.1. *Balance principle* assumes the choice, when forming a design concept, a variant of the visual perception of the territory:

even distribution of attention over the object, when using symmetrical zones, fragments, figure 1; the formation of asymmetric, but visually balanced configurations of zones, fragments, figure 2.



Figure 1. Symmetrical terrain fragments

Also used: the creation of asymmetric configurations, with a specially unbalanced design components, the division of fragments of the territory by composition, as components: foreground, background.

1. 2. **Focus principle** provides for the presence of a landmark on the object that attracts the main attention of visitors, for example: an artistic flower arrangement, MAF, woody plants, an entrance area of a house, a water body, a recreation area, for example - figure 3.



Figure 2. Asymmetric balance of the landscape, Japanese garden



Figure 3. Focal composition

1.3. **Simplicity principle** – limiting the diversity, number of plant species, materials, MAF, other components on the territory; ensuring a decrease in visual load when perceiving an object;

1.4. **Rhythm principle**, ensuring the recognizability and attractiveness of the object, due, in particular, to: repeated flower beds with the same color pattern; preservation of the observed design solutions when moving, walking around the territory; using the rhythm of color spots, which eliminates the monotony of the landscape.

1.5. **Analogy principle** involves the use of design solutions that are sufficiently close to the psychology of visitors, known and (or) used in other territories, providing the usual comfortable perception of the object being created.

The presented principles of landscape formation ensure the achievement of the required level of improvement and comfort [4, 5].

2. Typical methods of landscape design of objects

2.1. **Organization of space** using of volumetric, planar and linear compositions, as well as visual correction of the perception of the object [6, 7].

volumetric solutions: created using stone, relief, vegetation, architectural forms; planar fragments, based on: lawns, reservoirs, parterres, lawns, flower beds, rabatok; linear fragments of territories: paths, alleys, roads.

The perception of an object can be adjusted taking into account the peculiarities of vision: a visual approximation of a fragment of the landscape to the observer is ensured by the use of plantings with variegated, silvery and light-colored foliage, figure 4.



Figure 4. Hedge, shrub "Siberica" Doren white

2.2. *Formation of the color scale of the object* – a set of colors and their shades, in harmony with each other, is an urgent task, the solution of which largely determines the aesthetic perception, the attractiveness of the object, and the psychological impact. The design takes into account the following factors:

the palette of landscapes changes at least 9 times throughout the year; colors: orange, pink, yellow, red stimulate an increase in activity, create a good mood for the observer; ambient colors: blue, purple, green have a calming effect, help lower blood pressure, heart rate,

example - figure 5.



Figure 5. Activating color scheme of the flower bed by the garden path

The harmonious combination or contrast of the colors of the components of landscapes are created taking into account the need to eliminate color chaos, oversaturation of the object. The use of attractive color combinations is recommended: blue / orange, green / red, yellow / purple; selection, for components with different color combinations, differing in the area of fragments of the territory.

2.3. Taking into account the position of light sources and created shadows, in relation to fragments of an object, allows you to highlight the images of groups of plants, architectural forms, as well as to increase the level of comfort of being on the territory.

The specified required effect is provided in the morning hours of the day by the location of the determined landscape components to the south, east or north of the observation points. When the effect is oriented towards evening observation, the selected landscape components are located to the south, west or north of the observation points. Application of additional evening illumination of the territory - figure 6.



Figure 6. Evening artificial illumination of the landscape

2.4. **Lighting and component color** are mutually related in the visual perception of the landscape, are taken into account when solving design problems: red on a bright daylight hours visually brings the components of the landscape closer, and at dusk it is the background color, increases the depth of perception; blue color during daylight hours visually removes landscape components, is used to visually expand areas of the territory; violet, dark blue and black colors at dusk visually reduce the volume of the observation object; yellow color visually expands, increases the volume of the formed component of the territory; green balances other bright colors, which, in particular, is taken into account when creating decorative borders, lawns.

2.5. **Inclusion of small architectural forms into the structure of the object**, ensuring the achievement of functional and aesthetic comfort for a person. At the same time, the compositional consistency of the MAF with the surrounding buildings and landscape design is important. To enhance the expressiveness of space, relief modeling, the creation of artificial water fragments are used.

3. Types and composition of design project documentation

As a result of the implementation of the architectural landscape project, a set of documentation is formed:

3.1. General plan, basic scale: 1:500, which is drawn up taking into account the requirements for the object of landscape architecture;

3.2. Improvement plan of the facility, which includes layout drawings indicating the location and method of execution of the road and path network, MAF and decorative elements; layout drawings - part of the documentation sets containing a graphical representation of the location of the designed structures, fragments of the object, in relation to the existing reference bases; the specification indicates the equipment used, its operational characteristics;

3.3. Landscaping and flower arrangement plan with a description of the assortment of plants in the attached statement; it is possible to select a dendroplane for an object - a topographic plan that reflects the placement of trees and shrubs, and an inventory list;

3.4. Graduation drawings with spot elevations and earthwork specification;

3.5. Cost estimate, including the cost of planting material and work planned for the implementation of the project.

3.6. An explanatory note, which displays, explains the developed technical, dendrological, design solutions, and also provides a timetable for the implementation of the project.

An additional set of project documentation may contain:

3.7. Plan and estimate of dismantling works, with a list of fragments of the territory, large plants to be liquidated at the facility;

3.8. Documentation for the creation of new design fragments at the facility, in particular: pergolas, sports and playgrounds, a pond, fountains, slopes, retaining walls, special structures;

3.9. Drawings and descriptions, budget documentation for the manufacture of original small architectural forms and structures.

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列宁格勒州紫菀蒲抗生态特性及种子产量
**ANTIECOLOGICAL CHARACTERISTICS AND SEED
PRODUCTIVITY OF PHACELIA TANACETIFOLIA IN LENINGRAD
OBLAST**

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抽象的。 *Phacelia tanacetifolia* Benth. 来自 *Hydrophyllaceae* 科的一年生草本有毛植物，高达 80 厘米。它在北美西南部和墨西哥野生生长。它被栽培为一种多产的作物。 *Phacelia* 对生长条件的维护成本低，它在纯净状态下和与其他芳香植物一起生长良好。经常在不同时间播种，以形成开花传送带，加强蜜蜂的饲料基础和长期收集蜂蜜。 *Phacelia* 具有许多经济上有价值的特性。

我们研究了 *phacelia* 花的形态，它对异种受精和昆虫授粉的适应。 *phacelia* 开花的昼夜节律，白天和花发育不同阶段的花蜜分泌特征。我们还研究了种子、果实和种子生产力的形态。

对列宁格勒州条件下的 *phacelia tanacetifolia* 的研究表明，它具有生态可塑性，能很好地适应快速变化的气候。它具有很高的蜂蜜和种子生产力。 *Phacelia* 有望成为一种芳香植物、饲料、药用植物以及绿色肥料。

关键词： *phacelia tanacetifolia*，花，开花，授粉，花蜜分泌，蜜蜂，大黄蜂，种子，种子生产力。

Abstract. *Phacelia tanacetifolia* Benth. from the *Hydrophyllaceae* family is an annual herbaceous hairy plant up to 80 cm high. It grows wild in the southwest of North America and Mexico. It is cultivated as a melliferous crop. *Phacelia* is low maintenance to growing conditions, it grows well in the pure state and with other melliferous plants. It is often sown at different times to create a flowering conveyor, strengthen the feed base for bees and long-term honey collection. *Phacelia* has many economically valuable properties.

We studied the morphology of the phacelia flower, its adaptation to cross fertilization and insect pollination. Diurnal rhythm of phacelia flowering, features of nectar secretion during the day and at different phases of flower development. We also researched the morphology of seeds, fruits and seed productivity.

The study of phacelia tanacetifolia in the conditions of the Leningrad oblast showed that it has ecological plasticity, adapts well to a rapidly changing climate. It has high honey and seed productivity. Phacelia is promising as a melliferous, feed, medicinal plant, as well as a green fertilizer.

Keywords: *phacelia tanacetifolia, flower, flowering, pollination, nectar secretion, bees, bumblebees, seeds, seed productivity.*

Introduction

Phacelia tanacetifolia Benth. from the *Hydrophyllaceae* family is an annual herbaceous hairy plant up to 80 cm high. It grows wild in the southwest of North America and Mexico [1]. It is cultivated as a melliferous crop. Phacelia is low maintenance to growing conditions, it grows well in the pure state and with other melliferous plants. It is often sown at different times to create a flowering conveyor, strengthen the feed base for bees and long-term honey collection. Phacelia blooms richly and for a long time; its flowers emit a lot of nectar. Phacelia honey is used in folk medicine in case of gastrointestinal, cardiovascular diseases and for enhancing the immunity etc. [2]. A biochemical study of the top showed that it contains flavonoids, phenolcarboxylic acids, tannins, etc. [3]. In addition to the nectariferous properties, phacelia has other agronomic characters. So, it is sown on the fallow land, and after collecting nectar, it is used to feed animals fresh, in the form of silage and hay, or plowed up as green fertilizer. The yield of herbage of phacelia can reach 30 t/ha [4]. Even small areas of phacelia crops can serve as bait for pollination of other crops. For example, on seed crops of clover and alfalfa, the yield of seeds increases significantly if phacelia grows nearby [5]. Some Californian phacelia varieties are very beautiful and decorative.

