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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TECHNICAL SCIENCES

EARTH SCIENCES

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村庄的本质、形成历史和历史演变
THE ESSENCE OF THE VILLAGE, THE HISTORY OF ITS FORMATION AND HISTORICAL EVOLUTION

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摘要：本文探讨了“村庄”概念的起源，认为其拥有自身的自然、地域、社会经济、政治、精神和文化根源。此外，本文还探讨了村庄如何随着人们的劳动活动、生活方式、思维方式、历史发展阶段和生产性质的变化而演变。

关键词：村庄、村落、农民、人口、部落、经济、发展、聚落、研究。

Abstract. *This article examines the origins of the concept of “village,” which has its own natural, territorial, socioeconomic, political, spiritual, and cultural roots. It also examines how it has changed in response to people’s work activities, lifestyles, and ways of thinking, stages of historical development, and the nature of production.*

Keywords: *village, aul, peasant, population, tribe, economy, development, settlement, research.*

A village is a specific social space that has an important place in the development of society, is distinguished by its own natural, socio-economic activities in the organization of work, traditions, way of life and thinking, and the level and characteristics of the infrastructure of cultural and household services, “is a settlement where the majority of the population is engaged in farming, animal husbandry or other type of agriculture”[1]. As the lowest link of the administrative- territorial structure, the prosperity of the country and the well-being of the people are directly related to the fate and future of the villages. The origin of the Uzbek people goes back directly to the countryside. The village is connected with the domestic and foreign policy of the state in all respects, “...the great and sacred concept of motherland for mankind begins with the symbol of the village”[2] . A rural area is considered to be an area outside the city, where there are permanent agricultural land and residential areas, because the rural settlements constitute the socio-territorial unity of the society.

Villages were considered a more ancient form of settlement than cities. True, in ancient times, the first settlements were not called cities or villages. The emergence of villages was associated with the development of irrigated farming culture in the social division of labor. Irrigated agriculture was first carried out using natural water flow, then it developed on the basis of irrigation facilities (dam, canal, etc.) and tools (plough). Of course, the creation, maintenance and use of such structures, or in modern terms, irrigation infrastructures, required the work of a large community, the population living in one place and together. In this way, a community (society), a territorial unit of people, and permanent settlements appeared.

Farming is, by its very nature, individual work, in which the farmer relies on his own experience and way of thinking. A farmer is a large landowner, zamindar, village headman. “Fishlq” is understood as “a place, settlement, area whose population is mainly engaged in agricultural work[3]”.

According to Narshakhi, in Poykand in his time (VI-VIII centuries), a large landowner was called a “farmer” [4] . Academician A.Muhammadjanov explains that the word “peasant” became famous in the early Middle Ages as “village governor”. The philologist scientist H. Jabborov stated that the word “farmer” was created on the basis of Persian-Tajik language, and that it was actually used in the form of “dehygon” (dehy - villager and gon - plural suffix, that is, villagers). ” also mentions [5] . Nowadays, the meaning of this word has expanded and it is used as a person who cultivates various agricultural crops.

As a result of the separation of irrigated agriculture from animal husbandry, the development of crafts and trade on this basis, the next important stage of social and territorial division of labor began. Such changes in the life of society caused the separation and development of cities from villages. It is from this period that two forms of territorial organization of social life, i.e. villages and cities, appeared.

In the study of the history of the village, it is appropriate to associate the central place with the past. Because from the primitive meaning of the origin of the word “village” it is clear that this word was created by primitive hunters, herders, and herders. They called their original way of life a meadow (now a meadow). They lived in the meadows in spring, summer and early autumn, and in the village in late autumn, winter and early spring. Settlement in the history of Uzbekistan began at the last stage of the first stone age. This is a reality mile. avv. It happened in 500-150 thousand years. The capricious, ecological state of nature demanded a sedentary, stable, settled life in one place, living in a warm house and yard. BC in the previous 4th-2nd millennium, they changed from hunting to animal husbandry, from herding to farming. The origin of the first cities is also directly related to the villages. Therefore, the oldest cities of the Earth were formed in the territory of the Middle East, the present Israel, Jordan, and Syria.

The emergence and development of villages in such an evolutionary way occurred in accordance with LIMechnikov's concept of river (irrigated agriculture) civilization or culture. From this point of view, the history and culture of the East has been described as an inseparable unity of villages and cities. In other regions, the creation of villages differed in terms of space and time and took place in a different way.

In our context, villages means "village[6]". Because, even in the recent past, after completing summer and autumn field work (gardening, cattle breeding, farming), the local people returned to the villages to spend the winter with harvested grain, fruit, firewood and other necessary products (Russian steppe In regions where agriculture is developed, villages mean "selo", "stan", "stanitsa", i.e. stable settlements).

The appearance of the village concept has its own natural, territorial, socio-economic, political, spiritual and cultural reasons. It has changed in connection with people's labor activity, lifestyle and way of thinking, historical development stages, production characteristics. In the system of certain countries, its share is different. For example, in industrialized countries, their number is less, and in underdeveloped countries, it is more. In the last case, the share of agriculture is high, and the amount.

It has played of the rural population occupies the main place. An important role in the lifestyle of nomadic peoples in the regions of Central Asia, especially Uzbekistan, since the early Middle Ages and was considered as a place where they lived during the winter. This situation continued until the 16th and 17th centuries.

Poykand, which flourished as a trading town in the early middle ages (VI-VIII centuries), and each of its surrounding villages had its own rabat in Poykand, and during the winter, the population came to their rabat to spend the winter. Both the village and the city are considered here. In Narshahi's "History of Bukhara" it is noted that there were up to a thousand rabots in Poykand.

A village is a specific social space that has an important place in the development of society, is distinguished by its own natural, socio-economic activities in the organization of work, traditions, way of life and thinking, and the level and characteristics of the infrastructure of cultural and household services. It is connected with the domestic and foreign policy of the state in all respects, it occupies an important place in the strengthening of independence and the republic's entry into the world community.

Villages also perform a number of historical, economic, social, demographic, ecological and other tasks. In turn, agriculture or its economy is also different. Generally, agriculture is considered as a sector that produces agricultural products. But it is also a very complex system, and covers a number of areas besides agriculture in the "narrow" sense [7]. From this point of view, agriculture is con-

sidered as a separate taxonomic unit or link of the territorial organization of the economy (economy) as a whole, such as world economy, national (national) economy, urban economy, in a broad sense. must be interpreted.

According to the opinion of the Russian scientist A.V.Petrikov, territorial sub-system of rural society, which covers the set of social relations related to rural residents, rural life activities, socio-economic, territorial, it reflects the natural and historical-cultural complex, at the same time, the territory and its material objects" [8]. Thus, many scholars understand the rural area as an area with rural settlements that exist outside the city or as an interregional area. It can be said that one of the characteristics of rural areas is that they are considered as sources of many amenities.

When studying the history of villages, a methodological approach in the form of their own territorial and socio-economic system is appropriate. Based on this, a complex and systematic approach, territoriality and historicity, periodicity and sequence principles are also used in the study of villages. They are carried out on the basis of calculation, historical, comparative and other methods.

Geographers pay special attention to the natural-geographical conditions of the area in which they study rural areas. In particular, the climatic conditions of the place, topography, water and soil resources, and flora are important. Most of the villages in Uzbekistan were historically formed on the banks of hydrological branches or in their lower part. Streams, rivers, reservoirs and irrigation canals define the geography of villages in many ways. Large villages were formed on the basis of the development of irrigated agriculture, which requires a lot of manual labor, spreading of streams and canals (ditches) spread from them. An example of this is the villages formed in the streams of the Fergana Valley, especially in the lower part of the Sokh and Isfara rivers. A similar situation is observed in the lower reaches of the Zarafshan river, in the territory of the Karakol district. The name of Karakol district in Bukhara region means "big lake" (Turkish). Large villages were created in the Zarafshon stream by manual labor and by draining water. Archaeological sites found in the Zamonbobo massif prove this. Because it is recognized that this place was a place of farming 3 thousand years ago.

Villages are often located on hills, at the foot of mountains. Such a micro- geographical location is convenient both strategically and to prevent the increase of groundwater level.

The natural-geographic factor, location of villages in the desert, oasis and valley, mountain and sub-mountain regions, the form of housing construction characterizes their regional characteristics. Also, villages located in areas prone to various natural disasters (slides, landslides, floods, earthquakes, strong winds) do not have a favorable geographical location.

Thus, villages are more closely related to natural conditions than cities. As long as agriculture develops directly under the influence of natural and geographical

conditions, its influence on the geography of villages leaves no doubt. In addition, local construction materials - sand, gravel, lime, stone, etc. also play an important role in shaping the appearance of villages. Houses of villages located in streams and other hydrological branches, narrow mountain valleys will have a terrace-like shape, and residential areas will have an elongated, ribbon-like regional shape. The amount of water and the flow regime of streams, the narrowness or width of the valley, the availability of land suitable for farming also affect the demographic capacity of these places, the size and function of the villages. Usually, the villages in areas with scarce land are called “Zarkent”, “Zarhok”, that is, a small piece of land suitable for planting crops is valued as gold [9] . A group of Uzbek clans living in nomadic conditions in a number of villages along the Zarafshan River in Bukhara region settled and gave the village its name. For example, the villages of “Dormon” and “Zarmitan” are examples of this.

Economic sectors form the basis of the formation and development of villages. In this respect, villages are divided into three categories: specialized in agriculture, non-specialized in agriculture and mixed villages. On the other hand, the villages specializing in agriculture consist of villages engaged in horticulture and viticulture, irrigated farming, and cattle breeding. The ability of these agricultural sectors to “create a village” is also different. Relatively large villages are created in districts where irrigated agriculture is developed, and the residential addresses of the population engaged in animal husbandry are not very large.

Non-agricultural villages were formed on the basis of railway stations, meteorological stations, recreation and tourist areas, mineral resources, reservoirs and canals. The population of these villages will not be very large. Most of such villages do not have the status of a city or town due to the fact that their production potential is not large.

Mixed-type villages were created on the basis of the development of the above two sectors or, in general, on the basis of agriculture and related industries. The demographic potential of such villages can be relatively large. So, the size of the villages is determined by their function.

During the Savet period, villages were divided into two, i.e. promising and non-prospecting villages, from the point of view of urbanization. In fact, as long as any village, whether it is big or small, exists, it certainly has an economic (vital) base; because a village that does not have such a material basis will gradually disappear by itself.

While the size of the villages depends on their function, the conditions of providing services to the population and development of the service industry in such settlements are different. In areas where rural settlements are densely populated, a specific rural “agglomeration[10]” is formed, and “pendulum-like migration” is observed within them.

Areas of service to the population, for example, education, health care system, are organized in tiers in rural areas, and small villages have the lowest level of education or health care systems. As the villages grow larger, the objects related to these fields established in them also grow larger. For example, some of the largest villages have a college, technical or academic lyceum, a large library, a hospital, specialized stores, a market, a bank, and supermarkets.

Villages are also of great importance in the development of resorts and tourism. The fact that the majority of the population in Uzbekistan lives in rural areas, the emergence of new infrastructures in rural areas, the specific customs and traditions of rural life directly indicate that there are great opportunities for the development of rural tourism. Many countries in the world consider rural tourism as an important branch of ecological tourism.

Researchers present two classifications of "rural tourism": a) rural tourism is a type of activity directly related to farms, which is usually referred to as "Agrotourism" and is the historical starting point of rural tourism in developed countries; b) rural tourism is considered an activity based on the effective use of resources and assets in rural areas, and it mainly implies the maximum use of economic, social, and cultural resources available in the villages, and it is emphasized that the traditions of the villagers must be respected.

R. Khayitboyev, one of the scientists from Uzbekistan, believes that the main task of rural tourism development is to organize rural tourism services and tourism infrastructures based on the organization of business activities through the development of tourism in villages. At the same time, rural areas have great potential for local, religious, agro-tourism and eco-tourism development: various pilgrimage sites, fishing grounds or sycamores, caves and waterfalls, magnificent mountain or oasis landscapes, national folk games, ceremonies and weddings. ylar, food and clothes are also important for tourism. Also, various archaeological finds, mounds and mounds, ancient irrigation facilities serve as a factor in the regional organization of scientific and international tourism. For example, there are many such monuments in the Lower Amudarya and Surkhan valleys. It can be said that the organization and development of tourism with extensive use of available tourist resources in rural areas in tourism activities is very important in social and cultural life. This requires paying attention to these aspects when studying the history of the village.

The majority of the villagers are engaged in farming, animal husbandry or other types of agriculture [11]. The village differs from the city not only by the occupation of its inhabitants, but also by socio-economic, cultural, natural- geographic and lifestyle. The village is the lowest link in the administrative- territorial structure of the Republic of Uzbekistan, and its socio-economic characteristics are related to the extent to which the population uses the land, and the natural-geo-

graphical conditions of the place. Therefore, villages were historically large and small, and settlements were located accordingly. Flat, marshy and serunum soil, in general, large villages were located in places with favorable natural conditions. In flat, but water-poor areas (deserts and steppes), the population was more engaged in animal husbandry. In such places, villages are small, far from each other, mostly located near wells. In mountainous areas, villages are mostly located along streams and springs. Villages can also be divided into small settlements with a common center - village civil assemblies, economically and socially interconnected. They are divided into neighborhoods in Uzbekistan. Historically, the unification of neighborhoods into one village depended on the fact that the population was engaged in a certain type of agriculture, belonged to the same tribe, drank water from the same stream, held hashar, weddings and marakas together, etc. From ancient times, villages were governed by elected or appointed elders.

Ancient villages consisted of seasonal settlements of the population. Villages in the territory of Uzbekistan were originally created as a place for people to live in the winter season (hence the name "village"). As people gradually became engaged in agriculture and settled down, the villages increased and expanded. The clan associations formed during the period of primitive society were preserved even in the period of settlement, and one clan settled in one village. Today, some villages are named after that clan. For example, in the 18th-19th centuries in the Bukhara Emirate, the name of the "Do'rmon" clan meant the name of a village in 28 places. There are "Dormon" villages in 5 places in Bukhara and 2 places in Navoi. Later, as a result of the unification of clans into tribes, large or close villages appeared (Kenagas, Manaq, Mang'it, Mingli, Naiman, Mitan).

With the development of handicrafts and trade, new villages were created and expanded. Villages also appeared on caravan routes and river crossings: Yettikechuv, Qizilkechuv, Karakechuv, Langar and other crafts and trade developed, and agriculture began to separate, and cities appeared. Since the majority of the population lived in the villages in the early social structures, the main socio-economic and cultural features of the society were determined by the village life. In the early days, the village was governed by a community leader, then an elected community elder or community assembly.