Currently, a comprehensive study of phacelia is being carried out in many regions of Russia and abroad [6, 7, 8]. Breeding is carried out, varieties of phacelia have been bred [9]. Its melliferous and other useful properties are being studied [2, 5], sowing dates in different regions and the use of phacelia for greening agriculture in arid regions of Russia, etc., are being considered [10]. Our earlier antiecolological studies of phacelia and other melliferous plants showed that starting from the second half of August in the regions of the Leningrad oblast honeyflow from natural melliferous plants ends [11]. Therefore, sowing phacelia in areas located near an apiary later can provide bees with an additional source of nectar. Since the honey from the phacelia does not crystallize for a long time, it can be a complete food for bees in winter.

The aim of the study – to study the characteristics and duration of flowering, the nature of pollination, nectar secretion, the activity of bees and bumblebees, and to establish the melliferous capacity of the *phacelia tanacetifolia* in the conditions of the Leningrad oblast.

Materials, methods and objects of research

The object of the research was the phacelia *tanacetifolia*, variety "Natalia". The experiments were carried out in the collection nursery of medicinal and essential oil plants of St. Petersburg State Agrarian University. The soil of the plot is sod-podzol, highly cultivated. The humusness is 3.5-3.9%. Field area 7 m², tier is three-time. The dynamics of phacelia flowering and the flight rhythms of insect-pollinators were studied according to generally accepted methods. The nectar from the flower was extracted by ablation. The amount of sugars extracted from the flowers was determined by the Bertrand's method.

The summer of 2017 was cold and rainy, with average temperatures well below the long-term average. Precipitation in April, August and September exceeded the long-time average annual, and in the remaining months was close to norm. Temperatures were unevenly distributed in 2019: in April and May, the average monthly temperature was close to the norm, in June it exceeded it by 2.7 °C, and in July, it was below the norm by 3.4 °C. Sufficient moisture fell in April and September, and climate in the other months was torrid. June and July of 2021 turned out to be very hot and dry, the average monthly air temperature was significantly higher than the norm, the amount of precipitation for these months was only 32.6 mm. The temperature of the remaining months was close to the long-time average annual or slightly below the norm.

Research results

Sowing of phacelia was usually carried out in mid-June; seedlings appeared quickly i.e. in 8-12 days (Table 1). It usually takes 39-46 days from sowing to the beginning of flowering. Plant height at the time of flowering was 75-80 cm in 2017-2019 and 63-67 cm in 2021. Mass flowering lasted 10-12 days. During the years of research, the flowering of the phacelia lasted until the end of September and the beginning of October, which provided the bees with an additional source of nectar to replenish food reserves for the winter. The branching degree of the main stem of the plant was 1-2 shoots in 2017-2019, up to 7 shoots of the second order in 2021. Phacelia inflorescences are dense, densely pubescent curls, collected in semi-umbrellas. The opening of flowers in the curl occurs from the bottom up, while it unwinds, straightens and lengthens, reaching 7-9 cm in length. The number of flowers in curls, depending on the position on the plant, ranges from 23 to 45 pcs. During the period of mass flowering, up to 8 flowers are simultaneously revealed in the curl.

Table 1.

Dynamics of the onset of phenological phases of phacelia tanacetifolia in 2017-2021.

Year / Phenophases	Sowing	Seedlings	Branching of the main shoot	Budding	Flowering	Fruiting
2017	15.06	26.06	20.07	25.07	01.08	15.08
2019	17.06	29.06	21.07	27.07	05.08	15.08
2021	17.06	25.06	14.07	20.07	30.07	10.08

Phacelia flowers have very short pedicels, calyces 5.9-7.1 mm long, sepals are elongated lanceolate, pointed, densely covered with long straight hairs. Corolla is pink-purple, 7.9-9.0 mm long, with a tube and 5-lobed limb. There are 5 stamens; the anthers are small, bluish, on long blue filaments protruding from the corolla. The pistil column is filiform, long, deeply divided, covered with hairs in the lower part, also protruding from the corolla. A discal yellowish nectary is located under the ovary at the bottom of the corolla tube.

Phacelia is a cross-fertilizing plant. Its flowers have morphological and physiological behavior that limits self-pollination and promote cross-pollination. Phacelia flowers are characterized by dichogamy in the form of protandria i.e. the maturation of the anthers and stigma of the pistil at different times, as well as the spatial separation of the stamens and pistil - herkogamia.

The flowers of plants attract insects by providing them with food - nectar and pollen, which play a major role in cross-pollination. In addition to food, the bright color of flowers, the shape of the corolla, the smell and various patterns on the corollas attract insects-pollinators. These are the nectar indicators that give information about the location of nectar and pollen. Phacelia flowers are bright, collected in dense curls, well distinguishable against a background of green leaves. The tubular shape of the corolla with a 5-lobed limb serves as a landing area and attracts bees and bumblebees. Blue anthers with bright blue pollen are protruded far beyond the flower and attract pollinators. All this points to the entomophilous organization of phacelia flowers.

In multi-flowered curls, flowers are at different stages of development, both within the same plant and on the plantation as a whole. Visiting flowers with dusty anthers, insects transfer pollen grains to flowers, whose stigma is ready to receive pollen, and thus produce pollination. We studied the diurnal rhythm of phacelia flowering, nectar secretion, sugar productivity and visiting flowers by bees and bumblebees under favorable conditions. It is known that the daily flowering rhythm is associated with the process of pollination. Flowers open more at a time when pollinators are most active. Phacelia is characterized by the daytime

type of flower opening (Fig. 1).

According to our observations, the dynamics of flower opening depends not only on the illumination of the plant, but also on the air temperature. The opening of flowers in multi-flowered curls occurs with an interval of 1.5-2 hours at a temperature of 19-20 °C, at higher temperatures the interval is reduced. Flowers open from early morning until evening (21-22 h), but more flowers opened in the afternoon. The nature of pollinators visiting flowers coincides with the daily flowering rhythm.

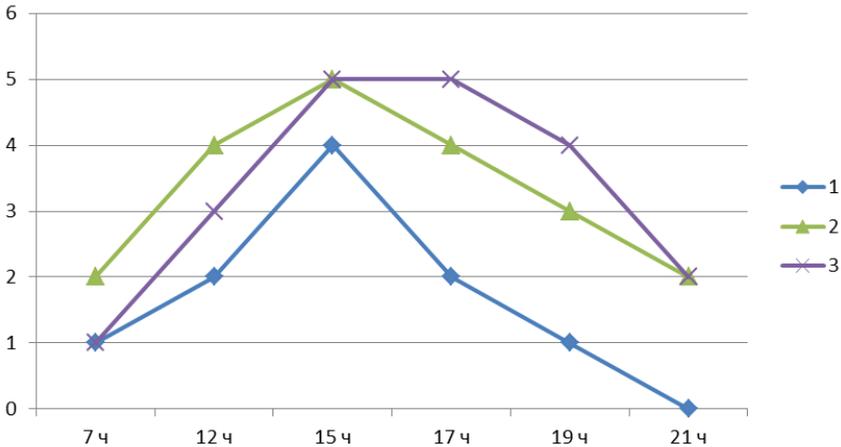


Figure 1. Diurnal type of opening of *phacelia tanacetifolia* and the flight of insect-pollinators (06.08.21): 1 - the average number of opened flowers in a curl, pcs; 2 - the average number of bees per 1 m²; 3 - average number of bumblebees per 1 m²

The nectarin flowers is produced throughout the day, the intensity of secretion depends on many factors, including weather conditions and the phase of development of the flower itself (Fig. 2). After the flower opens, the filaments are straightened and protruded outside the corolla. The pollen grains ripen, and the dusting of the anthers occurs. Later, the phase of the stigma's readiness to receive pollen begins. After pollination and fertilization, the corolla wilts, and the calyx remains with the developing ovary. During the opening phase of the flower, little nectar is produced and the sugar content in the nectar is 0.1 mg. The largest amount of nectar is produced in the phase of dusting of the anthers, much less in the stigma phase. During the withering of the corolla, the activity of nectaries gradually ends.

On a warm sunny day, the most intense nectar excretion was observed in the afternoon. Bees and bumblebees actively visited flowers throughout the day. In

the morning hours there were more bees, in the afternoon hours the number of bees and bumblebees was the same, and in the evening hours there were more bumblebees (Fig. 3).