Villages have changed and developed over the centuries in terms of appearance and construction. Over time, villages were formed and divided into three main classes: small villages (up to 1000 people), medium (1000-3000 people) and large (3000 people and more) villages [12]. The specialization of agriculture at different stages and related institutions, production and social infrastructure branches will be different.

The size of the villages depends on their specialization. In turn, the large or small number of inhabitants in villages affects the location of service and service

sector.Villages were established in ancient and newly acquired territories. As a result, the research of such aspects as housing construction, beautification, provision of production and social infrastructure, appearance in villages is a subject of great historical importance.

The demography of rural areas includes the following factors: the number of the population, its growth and location, the repeated formation of the population (birth, death, natural reproduction), the impact of the natural and mechanical movement of the population on the demographic situation, the age-sex composition of the population, the national composition of the population, and the demographic basis of the labor resource formation.

On the basis of the above indicators, relevant regularities or characteristics are determined. It uses„methods such as comparative comparison, grouping, periodicity and sequence" of the Russian Federation, several factors influence the development of rural areas. This includes production (in meeting the needs of society and the industry's need for raw materials), demography (in ensuring the demographic potential of the country), labor resources (in the use of able-bodied rural residents), housing (creating conditions for rural residents), territorial- communication (providing roads, electricity, drinking water, means of communication), ecological (preserving ecological balance in the area), cultural (preserving cultural-historical heritage) and social control of rural areas (maintaining social order and security in rural settlements providing support to state authorities) can be an example.

From the first days of independence, as a special part of the social sphere, special attention was paid to improving the rural lifestyle and increasing the income of residents. MABarg, PMBitsilli, M. Blok, Bolingbroke, B. Gubman, A. Gurevich, I. G. Droyzen, I. D. Kovalchenko, Y. Michelis, A. J. Toynbee, L. Fevr, E. Freeman, A. Xenopol are among the famous scientists of the methodology of the historical direction in the development of the theoretical and methodological foundations of the research. , the works of K. Jaspers and others were effectively used [13]. In particular, in evaluating and analyzing historical events, an attempt was made to study the socio-cultural sphere in close connection with other disciplines, relying on the works of M. Blok, L. Fevre and E. Freeman. Also, the opinion of the authors on this research topic was relied upon.

Social issues also play an important role in the study of rural history. In this, conditions such as the living conditions and lifestyle of the rural population, social infrastructure are analyzed. Currently, in Uzbekistan, great attention is paid to improving the infrastructure of rural areas. In this regard, issues such as the correct regional organization and development of the education and health care system, provision of clean drinking water and natural gas to the rural population are required to be comprehensively studied.

Also, retail trade and paid service sectors should be researched at the level of rural districts and rural citizens' assembly. In this case, contentment with absolute indicators cannot give complete conclusions. Therefore, in this regard, it is reasonable to use relative indicators, for example, data on how much trade or paid services are performed per capita.

In the health care system, regional characteristics such as rural medical centers, their density, the number of people they serve, the sphere of influence - the radius, are studied. At the same time, determining the health of rural residents, the level of morbidity, the types of diseases and their causes is also of great importance in the study of villages.

Rural areas are generally considered weaker in terms of socio-economic development than urban areas. The size of the cities, the strength of the innovation, investment and infrastructure potential, the multi-sectoral and highly developed economy, the wide range of opportunities for residents to live, study, receive treatment and work, and their influence play a leading role in the regional socio- economic system or complexes. ensures that it will play.

The village is subordinate to the city to a certain extent, providing it with agricultural raw materials, its inhabitants with clean air and water, and its economy with labor force. And the city supplies the village with qualified personnel, agricultural machinery, equipment, mineral fertilizers, building materials and modern service.

The development of the village requires the change of its social image in the future, the renewal of its place and role. Of course, the future of the village largely depends on the ongoing political, social, economic and spiritual reforms. Because due to the policy of the Soviet government in the field of agriculture, Uzbekistan was transformed into an agrarian farm. This caused a number of defects in the socio-cultural system of the country. During the Union period, the social problem of the village was interpreted in an abstract way, separated from human interests. "Human" interest was interpreted in the framework of elimination of "significant differences between the city and the countryside" in name only.

In the years of independence, a completely new approach to the countryside began in Uzbekistan. The establishment of new production relations requires saving the village from the raw material base, bringing industry closer to agriculture, changing the social system of the village, bringing its image to a new level. In solving the problem, first of all, it is important to take into account the dynamics of the labor force in the village and provide employment, and secondly, it is more important to anticipate the socio-political, cultural and educational processes that will arise from the growth of the rural population. Demographic trends are an important factor in the direction of social development of any country. About 50 percent of the population of Uzbekistan, that is, about 16 million people, lived in

rural areas. During this period, it was proposed that the population of working age would increase by almost 2 times. Or, if the number of permanent residents of Uzbekistan was 28.5 million people at the beginning of 2011, this indicator increased by 8.2 million people or increased by 1.4 times during 1990-2010 [14] .

If you study how the people living in today's village built their lives in the past, it becomes clear that they built their lives through hard and hard work. Eliminating these important social problems is one of the main issues in the constant focus of the country's politics.

Because the problems related to the life of the villagers are not just "peripheral problems" in a narrow range. It is difficult to imagine without radical changes in agriculture, of course. In order to ensure the change of the socio- cultural life of the villagers, to create the appropriate conditions: a) the improvement of the living conditions of the population; b) change of social life; c) level of activity; g) requires a fundamental change in the outlook and culture of the rural population. On this basis, the necessary conditions for the formation of attitudes within the framework of universal human dignity begin to emerge in the village.

In short, the approaches that reveal the essence of social and cultural life of villages have not been sufficiently developed in national practice. Of course, in the future, the formation of a new multi-criteria scientific direction, in which it will be strengthened with the issues that serve as the basis for the formation of the social and cultural life of villages, abandoning the view of the village as an area specialized in the agricultural sector, preserving its national values, forming and developing the human factor, it should be considered as a place to create suitable modern conditions for the population to live.

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锂诱导的体外人外周血细胞谷胱甘肽单元状态变化
LITHIUM-INDUCED CHANGES IN THE STATE OF THE GLUTATHIONE UNIT IN HUMAN PERIPHERAL BLOOD CELLS *IN VITRO*

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摘要：本研究比较了药理浓度和毒性浓度的锂离子对体外人红细胞和淋巴细胞谷胱甘肽系统的影响。结果发现，硫酸锂暴露不会改变红细胞中的谷胱甘肽-S-转移酶（GST）活性或还原型谷胱甘肽（GSH）水平。然而，毒性浓度的锂会抑制淋巴细胞中的 GST 活性，同时降低 GSH 水平。这表明锂离子诱导了淋巴细胞氧化还原状态的改变，而非红细胞的改变。

关键词：红细胞、淋巴细胞、谷胱甘肽-S-转移酶、还原型谷胱甘肽。

Abstract. *A comparative study of the effects of lithium ions at both pharmacological and toxic concentrations on the glutathione system in human erythrocytes and lymphocytes in vitro was conducted. It was found that lithium sulfate exposure does not alter glutathione-S-transferase (GST) activity or reduced glutathione (GSH) levels in erythrocytes. However, toxic concentrations of lithium inhibit GST activity in lymphocytes, while GSH levels decrease. This suggests that lithium ions induced changes in the redox status of lymphocytes, but not erythrocytes.*

Keywords: *erythrocytes, lymphocytes, glutathione-S-transferase, reduced glutathione.*

Lithium, in terms of its effects on the body, is a poorly studied essential microelement. It influences many metabolic processes, so abnormalities in its levels in the body often lead to health problems. Lithium salts are widely used in the treatment of mental disorders, but the mechanisms of its action on the body, particularly on blood cells, remain poorly understood. Our laboratory previously found that

exposure to lithium salts at toxic concentrations on human erythrocytes in vitro slightly reduces the level of reactive oxygen species and leads to modifications in the physicochemical state of membrane-bound proteins and lipids [1, 2]. Lithium ions influence the homeostasis of erythrocytes and lymphocytes in the body, but, unfortunately, the physiological and toxic ranges of lithium concentrations in the blood remain virtually unexplored. Depressive states are often accompanied by changes in the composition of white blood cell fractions, particularly relative neutropenia and relative lymphocytosis, and the use of lithium-containing medications helps normalize the composition of white blood cell fractions in patients with affective disorders [3]. Lithium salts have a strong immunomodulatory and anti-inflammatory effect [4].

The aim of this study was to compare the effect of lithium ions on the glutathione component of the antioxidant defense of human peripheral blood erythrocytes and lymphocytes in vitro.

Materials and Methods.

Donor blood obtained from the Republican Scientific and Practical Center for Transfusiology and Medical Biotechnology of the Ministry of Health of the Republic of Belarus was used in this study. Red blood cells were isolated by centrifugation at 1500 g for 5 min and washed three times in isotonic NaCl solution. Human peripheral blood lymphocytes (mononuclear cells) were isolated using a Histopaque-1077 density gradient by centrifugation (300 g, 30 min) and subsequent washes in PBS buffer. The cells were then exposed to lithium sulfate at pharmacological (0.5 mM - 3 mM) and toxic (6 mM and 10 mM) concentrations for 3 hours at 37°C with constant agitation. Glutathione status in the cells was assessed by glutathione-S-transferase (GST) activity and reduced glutathione (GSH) concentrations.

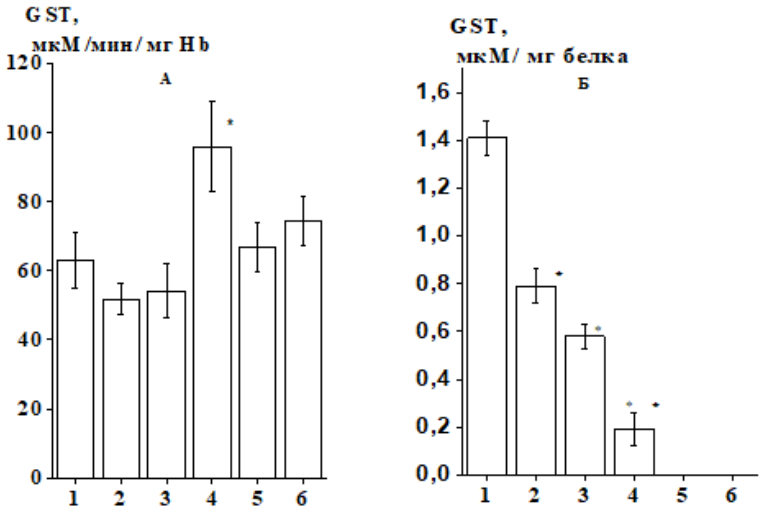
Results and discussion.

It is known that lithium salts at therapeutic doses can both reduce oxidative stress in rat brain cells, as evidenced by a decrease in catalase activity and GSH levels, and increase oxidative stress, as demonstrated in HEK293 cell cultures, where malondialdehyde concentrations and reactive oxygen species levels increased. GST plays a key role in redox-dependent cellular interactions, significantly contributing to cellular protection from the toxic effects of substances [5]. It is also known that, in addition to detoxifying compounds, GST plays a crucial role in the functioning of the antioxidant system. This occurs through the reduction of organic hydroperoxides to alcohols, using GSH as a cosubstrate.

We found that GST activity in erythrocytes increases upon exposure to only 3 mM lithium sulfate (Figure 1A). At pharmacological concentrations, enzyme activity tended to decrease, while at higher concentrations, it tended to increase. Regarding peripheral blood lymphocytes, as Figure 1B shows, lithium sulfate at

pharmacological concentrations significantly reduces GST activity, while at toxic concentrations, it completely inhibits it.

Thus, it was established that GST activity after exposure to lithium sulfate at pharmacological and higher concentrations did not cause significant changes in enzyme activity, while toxic concentrations of lithium ions inhibit glutathione transferase activity in peripheral blood lymphocytes.



Significance of differences in the analyzed parameter relative to the control ($p < 0.05$)* and ($p < 0.01$) **

Figure 1. *Activity of cytoplasmic glutathione-S-transferase in erythrocytes (A) and lymphocytes (B) exposed to lithium sulfate in vitro: 1 - control cells before incubation with Li_2SO_4; 2 - 0.5 mM Li_2SO_4; 3 -1 mM Li_2SO_4; 4 - 3 mM Li_2SO_4; 5 - 6 mM Li_2SO_4; 6 - 10 mM Li_2SO_4*

Table 1 presents data on changes in GSH content in erythrocytes and lymphocytes of peripheral blood depending on exposure to therapeutic (0.5, 1, and 2 mM) and toxic (6 and 10 mM) concentrations of lithium sulfate. Our experiments revealed no significant changes in reduced glutathione levels when erythrocytes were exposed to the studied range of Li_2SO_4 concentrations. It was shown that when lymphocytes were exposed to pharmacological concentrations of lithium sulfate, there was a tendency toward a decrease in GSH, while when these cells were treated with toxic concentrations, a significant decrease in the average GSH concentration was observed by approximately 20% and 50%, respectively.

Table 1

Change in reduced glutathione levels in peripheral blood cells after incubation in a medium containing lithium sulfate.

Li_2SO_4 concentration in the cell incubation medium, mM	**GSH level in red blood cells (%)**	**GSH level in lymphocytes (%)**
Control (cells before incubation with Li_2SO_4)	100	100
0,5	98,2±7,2	93,3±6,5
1	105,1±7,8	92,2±8,0
2	110,3±4,2	88,3±5,2
6	95,15±8,1	79,0±7,5*
10	90,4±6,3	51,7±5,5*

The mean glutathione concentration in control cells was taken as 100%.

Note: *Differences are significant compared to the control ($p < 0.05$).

The results obtained demonstrated differences in the responses of erythrocytes and lymphocytes to lithium sulfate. In erythrocytes, no changes in GST activity or GSH levels were observed under the influence of lithium sulfate, whereas after exposure of lymphocytes to lithium sulfate at concentrations of 6 mM and above, complete inhibition of this enzyme activity and a significant decrease in GSH concentration occurred, indicating a lithium-induced change in the redox status of lymphocytes, but not erythrocytes. Indeed, as we demonstrated using flow cytometry with 2',7'-dichlorodihydrofluorescein diacetate, the ROS level in lymphocytes at a toxic concentration of 6 mM lithium chloride increased by approximately 2-fold compared to the control, and at the maximum toxic concentration of 10 mM lithium sulfate, the increase in ROS level was approximately 20% compared to the control [6].