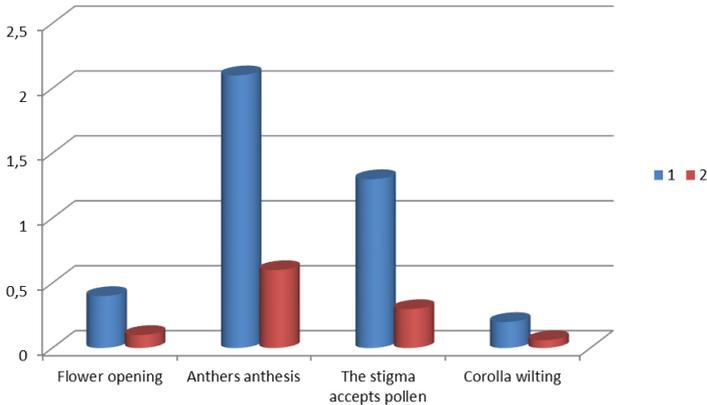


Figure 2. Dynamics of nectar excretion and the amount of sugar in the flowers of the phacelia tanacetifolia, depending on the phases of flower development: 1 - the amount of nectar in mg; 2 - the amount of sugar in the nectar in mg

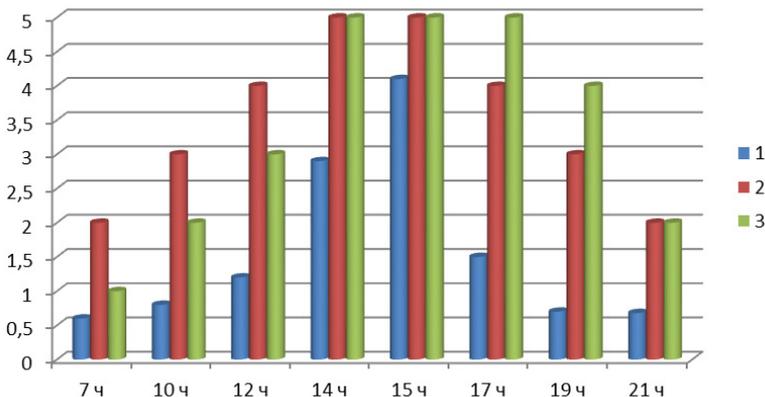


Figure 3. Dynamics of nectar excretion in the flowers of phacelia tanacetifolia and the nature of the flight of insects during the day (06.08.21): 1 - the average amount of nectar in a flower, mg; 2 - the number of bees per 1 m², pcs.; 3 - the number of bumblebees per 1 m²

The calculation of biological melliferous capacity was based on the amount of sugar in the nectar of a flower, the number of flowers in curls, the number of curls on plants, and the number of plants per m². The results are demonstrated in Table 2. The biological melliferous capacity of the phacelia is very high and depends on many factors; it reached almost 700 kg/ha in our experiments under favorable conditions.

The fruit of the phacelia *tanacetifolia* is an ovoid brown capsule 3.6 mm long and 3 ml wide. It opens vertically with two valves; at the top of the capsule there are white protruding hairs.

Table 2.
Indicators of melliferous capacity of phacelia tanacetifolia

Year	Average number of flowers per plant,	Sugar productivity of 1 flower, mg	Duration of flowering of 1 flower, days	Biological melliferous capacity, kg/ha
2017	81	1,20	2	558,7
2019	93	1,21	2	602,0
2021	210	1,06	1,8	695,6

4 oval-shaped seeds are formed in the capsule. On the outside, the seeds are convex, wavy-wrinkled, with cells in the deepening of wrinkles and with small dimples along the edge of the wrinkles. On antanal side, the seeds are dihedral. Coloring - from light brown to black.

The efficiency of plant pollination is determined by the level of seed productivity. In addition to pollinators, weather conditions directly and indirectly affect seed productivity. Therefore, 3-4 seeds are formed more often in a capsule in the lower flowers of the curl, in the upper flowers - 1, less often - 2 seeds, and the very last flowers of the curls of seeds almost do not form. Due to unfavorable weather conditions in 2017, which directly influenced the development of phacelia plants, and also impeded the active flight of pollinators, the coefficient of seed productivity turned out to be low (Table 3), 1 seed was formed in capsules, less often 2.

Table 3.
The level of fruit formation and seed productivity of phacelia tanacetifolia in 2017 and 2021

Year	Fruit formation, %	Seed productivity index, %	Weight of 1000 seeds, g
2017	86,7	38,3	1,32
2021	80,0	52,0	1,43

It should be noted that the dry and hot weather of the growing season of 2021 had a positive effect on the state of the phacelia *tanacetifolia*. The plants grew and developed well, branched strongly, bloomed profusely and for a long time, and did not suffer from drought. High seed and melliferous capacity was noted. This phenomenon can be explained by the origin of phacelia. Its homeland is the south-west of North America, where a hot and dry desert climate prevails, and the average annual air temperature is 20-24 °C.

Conclusion

The study of phacelia *tanacetifolia* in the conditions of the Leningrad oblast showed that phacelia *tanacetifolia* has ecological plasticity, adapts well to a rapidly changing climate. Insect-pollinators from the local fauna actively visited it. Phacelia has high melliferous and seed productivity. Sowing phacelia in mid-June provides bees and bumblebees with an additional source of nectar during August and September. Phacelia is promising as a late summer melliferous plant.

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马肌红蛋白尿的发病机制

PATHOMORPHOGENESIS OF EQUINE MYOGLOBINURIA

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抽象的。肌红蛋白尿症 – 这是一种急性疾病，其特征是严重的代谢紊乱、营养不良的变化和肌肉中乳酸和其他酸的积累、轻瘫或麻痹以及中枢神经系统的退行性变化、血液和尿液中出现肌红蛋白和其衰变产物（肌源性自体中毒）。马肌红蛋白尿症是麻痹性和地方性动物。第一种偶尔发生，第二种是地方性动物。该疾病迅速从潜伏病程转变为具有发展为轻瘫和瘫痪的临床表现病程。两种形式在许多症状、病理指标上是相同的，并且有条件地将它们组合在通用名称“肌红蛋白尿”下。这种病不是很了解。众所周知，麻痹性肌红蛋白尿症会影响 5 至 8 岁的严重类型、营养良好的马，但也注意到用于其他目的的马：运动、景点和轻度工作。该病更常发生在冬季和春季。肌红蛋白尿可作为一种过敏反应过程，在某些植物性食物对蛋白质进行初步致敏后发生。该病发生在长时间休息、被迫停工或大量单方面喂养后。导致这种疾病的原因是在黑暗和闷热的房间里发现了马。这种疾病的症状发生在工作开始时或工作后几个小时。冷却动物和通风会增加疾病的发生率。

关键词：肌白蛋白尿、坏死、麻痹、瘫痪、肌红蛋白、代谢紊乱、内科疾病、肌溶解症。

Abstract. *Myoglobinuria - This is an acute disease characterized by profound metabolic disorders, dystrophic changes and the accumulation of lactic acid and other acids in the muscles, paresis or paralysis and degenerative changes in the central nervous system, the appearance in the blood and urine of myoglobin and its decay products (myogenic autointoxication). Equine myoglobinuria is paralytic and enzootic. The first occurs sporadically, and the second is noted enzootically.*

The disease quickly passes from a latent course to a clinically expressed one with developed paresis and paralysis. Both forms are identical in a number of symptoms, pathological indicators, and conditionally they are combined under the general name "myoglobinuria". The disease is not well understood. It is known that paralytic myoglobinuria affects horses of a severe type, well-nourished, at the age of 5 to 8 years, although it is also noted in horses used for other purposes: sports, attractions and light work. More often the disease occurs in winter and spring. Myoglobinuria can occur as an allergic-anaphylactic process upon preliminary sensitization of certain plant foods with proteins. The disease occurs after a long rest, forced downtime or abundant one-sided feeding. The contributing cause of the disease is the finding of horses in dark and stuffy rooms. Symptoms of the disease occur at the beginning of work or a few hours after it. Cooling the animal and drafts increase the incidence of illness.

Keywords: *myoglobinuria, necrosis, paresis, paralysis, myoglobin, metabolic disorders, internal diseases, myolysis.*

Enzootic myoglobinuria (Myoglobinuria enzootica) occurs in areas where soils are poor in nutrients, macro - and micronutrients. This form of the disease occurs in farms with one-sided and inadequate feeding: hay from acidic soils, lack of proteins, carbohydrates, vitamins, calcium, phosphorus and trace elements - iodine, cobalt, copper, etc.

With prolonged rest, the skeletal muscles of the horse are in a semi-relaxed state, which leads to a decrease in redox processes in them. I. Marek explains the development of the pathological process in paralytic myoglobinuria by auto-intoxication. Due to overstrain after rest, glycogen is intensively decomposed in the muscles with the formation of lactic acid and under-oxidized products. High acidity of muscle tissue leads to its numbness due to the coagulation of myosin. Then myoglobin dissolves, muscle degeneration begins (fatty degeneration). Dystrophic changes occur in the liver, myocardium, kidneys and spinal cord; the latter is the cause of paralysis of the pelvic limbs. P. 3. Gzhitsky indicates that with hypofunction of the insular apparatus of the pancreas, the content of sugar and creatine in the blood rises, which leads to an accelerated breakdown of phosphogen and glycogen; resynthesis of the latter becomes impossible. A.P. Onegov et al. note that as a result of metabolic disorders due to malnutrition, a large amount of acidic products (acidosis, toxemia) accumulates in tissues and organs, which leads to hardening of one or another muscle group, disintegration of myofibrils, myoglobin and the release of the latter with urine. Deep biochemical changes occur in muscles, glycogenesis, phosphogenesis, synthesis of adenylenephosphoric acid, etc. are disrupted. A.V. Sinev, A.G. Smirnov believe that the loss of myoglobin is essential in the development of the disease. A.V. Zharov explains the development

of the disease by increased breakdown of glycogen in muscles, the accumulation of under-oxidized products of lactic acid metabolism and the development of myogenic autointoxication. As a result of acidosis, the acid-base balance of the blood decreases, dystrophic changes in the heart muscle, kidneys, liver, lumbar and sacral spinal cord develop, resulting in the appearance of paralysis and paresis. Acidosis causes the release and excretion of myoglobin and its decay products in the urine (urine is reddish or brown-red).

Inadequate and unilateral feeding of horses and foals causes changes in metabolism, causes deep dystrophic changes in the liver, skeletal muscles, myocardium and other organs. Muscles lose their contractile function, sick horses cannot move independently. All of the above reasons contribute to a decrease in resistance, reproductive capacity and large mortality of young animals.

Symptoms of paralytic myoglobinuria appear during work, after one or two days of rest. The horse begins to sweat, his breathing quickens, the shakiness of the pelvic limbs appears (bending over). She falls to the ground in a state of excitement, tremors are noted, her eyes are widened, makes attempts to get up, but, exhausted, falls on her side. The sensitivity of the skin initially persists, but after 2-3 days anesthesia occurs in the pelvic extremities. Affected muscles of the back, croup, pelvic limbs are tense, hard and painful. Due to strong swelling, they are sharply delimited by furrows from adjacent healthy muscles. When worried, the horse injures certain parts, especially the head. The body temperature is initially normal, but during strong arousal it rises to 39.5°C. The heartbeat is quickened, at first the tones are intensified, later weakened, especially the first tone. The appetite is preserved, the thirst is intensified. Peristalsis is somewhat weakened. At the beginning, the act of urination is preserved, but later paresis of the bladder is noted. The urine is cherry-colored, dark brown or brownish. In addition to myochrome, a large amount of urea, protein and glucose are found in it. The blood coagulates slowly, the serum is pink due to oxyhemoglobin. The number of erythrocytes and hemoglobin is within normal limits or slightly increased. The sugar content is sharply increased - from 167 to 267 mg%, the alkaline reserve is reduced by 2-3 times. Hypocalcemia. The content of lactic acid, creatine and inorganic phosphorus is increased. Paresis and paralysis of the affected limbs appear. On the 2-3rd day of illness, with severe course, bedsores are formed, which turn into gangrene. Equine enzootic myoglobinuria is characterized by the duration of the premorbid period - from 2-3 weeks to 3 months. During this period, sick horses are noted for rapid fatigue, tremors, and functional insufficiency of the cardiovascular system. With physical overstrain or exposure to other unfavorable factors, progressive stiffness of the movements of the thoracic and pelvic limbs, unsteadiness of the rear, swelling and hardening of the muscles of the croup, back, masseters and lips are observed. Frequent fibrillar tremors of the triceps brachii.

In the affected muscles at the onset of the disease, there are no tendon reflexes, sensitivity and mechanical excitability, later they are restored. General depression is revealed. Swelling appears on the dewlap, abdomen, scrotum on days 2-5. Foals have erythematous stomatitis, ulcers of the oral mucosa; the tongue swells a lot and does not fit into the oral cavity, glossitis is sometimes noted; the muscles of the head are mainly affected, especially the masseters. Taking food and even water becomes impossible. The animal dies from exhaustion. The acidity of gastric juice decreases, its digesting power is reduced several times, achilia sets in. Intestinal peristalsis is weakened, defecation is impaired, colic often appears. Bladder paresis. Urological symptoms are the same as in paralytic myoglobinuria. The blood serum of foals is milky in color, and in adults it is often opalescent (presence of lipids). Hemoglobin and erythrocytes are within the upper physiological limit. Aneosinophilia, basopenia, lymph - and monocytopenia, neutrophilia with hyporegenerative nuclear shift are noted.

Pathological changes

The subcutaneous tissue in the area of the dewlap, the abdomen is edematous and infiltrated. Mucous membranes with a bluish tinge, edematous. The muscles are pale, resemble cooked meat, especially in the croup, back, and masseters and triceps muscle of the shoulder. With a prolonged course in the muscles, especially in the masseter and myocardium, fibrosis occurs. The external muscles become denser, and in the intermuscular connective tissue, serous edema, hemorrhages. During histological examination, carbohydrate, granular, fatty degeneration is established in the affected muscles. Sometimes the development of hyalinosis of myofibrils, their decay and the development of waxy necrosis is observed. In protracted cases of the disease, dystrophic changes are accompanied by the development of granulation tissue in the lesions, with its transformation into scar tissue. (fig 1,2)

In the acute course of the disease, irreversible dystrophic-degenerative changes in skeletal muscles prevail (in the form of melting of muscle tissue with preservation of the sarcolemma (fig. 3), myocardium and massive hemorrhages and stagnant processes in all tissues and organs.

In the pancreas and thyroid glands, adrenal glands and pituitary gland, dystrophic-inflammatory processes and partial atrophy of glandular cells are observed. The spleen is slightly enlarged, with punctate hemorrhages under the capsule. In some cases, a productive process is noted (fig 4). Lungs are reddish in color, a bloody foamy liquid flows from the incision surface. In the lung tissue, congestive hyperemia, perivascular edema, focal compensatory emphysema, focal pneumonia or purulent bronchopneumonia can be found due to the ingress of a foreign body into the bronchi as a result of pharyngeal paralysis (fig. 5.6).

Heart - changes in the myocardium are similar to changes in skeletal muscles. As a result of the development of granular and fatty degeneration. The myocardium is flabby, gray in color. The heart muscle takes on the appearance of boiled meat. Hemorrhage under the epicardium and endocardium. The right atrium is usually dilated.

Liver and kidneys - changes are characterized by the development of granular and fatty degeneration (fig. 6), acute congestive hyperemia, focal necrosis is possible. The liver and kidneys are enlarged, swollen, flabby. Due to the development of protein-fatty degeneration and acute congestive hyperemia, the surface of the liver incision has a muscat color. In the glomeruli and tubules of the kidneys during histological examination, a large amount of myoglobin and focal hemorrhage are noted, in addition, in the tubules, cylinders are formed from cells of desquamated epithelium. (fig. 8.)

Bladder - the mucous membrane is hyperemic. Urine is reddish or reddish-brown in color. The change in the color of urine is due to the entry of dissolved myoglobin into the blood and its excretion in the urine (myoglobinuria).

In the central nervous system - changes are characterized by perivascular and pericillary edema or (dropsy) dystrophy of nerve cells, congestive hyperemia and the development of encephalomalacia. The vessels of the brain and its membranes are overflowing with blood. Due to the development of hydropic dystrophy, edema of the brain and its membranes develops, as well as softening of the brain.

Treatment

Sick horses are provided with complete rest, soft bedding, and a separate, well-ventilated, draft-free room. They are turned over from side to side 2-3 times a day. It is necessary to carry out daily catheterization of the bladder in order to free it from urine, the rectum is cleaned of feces using warm alkaline enemas. Every day you need to add 30-50 g of bicarbonate of soda to drinking water. The diet of sick animals should include cereal hay, wheat bran or oatmeal talkers, carrots, hydroponic greens, green grass.

To eliminate hypoproteinemia and restore the amino acid balance, milk is given (3-5 liters per day). Foals are injected with talkers through the nasoesophageal tube.

Pharmacotherapy: Glauber's salt - 200-250 g, bone meal, chalk, iodized salt; intravenous administration of 3-5% sodium bicarbonate solution - 300-400 ml; with heart failure - caffeine and up to 40 ml of camphor oil; intravenous administration of a 0.25% solution of novocaine in an amount of 400-500 ml for 2-3 days.

To reduce the sugar level, insulin is injected intramuscularly, 200-300 units, for 3-4 days. Penicillin therapy is carried out against streptococcal infection.

Physiotherapy: daily massage of muscles, masseters, back, croup and affected limbs; infrared irradiation or ironing through two layers of blanket with a hot iron.

Prevention of paralytic myoglobinuria - on non-working days, they reduce the daily ration by 20-25% and arrange for the horses. Improves stable ventilation. For the diagnosis of enzootic myoglobinuria (to clarify the premorbid state), once a month, clinical and physiological studies, diagnostic measures or medical examination are carried out.

They organize full and varied feeding of horses in winter. In the second half of winter and early spring, they give carrots, hydroponic greens, grass and coniferous flour, in summer - grazing or regularly giving green grass to feeders. In dysfunctional farms in terms of enzootic myoglobinuria, horses are examined.

The diagnosis is made according to the leading symptoms: paresis of the pelvic limbs and paralysis, muscle stiffness, the presence of myochroma in the urine. Enzootic myoglobinuria is diagnosed on the basis of the premorbid period, lesions of the masticatory muscles and muscles of the tongue, due to the massive spread of the disease it is endemic.

Differential diagnosis. Myoglobinuria should be distinguished from hematuria by urological tests and sediment microscopy, from myositis and muscle rheumatism. With these diseases, the composition of urine does not change. It is also necessary to differentiate the clinical symptoms observed in myoglobinuria from those in traumatic injuries of the spine and fractures of the pelvic bones.