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消除储备以延长平均寿命
ELIMINATION RESERVES FOR INCREASING THE AVERAGE LONGEVITY OF LIFE

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摘要：衡量人口健康状况最直观的指标之一是平均预期寿命。该指标积累了与年龄相关的死亡率数据，是衡量不同人群健康状况的更可靠指标。同时，不同的疾病对人口生存能力造成的损害也不同。为此，本研究旨在运用托马斯•格雷维尔方法研究各种死因对平均预期寿命缩短的影响。所得数据有力地证明了这样一个事实：消除脑血管病变（城市劳动年龄人口的死因之一）可以为提高此类人群的平均预期寿命提供足够明显的消除储备。

关键词：预期寿命，托马斯•格雷维尔技术，提高平均预期寿命的储备。

Abstract. *One of the most visible indicators for characterizing the health of the population is the indicator of average life expectancy. This indicator accumulates age-related data on mortality and is a more reliable indicator of the health of various population groups. At the same time, different diseases cause different damage to the viability of the population. In this regard, the purpose of the study was to study the impact of individual causes of death on the reduction of average life expectancy using the Thomas Greville method. The data obtained convincingly testify to the fact that the elimination of vascular lesions of the brain, as a cause of death of the city population at working age, gives a sufficiently tangible elimination reserves of increasing the average life expectancy of this category of the population.*

Keywords: *life expectancy, Thomas Greville technique, reserves of increasing the average life expectancy.*

Today, the national state project “Long and Active Life” is being actively implemented in the country. One of the most illustrative indicators for characterizing the health of the population is the average life expectancy (ALS). This indicator cumulates age-specific mortality data and is a more reliable indicator of the health of various population groups. At the same time, various diseases cause varying damage to the viability of the population [1-2]. In this regard, the aim of the study was to study the influence of individual causes of death on the reduction of average life expectancy.

Material and methods of the study. To study the influence of mortality from individual causes on the average life expectancy of the population, we used the construction of hypothetical life tables with the complete elimination of mortality from each of the causes. For this purpose, we used the methodology of the American demographer Thomas Greville I and II. It allows us to answer the following questions: what is the proportion of people of a certain age who, under the mortality conditions reflected in the table coefficients, will ever die from infectious diseases, cancer or an accident; or how much would the average life expectancy increase with the complete elimination of one of the causes of death.

Results and discussion. The calculation results are presented in Table 1.

Table 1

Reduction in the average life expectancy of people of working age in Moscow (both sexes) with mortality from one of the causes in years according to the T. Greville method (2022)

Age	Diseases of the circulatory system	Neoplasms	Injuries	Diseases of the respiratory system
15 - 19 years old	9,7	17,8	15,7	21,3
20 - 24 years old	9,3	17,4	15,7	20,9
25 - 29 years old	8,8	16,9	15,8	20,4
30 - 34 years old	8,2	16,3	15,8	19,8
35 - 39 years old	7,6	15,6	15,8	19,0
40 - 44 years old	6,9	14,7	15,7	18,2
45 - 49 years old	6,1	13,8	15,4	17,1
50 - 54 years old	5,3	13,7	14,8	15,9
55 - 59 years old	4,2	11,3	13,8	14,0

When analyzing the obtained data, the following features can be noted. The loss of average life expectancy decreases with increasing age, but the rate of this process is not the same for different classes of diseases. The highest rate of decline was noted for deaths from diseases of the circulatory system (130.9%). It should be noted that a large role is given to the treatment of cardiovascular diseases in the

country [4, 5]. Next come neoplasms (the rate of decline is 57.5%), diseases of the respiratory system (the rate of decline is 52.1%), and injuries (the rate of decline is 13.8%). The loss of average life expectancy decreases with increasing age, both in men and women, but the rate of this is not the same for different classes of diseases.

Further, at the next stage, we subjected diseases of the circulatory system to a more detailed analysis. When analyzing the obtained data, the following features were revealed. The age-related rate of decline in this indicator for all nosological forms is significantly more pronounced in men than in women. The highest rate of decline (in men) was observed in deaths from ischemic heart disease (83.2%) and cerebrovascular lesions (67.4%). In women, the highest rate of decline was observed in deaths from ischemic heart disease (29.3%) and cerebrovascular lesions (22.9%).

When eliminating all diseases of the circulatory system as a cause of death for men of working age in Moscow, an increase in the average life expectancy of 18-19 years (on average, at different ages) is observed. But the significance of individual diseases is not the same. Thus, the greatest increase is due to ischemic heart disease and cerebrovascular lesions. It should be noted that the increase in the average life expectancy when eliminating one of the diseases of the circulatory system decreases with increasing age, both in men and women. But on average, if for women the life expectancy, excluding mortality from cerebrovascular lesions, increases by 6 years, then for men this increase is 33 years, and, on average, for the working-age population it increases by 18 - 19 years.

Conclusions. The presented data convincingly indicate that the elimination of cerebrovascular lesions as a cause of death of the city's working-age population provides quite tangible elimination reserves for increasing the average life expectancy of the working-age population.

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形态学检查在胃癌早期诊断中的作用：研究幽门螺杆菌菌株的重要性
MORPHOLOGICAL EXAMINATIONS IN EARLY DIAGNOSIS OF GASTRIC CANCER: THE IMPORTANCE OF STUDYING H.PYLORI STRAINS

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摘要：作者对100例感染H. pylori的胃病患者及20例对照组进行了形态学检查及H. pylori致病菌株检测，探讨其对胃癌早期诊断的意义。研究结果表明，慢性胃炎患者胃黏膜H. pylori感染程度较弱，炎症改变强度较低，CagA基因可作为H. pylori致病状态的标志基因。

关键词：H. pylori致病菌株，慢性胃炎，内镜检查，胃黏膜，ureC和CagA基因，活检，分子遗传学检查，OLGA和OLGIM系统，萎缩，肠化生。

Abstract. *The authors studied the significance of morphological examinations and pathogenic strains of H. pylori in 100 patients with gastric diseases infected with H. pylori and 20 people who formed a control group for the early diagnosis of gastric cancer. The results of the study showed that a weak level of H. pylori infection of the gastric mucosa in chronic gastritis is associated with a low intensity of inflammatory changes, and the CagA gene can be used as a marker gene for the pathogenic status of H. pylori.*

Keywords: *pathogenic strains of H. pylori, chronic gastritis, endoscopic examinations, gastric mucosa, ureC and CagA genes, biopsy, molecular genetic examinations, OLGA and OLGIM systems, atrophy, intestinal metaplasia.*

In 2022, 20 million new cancer cases were registered worldwide, and 9.7 million deaths were recorded. 53.3 million cancer patients survived 5 years after diagnosis [3]. Approximately 1 in 5 people will develop cancer during their lifetime. According to IARC, the incidence is 12 times higher in less developed and devel-

oping countries than in developed countries [11]. Several factors contribute to the development of cancer, one of the main factors of which is Helicobacter pylori (H. pylori). Studies have shown that aggressive strains of H. pylori are confirmed to cause severe forms of the disease [5, 9]. In addition, molecular genetic factors of a person have been confirmed to play an important role. Gastric cancer ranks 2nd in the structure of oncological diseases in our country, with an incidence of 6.8 per 100,000 population (2022). In our country, gastric cancer, regardless of etiopathogenetic factors, is treated mainly on the basis of oncological principles, and unlike other types of cancer, the 5-year survival rate does not exceed 50% even in early stages [6]. The high aggressiveness, moderate sensitivity to radiation and chemotherapy indicate the need to focus on the molecular genetic factors of this disease and develop personalized treatment methods in the future [7, 12]. To date, gastric cancer and precancerous lesions in our country have not been sequenced or genotyped by exome, labeled, expression-based marker genes, marker polymorphisms, and have not been thoroughly analyzed for regionally specific H. pylori strains and disease-associated polymorphisms [1, 8]. Therefore, the percentage of patients diagnosed at an early stage of cancer remains quite low. Of course, morphological examinations play a key role in the early diagnosis of gastric cancer and help to identify precancerous changes in the gastric mucosa due to H. pylori infection [3, 5]. Numerous literature reviews have shown that the risk of gastric cancer is higher in patients with advanced age, gender (more men than women), atrophic gastritis, intestinal metaplasia and gastric dysplasia than in patients with other precancerous diseases (for example, gastric polyposis), and aggressive strains of H. pylori are involved as their “conductors” [4, 10]. This, in turn, requires a serious and individual approach to precancerous diseases.

The aim of the study was to study the importance of morphological examinations and pathogenic strains of H. pylori in the early diagnosis of gastric cancer.

The object of the study was 100 patients with gastric diseases infected with H. pylori, the subjects of which were molecular genetic examinations, morphological examination materials from targeted biopsy samples to detect pathological changes in the gastric mucosa.

Methods of the study. All patients were divided into three study groups depending on the nosology of the pathological process, and their results were studied comparatively: 80 patients with chronic gastritis 80 patients with chronic gastritis (chronic atrophic gastritis (CAG) and chronic non-atrophic gastritis (CNAG)), and 20 patients with gastric cancer (GC) and a control group consisting of 20 healthy people.

All patients underwent gastroscopy and a five-point gastric biopsy. Based on the studied material, a morphological study of biopsies was conducted to identify preneoplastic changes (fibrosis, atrophy, intestinal metaplasia (IM), dysplasia) in patients with gastric diseases infected with H. pylori (Table 1).

Table 1

Morphological incidence of gastric diseases infected with H. pylori (based on the study of biopsies taken from the gastric mucosa), n=120

Nosology	Histological signs							
	Foveal hyperplasia		Fibrosis		Atrophy		Intestinal metaplasia	
	Abs	%	Abs	%	Abs	%	Abs	%
CNAG, n=44	21	47,7	7	15,9	2	4,5	1	2.2
CAG, n=36	25	69,4	11	30,5	31	86,1	5	13,8
GC, n= 20	16	80	10	50	17	85	9	45
control group, n=20	6	30	2	10	3	15	2	10
Total, n=120	68	56,6	30	25	53	44,2	17	14,2

Explanation: CNAG-chronic non-atrophic gastritis, CAG-chronic atrophic gastritis, GC-stomach cancer

The table shows that, depending on the nosological form of gastric diseases infected with H. pylori, the morphological appearance differs in the variability of gradations. The results obtained indicate that the intensity of morphological signs depends on the nosological forms of gastric diseases infected with H. pylori. In general, gastric diseases infected with H. pylori were morphologically manifested by atrophy of the gastric mucosa - 44.2%, fibrosis - 25%, and intestinal metaplasia of varying degrees - 14.2%. The analysis of morphological studies, which included qualitative and quantitative indicators, shows that diseases infected with H. pylori are characterized by variable changes in the gastric mucosa. In all studied nosological groups, morphological changes according to the OLGA system were zero or I degree: 27.2% and 15.1%, respectively. Intestinal metaplasia was observed in only 7.3% of cases in all groups according to the OLGA system. When analyzed using the OLGIM system, the same morphological changes showed a different rate. Intestinal metaplasia of stages I and II was detected in 17.6% and 10.8% of cases, respectively. The study showed that irreversible stages III and IV of intestinal metaplasia were detected in 11.2% and 5.6% of patients, respectively. CG and GC were accompanied by varying degrees of activity of the local inflammatory process. The general interpretation of the results obtained showed the feasibility of using the above systems, since it is morphological analysis from the point of view of detecting atrophy and intestinal metaplasia that can be the most basic platform for creating a further strategy of therapeutic measures. Therefore, it is a predictive risk factor for the development of neoplastic changes, detected in 17.6% of patients with stage II and III according to the OLGA system and in 17.7% of patients with stage III and IV according to the OLGIM system. If this indicator was not observed in our studies in CNAG, then in CAG it is very rare and in GC it has the most accurate indicator.

The ureC (glm) gene of H.pylori bacteria was amplified using the Real time PCR method in the feces of all 120 people in the study group. In order to determine the pathogenic status of the identified H.pylori bacteria, PCR amplification of the EPIYA motif of the CagA gene was performed.

Analysis of the obtained PCR results showed that 95 (79.1%) of the 120 people examined had H.pylori ureC gene amplification, while 25 (20.8%) patients did not have the ureC gene. The detection rate of H.pylori in all nosological groups was 1.5 times higher than in the control group (84% and 55% of cases), and it was confirmed that H.pylori bacteria are a risk factor for the development of these diseases ($\chi 2$=8.4; p=0.001). In a control group of 20 healthy individuals, 11 (55%) had the ureC gene detected, while 9 (45%) did not (Table 2).

Table 2

Statistical analysis of H.pylori ureC gene in gastric diseases

Nosological groups	*H. pylori UreC positive or negative*				**Statistical difference**					
	n+	**%**	**n-**	**%**	**χ2**	**p-value**	**Relative risk**		**Odds ratio**	
							RR	**95%CI:**	**OR**	95%CI:
CNAG, n=44	36	81,8	8	18,2	5,07	0,012	1,6	1,0-2,7	3,6	1,1-12,0
CAG, n=36	31	91,6	5	8,3	6,6	0,004	2,0	1,0-4,3	4,9	1,3-19,4
GC, n=20	17	85	3	15	4,3	0,01	2,4	0,87-6,7	4,4	1,0-24,4
General group n=100	84	84	16	16	8,4	0,001	1,3	1,0-1,8	4,2	1,4-12,1
Control group, n=20	11	55	9	45	-	-	-	-	-	-

Explanation: CNAG-chronic non-atrophic gastritis, CAG-chronic atrophic gastritis, GC-gastric cancer

H. pylori was confirmed to be a significant risk factor for the development of CNAG, CAG and GC (p=0.001).

In order to determine the pathogenic status of H. pylori and to study its association with the disease, the CagA gene was obtained and the association between the H. pylori CagA gene and the development of the disease was studied.

The results showed that the CagA gene was detected in 69 (78.4%) of 84 patients, while it was not detected in 19 (21.5%). Of the 11 control subjects, the CagA gene was detected in 6 (54.5%) of 11 subjects, while it was not detected in 5 (45.4%) (see Table 3). Analysis of the CagA gene by nosological groups showed that the percentage of detection of the pathogenic CagA gene increased with the development of the disease. Analysis of the study results showed that, unlike healthy controls in the control group, the CagA gene was detected 1.5 times

more often in patients with H. pylori-associated gastric diseases (78.4% / 54.5%, respectively).