The prognosis is cautious, but unfavorable in the clinical form. Mortality in paralytic myoglobinuria reaches 70%, and in enzootic - 70-80%. With recovery, the disease may recur. Performance, even after a mild stage of the disease, is reduced.

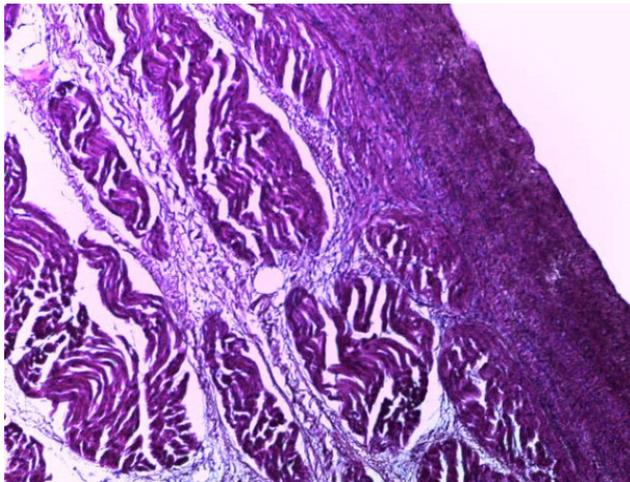


Figure 1. Superficial muscle thickening and deep muscle edema. Staining with hemotoxylin and eosin, X400 mag.

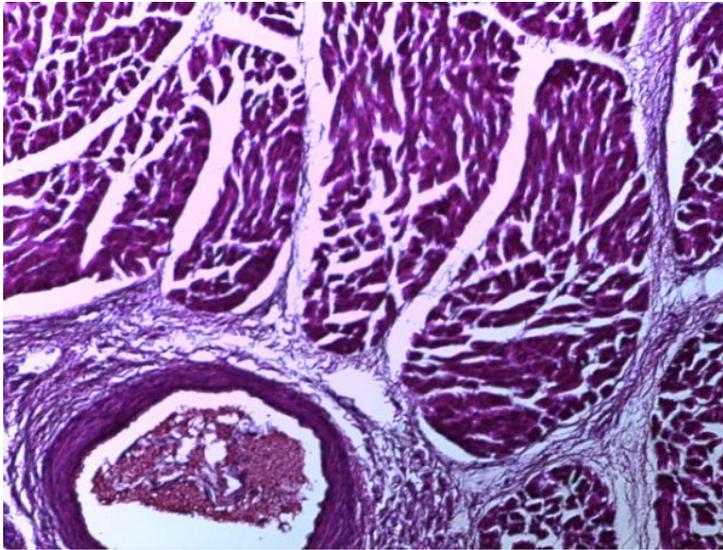


Figure 2. Deep muscle edema, perivascular edema and congestive vascular hyperemia. Staining with hemotoxylin and eosin, X400 mag

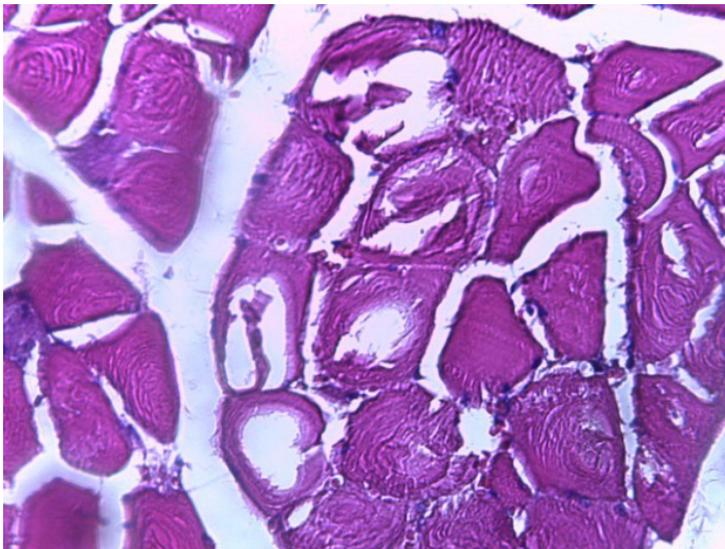


Figure 3. Muscle tissue melting and necrosis
Staining with hemotoxylin and eosin, X600 mag

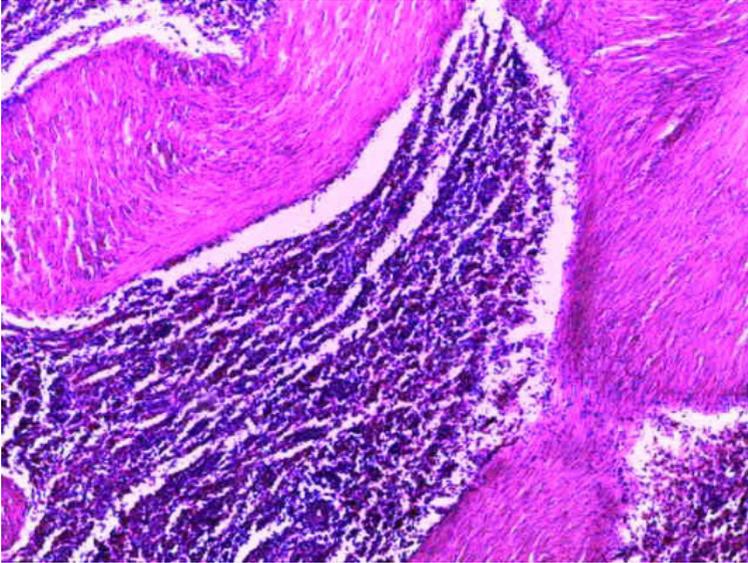


Figure 4. *Overgrowth of connective tissue in the spleen
Staining with hemotoxylin and eosin, X200 mag*

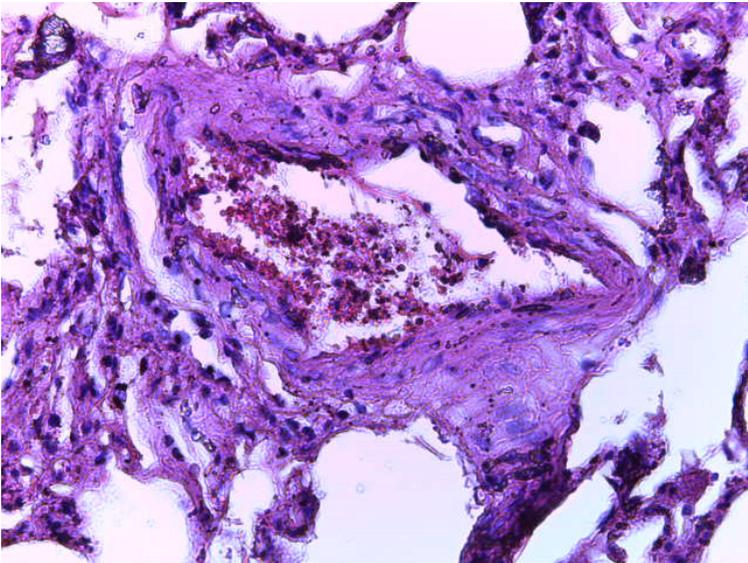


Figure 5. *Congestive pulmonary vascular congestion, perivascular edema,
Compensatory emphysema. Staining with hemotoxylin and eosin, X400 mag*

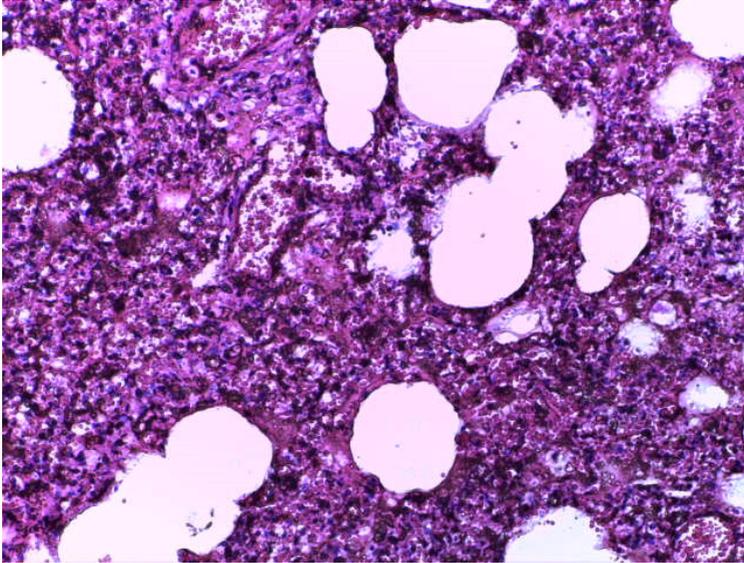


Figure 6. Focal pneumonia. Staining with hemotoxylin and eosin, X200 mag

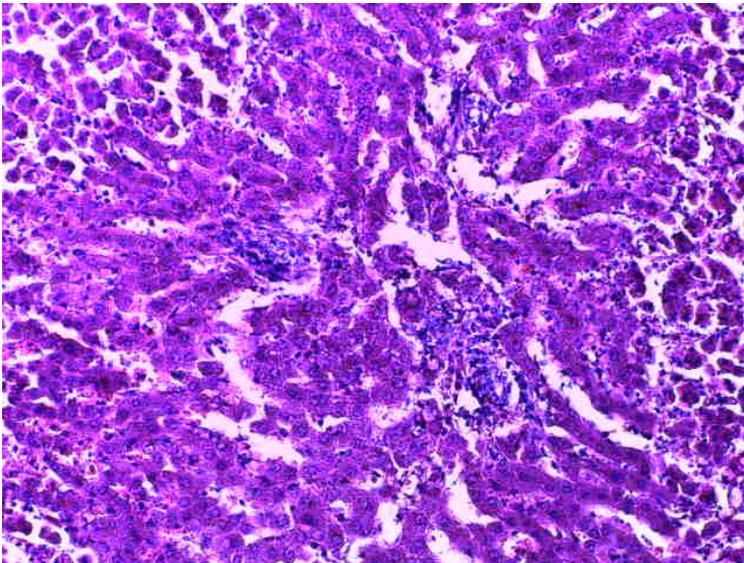


Figure 7. Granular fatty degeneration of hepatocytes. Staining with hemotoxylin and eosin, X200 mag

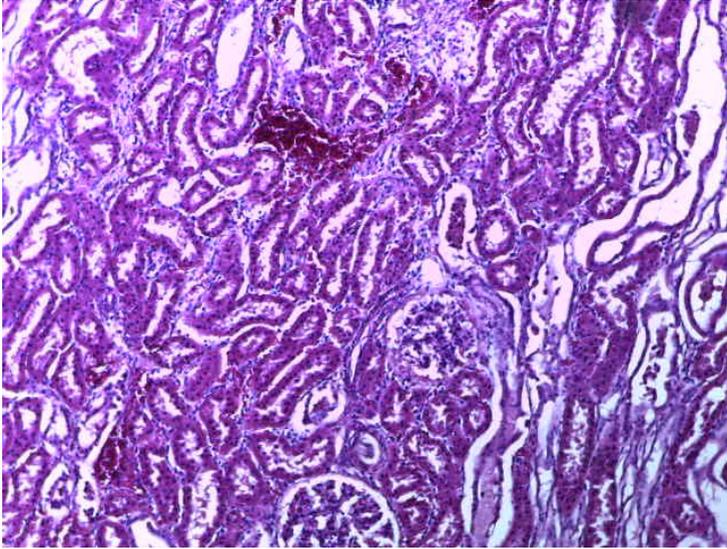


Figure 8. Focal hemorrhages in the kidneys and the formation of cylinders in the tubules. Staining with hemotoxylin and eosin, X200 mag

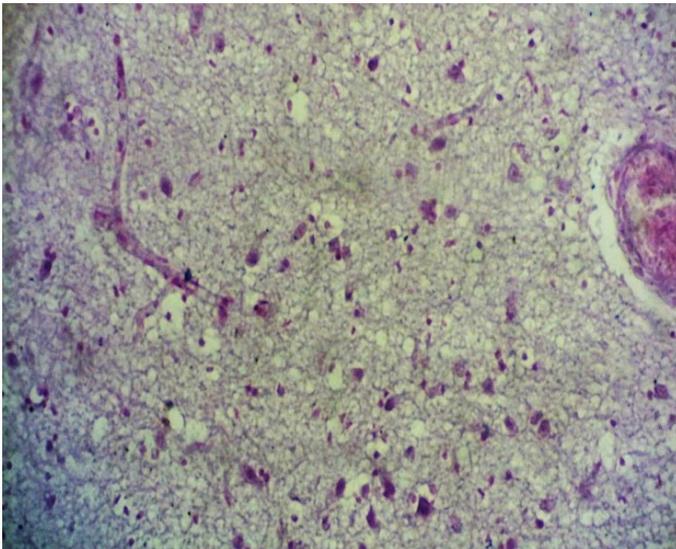


Figure 9. Congestive hyperemia, perivascular, pericellular edema of brain tissues Staining with hemotoxylin and eosin, X100 mag

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早期胚胎后个体发育中火鸡胸腺的形态发生
**MORPHOGENESIS OF THE TURKEY THYMUS IN EARLY
POSTEMBRYONIC ONTOGENESIS**

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注解。为了鉴定白胸品种火鸡胸腺的宏观和微观形态变化，在年龄方面对胸腺进行了解剖学和组织学研究。宏观形态指标的测定采用目视法、称重法和数学方法。通过 Van Gieson、苏木精和伊红以及 Romanovsky-Giemsa 对组织切片进行染色，研究了器官的组织学结构。

所进行的研究结果表明，火鸡胸腺的形态发生以年龄方面的发育周期性为特征。在新生儿期 - 直至 4 周龄，腺体的重量和线性参数增加。同时，观察到实质的增加和结缔组织间隔的宽度，淋巴细胞的百分比。随着血管的形成，也揭示了神经纤维向实质中的萌发。

关键词：胸腺；胸腺；形态学；火鸡。

Annotation. *In order to identify macro- and micromorphological changes in the thymus in turkeys of the White Broad-chested breed, anatomical and histological studies of the thymus in the age aspect were performed. Macromorphological indicators were determined by the method of visiography, weighing and mathematical techniques. The histological structure of the organs was studied by staining histosections by Van Gieson, hematoxylin and eosin and by Romanovsky-Giemsa.*

As a result of the conducted studies, it was revealed that the morphogenesis of the thymus in turkeys is characterized by the periodicity of development in the age aspect. During the newborn period - up to 4 weeks of age, the weight and linear parameters of the gland increased. At the same time, an increase in parenchyma and the width of connective tissue septa, the percentage of lymphocytes were observed. With the formation of blood vessels, the germination of nerve fibers into

the parenchyma was also revealed.

Keywords: *thymus; thymus; morphology; Turkey.*

Introduction

Turkey breeding is an important source of increasing the production of high-quality poultry meat and is a very effective branch of modern poultry farming [3, p. 5]. Among all breeds, a special place is occupied by turkeys of the White broad-chested breed, characterized by good meat qualities, precocity, high presentation of the carcass, high egg production. And therefore, in order to increase the resistance and productive qualities of poultry, knowledge of the morphofunctional features of the organs of immunity of birds, in particular the thymus, which is the central organ of immunogenesis, is necessary. In this connection, the study of the morphology of immune organs is one of the important problems of modern biological science.

Many researchers have studied the morphology of immunocompetent organs in birds (D. A. Zinchenko, 2019; Pronin, V. V., 2017, Huralska, S. et al., 2020, Pavlova, A. V. et al., 2020, etc.). Despite this, the morphological and functional characteristics and dynamics of the formation of the organs of the immune system of turkeys, and thymus in the age aspect, has not been studied.

The purpose of the study: to study the morphogenesis of the thymus of turkeys of the White Broad-chested breed in early postembryonic ontogenesis.

Material and methods of research

The material for the research was pieces of the thymus of turkeys of a White broad-chested breed of 1-, 3-, 4-week-old from clinically healthy birds. Macro- (absolute, relative mass, largest diameter and length) and micromorphological parameters of the thymus were determined. The pieces of organs were fixed in a 10% neutral formalin solution and poured into paraffin. Finished histosections, 5-7 microns thick, were stained with hematoxylin and eosin and according to Romanovsky-Giemsa.

Literary review

The analysis of the scientific literature shows that the study of the morphogenesis of the immune organs of birds, in particular turkeys, is not fully covered.

One of the central organs of the immune system in birds is the thymus. In the thymus, T-lymphocytes are formed from stem cells, which provide cellular immunity reactions. [2, p. 204].

All organs of the immune system, thanks to neurohumoral mechanisms of regulation, function as a whole. By the time of puberty, partial or complete involution of the immune system organs occurs [5, p. 1272].

Zinchenko D.A. (2019) determined that the thymus in turkeys lay under the skin in the neck area along the jugular veins and consisted of two lobes. Each lobe

consisted of 6-8 bean-shaped lobules. In birds of diurnal age, linear and weight indicators of the thymus were minimal. With age, the length and weight of the organs increased, after puberty – decreased.

The histomorphology of the thymus in chickens is described in Huralska, (2020). The thymus is an epithelial-lymphoid organ covered with a connective tissue capsule. The partitions separating the parenchyma of the organ into lobules depart from the capsule. The lobules consist of cortical and cerebral layers, each of which contains lymphoid cells. There are also thymus corpuscles in the brain area, the number of which increases with age [4, p.460].

Thus, the thymus is a key organ of immunogenesis. The thymus matures and differentiates the population of T-lymphocytes responsible for the reaction of cellular immunity. With the onset of puberty in birds, these organs undergo partial or complete age reduction [2, p. 206].

The analysis of specialized literature shows that the features of the age macro- and microstructure of the thymus of turkeys are insufficiently studied. In our work, we will study these aspects in more detail.