In healthy people, the incidence of ureC gene-positive patients with no CagA gene was 2.8 times lower than in patients with nosocomial disease (21.5% versus 45.4%). According to the data obtained, the CagA gene, which determines the pathogenicity of H. pylori, had an aggravating effect on the course of gastric diseases associated with all its forms. The CagA gene significantly increased the risk of developing the disease by 2.9-6.2 times. Analysis of the data obtained indicates the role of the CagA gene as a factor in the development of severe forms of gastric diseases, which was confirmed by a 2.9-fold increase in the risk of developing CABG in patients with a positive CagA gene ($\chi2$=8.4; p=0.002; OR=2.9; 95%Cl 1.4-6.5) and a 6.2-fold increase in the risk of gastric cancer compared to the control group ($\chi2$=8.6; p=0.001).

Table 3

Association of the CagA gene with H. pylori–associated gastric diseases

Groups	Number				Statistical difference					
	n+	%	n-	%	$\chi2$	p-value	Relative risk		Odds ratio	
							RR	95%CI:	OR	95%CI:
CNAG, n=36	26	72,2	10	27,8	4,6	0,015	1,4	1,0-2,2	4,4	1,0-20,0
CAG, n=33	26	78,8	7	21,2	6,8	0,004	1,7	1,0-2,9	6,1	1,4-30,6
GC, n=19	14	73,7	5	26,3	4,0	0,02	1,8	1,0-3,8	4,6	1,0-25,8
General group, n=88	64	72,7	24	27,3	6,0	0,007	1,2	1,0-1,5	4,6	1,2-19,3
Control group, n=11	4	36,3	7	63,6						

Explanation: CNAG-chronic non-atrophic gastritis, CAG-chronic atrophic gastritis, GC-gastric cancer

Of the 88 patients with the H.pylori ureC gene, 19 (21.5%) did not detect the CagA gene. Perhaps the H.pylori bacteria present in these patients lack the CagA gene or have strains that contain motifs other than the A motif (B, C, D, E). Another hypothesis is that these isolates may have the CagA gene, but there may be a nucleotide mutation at the primer binding site. Analysis of the association of the CagA gene with nosological groups indicates its leading role in the development of severe forms of the disease. It is clearly seen that the CagA gene is a risk factor for the development of severe forms of gastrointestinal diseases. In terms of diagnostic efficiency (AUC-classifier), the CagA gene showed an average indicator (61.8-66.8 %), in all diseases. This means that the CagA gene can be used as a marker gene in the diagnosis of pathogenic or non-pathogenic strains of H.pylori.

Conclusions:

1) In chronic gastritis, the weak level of infection of the gastric mucosa with H. pylori is associated with a low intensity of inflammatory changes.

2) The results of the study showed that the CagA gene is a risk factor for the development of gastrointestinal diseases and that this gene can be used as a marker gene for the pathogenic status of H. pylori.

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严重遗传综合征的功能恢复：细胞疗法治疗天使综合征的临床经验
FUNCTIONAL RECOVERY IN SEVERE GENETIC SYNDROMES: CLINICAL EXPERIENCE OF CELL THERAPY IN ANGELMAN SYNDROME

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摘要：尽管医疗技术、实验室诊断和靶向治疗手段已显著发展和扩展，但遗传性疾病仍然是现代医学面临的一大挑战。由于缺乏针对病因的治疗，患有遗传性疾病的儿童仅接受对症治疗，以稳定病情、缓解危及生命的因素，甚至无法促进受损器官的部分功能恢复。天使综合征是一种罕见且严重的遗传性疾病，其特征是精神运动发育迟缓、癫痫发作和品行障碍。患有该病的患者通常发育和社会化预后不良。干细胞移植是治疗各种遗传性疾病、神经退行性疾病和自身免疫性疾病的一种有前景的方法。本文描述了两例确诊为天使综合征的患者，他们接受了以干细胞移植为主要方法的联合治疗。本文利用患者的体格检查数据、神经系统和心理状态评估、神经影像学和功能医学检测方法以及激素、线粒体和免疫状态的实验室检测，分析了患者的健康结果。结果显示，患者的精神运动发育显著改善，实验室指标和功能指标也呈现积极变化。因此，该联合疗法有望成为治疗伴有严重神经系统损伤的严重遗传性疾病患者的一种有前景的方法。

关键词：安格曼综合征；智力和言语发育迟缓；干细胞；细胞疗法。

Abstract. *Genetic pathologies remain a major challenge in modern medicine, although medical technologies, laboratory diagnostics, and targeted therapy tools have significantly developed and expanded. Since etiopathogenetic therapy is not provided, children with genetic disorders receive only symptomatic treatment stabilizing their status and mitigating life-threatening factors, but not contributing to even a partially functional recovery of damaged organs. Angelman syndrome is a rare and severe genetic pathology characterized by delayed psychomotor development, seizures, and conduct disorders. Patients with this diagnosis have, in general, a poor prognosis for development and socialization. Stem cell transplantation is a promising approach to treating various genetic,*

neurodegenerative, and autoimmune diseases. The article describes two clinical cases of patients with verified Angelman syndrome who received a combination therapy with stem cell transplantation as a key method. Health outcomes were analyzed using the data of physical examination, assessment of neurological and psychological statuses, testing methods of neuroimaging and functional medicine, and laboratory testing of hormonal, mitochondrial, immune states of patients. The results showed a significant improvement in patients' psychomotor development and a positive dynamic in laboratory and functional indicators. Therefore, the studied combination therapy approach could become a promising method for treating patients with severe genetic diseases accompanied by serious nervous system damage.

Keywords: *Angelman syndrome; delayed mental and speech development; stem cells; cell therapy.*

Introduction

Genetic syndromes play a significant role in the etiology of psychomotor development delays and autistic-like behavioral disorders among pediatric patients. Contemporary studies describe a whole range of genetic diseases with various types of inheritance, which lead to some sort of disruption in the development and maturation of the nervous system. However, they are all unified by the overall lack of etiopathogenetic treatment and an unfavorable prognosis in terms of restoring the functions of the nervous system. In most cases, patients with genetic syndromes receive symptomatic treatment (correction of seizures with the use of antiepileptic drugs, behavioral disorders with the help of neuroleptics, basic physical rehabilitation work for changes in muscle tone, etc.), which is carried out with the aim to stabilize relatively the patient's state with no expectation of even partial restoration of the functionality of the nervous system in the form of motor and speech progress at all.

Achieving symptomatic stabilization of patients with genetic disorders undoubtedly improves their survival, however, multidisciplinary assistance provides far more great chances for improvement in psychosocial status and, overall, the prospects for social adaptation of the described contingent. Over the past three decades, large studies of new therapeutic strategies, including cellular therapy, have been conducted worldwide.

The prospects for using cell therapy for various genetic diseases are greatly numerous [1, 2]. On the one hand, experimental studies fous on studying cell therapy using genetically normal or genetically modified cells as a gene-supplemental approach that allows the introduction of normal copies of the gene [3, 4], while on the other hand, the practical aspect of the application of cell therapy is of interest due to its immunomodulatory, anti-inflammatory, bactericidal, anti-hypogenic and to a greater extent paracrine effects [5]

Stem cells have a number of specific characteristics that make them attractive for therapeutic use in a variety of diseases, both genetic and autoimmune, and conditions associated with cell and tissue damage. Stem cells are non-immunogenic, have minimal oncogenicity and a short lifespan *in vivo* with the highest regenerative potential at the same time due to the ability to detect the damaged chip and direct its response to initiate recovery processes [6, 7]

The clinical picture of Angelman syndrome is caused by a disruption of maternal- and paternal- imprinted UBE3A, which encodes E3 ubiquitin ligase. Four mechanisms have been identified that render maternal inherited UBE3A non-functional, the most common of which is deletion of maternal chromosome region 15q11-q13. Notably, duplication of the same chromosomal region is one of the few typical persistent genetic abnormalities associated with autism spectrum disorders, occurring in >1 - 2% of all cases of autism spectrum disorders.