Research results. As a result of the research, it was revealed that the thymus of turkeys of the White broad-chested breed consisted of the right and left parts, which were located under the skin on both sides of the neck, had a grayish-pink color (Fig.1). Each half of the gland began at the level of 3-4 cervical vertebrae and ended at the entrance to the thoracic cavity of the body. Each part of the organ had 6-8 bean-shaped lobes of elastic consistency. All the lobes of the loose connective tissue were combined into a single weight. In turkeys in the first month of life, the shape of the thymus lobes is more often bean-shaped and convex-oval.

In week-old turkeys, the absolute mass of the organ was 0.09 ± 0.05 g, relative - $0.037 \pm 0.01\%$. The left part of the organ is longer than the right: 2.77 ± 0.11 cm and 2.00 ± 0.07 cm, respectively (Table 1).

Histological examination revealed that each lobe of the organ was covered with a connective tissue capsule having an uneven thickness. In the places where the blood vessels were located, it was thicker. The capsule consisted of loose unformed connective tissue, where collagen fibers predominated and elastic and reticular fibers were contained in insignificant amounts. Fibrocytes were located among the fibers.

Each lobe of the thymus consisted of lobules, the number of which depended on the size of the lobes. In small and medium lobules, the cortical and cerebral zones were not differentiated. The lobules were densely populated with large and medium lymphocytes, among them small lymphocytes and single reticuloepithelial cells were detected in small numbers.

Table 1.
Macromorphological parameters of the thymus of White broad-chested turkeys (n=5)

Age of the bird, week	Live weight of the bird, g.	Absolute mass of the thymus, g.	Relative mass of the thymus, %	Length of the thymus, cm	
				of the right part	of the left part
1	253,33±0,57	0,09±0,05	0,037±0,01	2,00±0,07	2,77±0,11
3	350,00±0,94	0,59±0,03	0,168±0,01	3,93±0,11	5,57±0,11
4	440,00±0,04	0,73±0,04	0,161±0,01	4,67±0,15	6,73±0,15

In large lobules, the cortical and cerebral zones were distinguished more clearly (Fig. 2). Due to densely located lymphocytes, the cortical zone is darker colored. Lymphocytes are predominantly small in size. The lighter-colored brain area consisted of large and medium-sized lymphocytes and lymphoblasts. There were also singly located reticuloepithelial cells.

Thymus corpuscles in the form of a small focal cluster of epithelial cells were detected in the medulla of large lobules. Their number varied from 1 to 3. Around the thymus bodies, the number of thymocytes is less than in the cortical substance of the organ. The circulatory system is represented by a weakly expressed network of vessels of the microcirculatory bed, which were located in the interlobular connective tissue.



Figure 1. *Thymus of 4 week old turkeys*

In 3-week-old turkeys, weight and linear indicators increased: absolute weight to 0.59 ± 0.03 g, relative weight was $0.168 \pm 0.01\%$. The length of the left lobe at this age was 5.57 ± 0.11 cm, and the right lobe was 3.93 ± 0.11 cm. The size of the lobes also increased, the number of lobules in them also increased.

In small lobules, the corpuscles of Ghassal were not detected, but they began to be determined not only in large, but also in medium lobules. The number of them varied from 2 to 4.

There were small lobules on the periphery. In them, the cortical and cerebral zones, as before, were not differentiated. The central position in the lobes was occupied by well-formed lobules, where the separation between the cortical and cerebral layers was clearer. At the same time, the number of vessels increased and thickening of the thickness of the interlobular septum was noted.

Linear indicators continued to increase in 4-week-old turkeys. So the length of the left lobe was 6.73 ± 0.15 cm, the right - 4.67 ± 0.15 cm. There was a slight increase in absolute mass to 0.73 ± 0.04 g. The relative mass, on the contrary, decreased to $0.161 \pm 0.01\%$. The slices increased in size. Medium and large lobules were more common, in which there was a clear division into cortical and cerebral zones. The number of thymus cells in these lobules increased to 2-5.

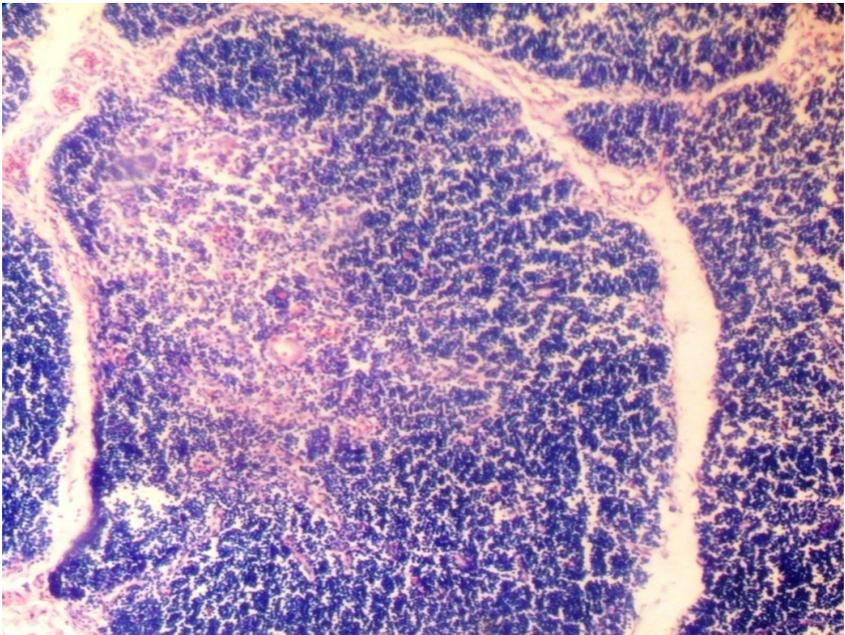


Figure 2. Thymus of turkeys 3 weeks of life

Small lobules were also located along the edges, where there was no clear division into zones. No Ghassal corpuscles were found in such lobules. Blood vessels were well formed in the interlobular connective tissue, the walls of which were noticeably thickened.

Conclusion. After studies of the central organs of immunity of turkeys of the White broad-chested breed of 1-, 3-, 4-week-old, it was revealed that the thymus consisted of right and left formed parts. As the organ developed, the absolute mass increased, and the relative mass began to decrease by the age of 4 weeks. At the same time, there was a change in linear indicators in the direction of their increase.

Histological examination showed a clear formation of lobules with their division into cortical and cerebral zones. The parenchyma of the lobules was represented by small, medium and large lymphocytes, reticulocytes, as well as thymus corpuscles.

At the same time, an increase in both the absolute and relative mass of the fabricium bag was observed. The linear indicators of the organ also increased.

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牛急性呼吸系统疾病的病因和风险降低
**ETIOLOGY AND RISK REDUCTION OF ACUTE RESPIRATORY
DISEASES IN CATTLE**

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抽象的。 幼牛呼吸器官的病变仍然是畜牧业经济损失的主要原因，包括对小牛健康的负面影响、它们的死亡以及缺乏患病和康复动物的产品。 在一些农场，与强制屠宰相关的小牛死亡达到40-55%，患病和康复动物的饲料回报率下降了2-3倍。 尽管引进了先进的畜牧业技术、改善了饲料基础以及使用了新的现代药物和防治动物疾病的计划，但牛呼吸系统疾病的紧迫性并未减少。 造成这种情况的主要原因是呼吸系统疾病的多因素性质，即导致呼吸系统疾病和导致其发生的因素很多。

关键词：呼吸系统疾病，牛，小牛。

Abstract. *The pathology of the respiratory organs of young cattle remains the main cause of economic losses in animal husbandry, which consist of a negative effect on the health of calves, their death, and the lack of products from sick and recovered animals. In some farms, the death of calves in conjunction with forced slaughter reaches 40-55%, and the return on feed for sick and recovered animals decreases 2-3 times. Despite the introduction of advanced technologies for animal husbandry, improvement of the fodder base and the use of new, modern drugs and schemes for combating animal diseases, the urgency of respiratory diseases in cattle is not decreasing. The main reason for this situation is the multifactorial nature of respiratory diseases, that is, there are many factors both causing respiratory diseases and contributing to their occurrence.*

Keywords: *respiratory diseases, cattle, calves.*

Introduction

The pathology of the respiratory organs of young cattle remains the main cause of economic losses in animal husbandry, which consist of a negative effect on the health of calves, their death, and a decrease in production from sick and recovered animals. In some farms, the death of calves in conjunction with forced slaughter reaches 40-55%, and the return on feed for sick and recovered animals decreases 2-3 times.

Despite the introduction of advanced technologies for animal husbandry, the improvement of the fodder base and the use of new, modern drugs and schemes for combating animal diseases, the urgency of respiratory diseases in cattle is not decreasing. The main reason for this situation is the multifactorial nature of respiratory diseases, that is, there are many factors both causing respiratory diseases and contributing to their occurrence.

In recent years, the farms of the Sverdlovsk region of practically all forms of ownership have faced the problem of increasing and maintaining high productivity, premature culling and death of animals. The drive to increase productivity is another factor contributing to the higher susceptibility of animals to respiratory infections.

Infectious rhinotracheitis viruses of cattle (IRV of cattle), viral diarrhea of cattle (VD of cattle), as well as bacteria of the Pasteurellaceae family - *M. haemolytica* and *P. multocida* play a leading role in the occurrence of respiratory diseases. According to most researchers, respiratory diseases are recorded mainly in young cattle at the age of 1-6 months [1-4,13,14,15].

The clinical signs of respiratory diseases caused by different pathogens are often very similar. When planning and carrying out antiepidemiological measures, the results of laboratory diagnostics, based on the integrated use of traditional virological, bacteriological and molecular genetic research methods, are of great importance [7,16,17].

Results and discussion

The study of the prevalence of lung diseases creates a prospect for the development of prevention of this pathology. Prevention of respiratory infections leads to a decrease in the incidence of chronic diseases, which can be one of the causes of the formation of lung diseases. The use of methods of immunization of breeding stock of cattle and young animals will help reduce the incidence of these infections. It is known that the best way to prevent lung disease in young animals is to optimize the antenatal state of the fetus by immunizing the adult herd [5,12].

The main causes of respiratory diseases in young cattle are biogenic factors:

various viruses, such as the causative agent of infectious rhinotracheitis, parainfluenza type 3, viral diarrhea - diseases of the mucous membranes, respiratory syncytial infection, adenoviruses and others. Currently, more than 20 viral agents are known in the world that are involved in or cause respiratory diseases in cattle. [5,6,11].

Despite the mass vaccination, the incidence of cattle with parainfluenza type 3 and infectious rhinotracheitis has not decreased in recent years and remains at the level of 25 - 27% and 19 - 25%, mainly in commercial agricultural enterprises.

Typically, viruses infect the mucous membranes of the upper respiratory tract, causing acute respiratory viral infections (ARVI). Bronchopneumonia is mainly caused by bacteria that live in the nasal cavity of calves (commensals) or in the surrounding air, on the surface of walls, fences, floors, and care items. In most cases, these are enterobacteria, streptococci, staphylococci, pasteurilla, enterococci, *Pseudomonas aeruginosa*, less often representatives of other families and species [8-10].

According to our research, the main predisposing factors contributing to the onset and development of diseases of the respiratory system in cattle are:

- high room humidity (relative humidity not higher than 70%);
- increased concentration of harmful gases (ammonia - no more than 0.01 mg/l, carbon dioxide - no more than 0.15 mg/l, hydrogen sulfide - no more than 0.005 mg/l);
- increased microbial contamination of premises (no more than 50 - 70 thousand microbial bodies/m³ of air);
- crowding;
- lack of active exercise and solar insolation;
- violation of feeding, including a deficiency in the diet of protein, macro- and microelements, vitamins, poor quality feed, including mycotoxin damage to feed;
- recruiting of groups without taking into account anatomical and physiological development and the immune background, recruiting groups with animals of different ages;
- lack of sanitary breaks and technological disinfection

Table 1 presents data on the incidence and mortality of cattle from acute respiratory diseases in the Sverdlovsk region.

Table 1.

Lung diseases of infectious etiology of cattle in agricultural enterprises of the Sverdlovsk region in 2010-2020

Years	Morbidity (n)		Cattle mortality from infectious diseases (n)	
	Total, heads	including cattle, heads	% of the total case	Total, heads
2010	6751	2521	2.5	436
2011	5756	1856	2.2	295
2012	4547	618	2.2	243
2013	2365	984	2.7	313
2014	4634	2061	3.4	340
2015	3520	2438	1.7	139
2016	2066	986	3.4	195
2017	3218	2380	2.1	156
2018	3214	1528	5.1	384
2019	3884	634	3.9	212
2020	1073	456	2.7	145

Analysis of the data of veterinary reports of regional state veterinary institutions of the Sverdlovsk region from 2010 to 2020 indicates a significant decrease in the number of cattle (1.6 times). At the same time, only in recent years, the mortality of cattle to herd turnover and births has significantly decreased, there has been a stable trend towards a decrease in the death of animals from acute respiratory diseases, on average, by 3 times (table 1).

To exclude high humidity and gas content in the premises, it was recommended to adjust the ventilation system and provide animals with a sufficient amount of bedding, to exclude drafts and hypothermia. The simplest indicator of the gas-humidity state of the air is the presence of condensation on the ceiling and the smell of ammonia. The use of fluffy lime to reduce the humidity of rooms is undesirable, since during cleaning a lot of dust rises into the air, which leads to irritation of the mucous membranes of the respiratory tract and dust aspiration.

When group placement of calves, overcrowding should be avoided, the norms for placing animals should be observed, since violation of the norms leads to the accumulation of harmful factors that contribute to the development of respiratory diseases, including pathogenic and conditionally pathogenic microflora, as well as the rapid re-infection of calves in the event of an outbreak of viral or bacterial infection.

In the prevention of respiratory diseases in calves, we used drugs that increase nonspecific (natural) resistance: vitamins and immunocorrectors. Their use is especially necessary in stressful situations: when regrouping, moving or transporting animals, during the period of sharp jumps in air temperature, as a rule, in the autumn-winter and winter-spring periods.

For the specific prevention of respiratory diseases in calves, various vaccines, both domestic and imported, were recommended. Vaccines can be inactivated (killed) and attenuated (made from live pathogens weakened in laboratory conditions), monovalent and associated, including various types of viral, bacterial or viral and bacterial pathogens. The choice of the vaccine was determined by the epizootic situation on the farm, the etiological structure of pathogens, the direction of antiepidemic measures (prevention of the disease or the elimination of an outbreak), the immunogenicity of the vaccine and indications for use in livestock of various ages and physiological conditions. [1].

When choosing a specific vaccine, there was a preliminary laboratory research in the Sverdlovsk Regional Veterinary Laboratory: serological - to determine the etiological structure of pathogens of viral infections circulating in the farm, the intensity and duration of colostral immunity, the age of the first vaccination of calves, and bacteriological - to determine the etiological structure of pathogens of bacterial etiology and an effective antimicrobial agent in case of further therapy.

We note that the basis of vaccine prophylaxis is the creation of persistent herd immunity, which is controlled by serological studies, for which, 21-30 days after the last immunization, blood was taken from 5-10 animals of each age group and the serum was sent to the laboratory for research. In the presence of specific antibodies in the blood of animals in titers 1:32 - 1:256 in RNGA or RTGA, post-vaccination immunity is considered tense, that is, it is capable of protecting the animal from disease upon contact with the causative agent of a respiratory viral infection. The duration of post-vaccination immunity was determined by serological studies 3 and 6 months after immunization. When animals with specific antibody titers below 1:16 were found, the livestock was revaccinated and the immunization schedule was adjusted [13].

Bovine respiratory disease (BRD) is a major concern in both beef and dairy cattle, but beef calves overwhelmingly develop BRD symptoms during the first weeks after arriving at the feedlots. These cases occur after weaning from the mother.

So, calves from different producers were grouped in lots for sale on fattening. Cross-contamination between calves of different origins (potentially carrying different pathogens) together with increased stress from the batching process increased the risk of developing BRD symptoms. An algorithm was developed to create batches with the minimum possible number of sources of origin, while

respecting the restrictions on the number of calves. We tested this algorithm on a dataset of 137,726 weaning calves grouped in 9701 calves and calculated an index that assesses the risks of developing BRD due to batch composition, taking into account the four pathogens involved in the BRD system. While increasing the heterogeneity of lots in calf weights, which is not expected to have a significant impact on performance, our algorithm has successfully reduced the average number of shipments in the same lot and their risk index. Both this algorithm and the risk index can be used as part of a decision-making tool to assess and possibly minimize the risk of BRD in batch creation, but are generic enough to assess the health risk of other production animals and optimize the uniformity of the selected characteristics [13].

Respiratory diseases are the most important sanitary and economic manifestation in several branches of animal husbandry, such as dairy and beef cattle breeding.

Clinical signs of acute respiratory diseases in the RF include complexes of pathogens, namely bacteria (for example, *Mannheimia haemolytica*, *Pasteurella multocida*, *Histophilus somni*, *Mycoplasma bovis*) and viruses (for example, respiratory syncytial virus, viral diarrhea, bovine herpesvirus-1 and parainfluenza type 3).

Conclusion and proposal

One of the economically important problems of livestock farms in the Sverdlovsk region is infectious diseases of the lungs of cattle. The massive nature and stationarity of lung diseases indicate that they do not arise by chance, but are caused by the impact on the animal organism of numerous adverse factors with the obligatory carriage of pathogens. Undoubtedly, regional fluctuations in the prevalence of diseases of the respiratory tract are associated with natural and climatic differences, the peculiarities of the technology of raising animals, the disadvantage of an agricultural enterprise for viral and bacterial diseases (infectious rhinotracheitis, viral diarrhea - mucosal disease, parainfluenza type 3, pasteurellosis, chlamydia, etc.). However, it is hardly possible to explain all the diversity in the breadth of the prevalence of respiratory diseases only by the listed circumstances. The difficulty in interpreting the available data is largely due to methodological problems arising in the analysis of the results of epizootic studies. First of all, it should be noted that ideas about the nature of lung diseases have changed over the past decade, which is accompanied by a revision of the definitions of the disease, and, accordingly, the diagnostic criteria.

The main prevention of acute respiratory illness involves vaccinating calves before weaning and minimizing transport distances.

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