Although overall brain morphology and neural projection connectivity appear largely normal in Angelman syndrome mouse models, major functional defects are found at the level of context-dependent learning, as well as impaired maturation of the hippocampus and neocortical circuits [8, 9]. Though these data demonstrate the crucial role of ubiquitin-protein-ligase E3A in synapse development, the mechanisms by which ubiquitin-protein-ligase E3A deficiency leads to the pathophysiology of Angelman syndrome in humans remain poorly understood [10]. However, recent investigations have shown promising potential to restore impaired function in patients with Angelman syndrome, which has renewed hope that an effective treatment strategy may be found.

Despite the different variants of the mechanism of formation, the clinical picture of Angelman syndrome is quite typical. Among 80% and 100% of children with the syndrome have mental and motor developmental delays, speech impairment, undesirable behavior, ataxia, hand stereotypes, apraxia of hand movements, squinting, and excessive salivation. The epileptic seizures were reported among more than 70% of the children, and all patients, regardless of seizures, exhibited the same patterns on the electroencephalogram as Angelman syndrome (high-amplitude synchronous delta waves).

Despite a fairly typical clinical picture, it is not uncommon for patients with Angelman syndrome to be observed exclusively by psychiatrists for long periods of time without verification of the genetic syndrome. Genetic abnormalities in the chromosome area 15q11-q13 are among the most common of all mutations found in ASD and account for approximately 1-2% of all cases [11, 12]. Moreover, recent reports suggest that 15q11-q13 copy number variants are associated with autism [13]. The article describes two clinical cases of genetically confirmed Angelman syndrome with gross psychomotor retardation and resistance to standard symptomatic treatment in the anamnesis. One of them was diagnosed with

"Angelman syndrome" as an infant, and the other was diagnosed much later, resulting in the child being treated by specialists exclusively as a patient with ASD due to a typical clinical picture.

Patients have been examined by a team of doctors, including a neurologist, a geneticist, a psychiatrist, and undergo a preliminary comprehensive laboratory and functional examination. Based on our own positive clinical experience with cord blood stem cell therapy among children with psychomotor developmental delays of various etiologies, a decision was made and consent from external representatives to perform stem cell transplantation among the patients described in the article was obtained. Both children underwent therapy to correct neuroinflammation as measured by appropriate assays prior to stem cell transplantation, infusion-detoxification therapy based on laboratory toxicology, and antioxidant therapy.

Description of the clinical cases

Case Study 1. Patient A., 2 years old. The medical history indicates that the patient is being raised in a happy, intact family. This is the third pregnancy (1st - vaginal, 2nd - healthy female), that was generally normal and the child was born full-term.The childbirth was spontaneous, birth weight was 3050, and the Apgar score was 8/8. Since birth, A. had been developing with a delay in psychomotor development, and was therefore monitored by a neurologist at his place of residence. He underwent courses of therapeutic and prophylactic massage and nootropic therapy, but the treatment did not bring the desired result.At the time of scheduled hospitalization, when being examined, the child looks significantly younger than his age, is hypotrophic, hypotonic, and is examined in his mother's arms. The skin is pale, dry, with foci of atopic dermatitis. The extremities are cold and clammy. The teeth are widely spaced, with Priestley's plaque and enamel hypoplasia, and there is no prognathism. Brachycephaly is eviently obvious. There are no other dysmorphisms. On auscultation, breathing is harsh. The abdomen was distended, disproportionately enlarged compared to the limbs, with pronounced gas formation.

During examination, the patient is hyperactive, exhibiting multiple stereotypical chaotic movements, a sharply reduced ability to concentrate and focus, and occasional strabismus. His reaction to speech is reduced, and he thrust his tongue out, which is accompanied by short-term synkinesis.

The eye slits are equal. The pupils are round, D=S, and react well to light. According to the mother, feeding is complicated by frequent and profuse regurgitation. The child's mood is unstable, and he has difficulty differentiating between "friend" and "foe." He cannot sit up or roll over independently. The child has had problems falling and staying asleep since birth, and frequent manifestations of gastrointestinal dysfunction, such as constipation.

All of these symptoms are characteristic of Angelman syndrome, but are not specific ones. Taking into consideration the severe immunometabolic syn-

drome, the child is admitted to hospital for intensive detoxification and anti-inflammatory therapy. As the general condition improves, it is advisable to establish a genetic diagnosis, determine the prognosis alongside with long-term treatment options.

Genetic testing revealed a de novo deletion at 15q11-q13o on the maternal chromosome copy. It should be noted that a deviation from the typical Angelman syndrome phenotype does not exclude a true Angelman syndrome mutation. Some mutations in the UBE3A gene result in milder phenotypes than typical Angelman syndrome; patients with them do not meet all the clinical criteria for Angelman syndrome, and their disease may have a largely atypical course.

Genetic testing revealed a deletion 15q11-q13o on the copy of the maternal chromosome, which arose de novo. Laboratory tests of the child revealed an increase in neuroinflammatory markers (HSE 28.44 c100 0.130), antinuclear factor (ANF 1:640), an increase in lactic acid in the blood (3.43) and liver enzymes, a total decrease in the concentration of steroid hormones in the blood and saliva with ACTH at the lower limit of normal, a marked increase in the concentration of eosinophilic cationic protein (123 ng/ml), as well as a gross increase in the concentration of tartaric, caffeic acids, arabinthol and arabinose in the urine. Immunological studies showed a moderately pronounced immunodeficiency status. Thus, against the background of a pronounced systemic inflammatory process, a recurrent hypercatabolic-hypermetabolic syndrome with a severe deficiency of the anabolic component is noteworthy. The systemic inflammatory process has autoimmune features, affecting muscle structures and collagen structures (with an increase in the concentration of saccharopine, pipecolic acid, sarcosine in the blood, as well as pyroglutamic acid in the urine) with a concomitant increase in the amount of antibodies to DNA and collagen. According to metabolomic studies, mitochondrial dysfunction of a mixed nature with transient blocks of intramitochondrial beta-oxidation and losses of medium-chain fatty acid metabolites, up to the picture of MCAD based on the results of organic acids, was verified. Transient laboratory-verified metabolic crises did not lead to full-blown metabolic acidotic crises, but provoked an aggravation of the deficiency state. The spectrum of changes in the metabolic profile is associated not so much with the genetic pathology identified in the child, but with the epigenetic state of immunomitochondrial diathesis, progressive catabolic syndrome against the background of immunodeficiency status and a chronic inflammatory process. Moreover, the disturbance of neurosteroid and neurotransmitter metabolism was secondary in nature against the background of a transient partial block of the hydroxylase enzyme system, the accumulation of by-products of aromatic amino acid metabolism, which further aggravated the intoxication syndrome. The intoxication syndrome was also aggravated by

severe invasive candidiasis that developed within the immunocompromised patient.

In our opinion, the summative antigen load and the resulting neuroinflammatory damage to the nervous system in an immunodeficient and hormonally weakened child with reduced compensatory potential turned out to be the leading cause of the severity of psychomotor retardation along with the consequences of the existing genetic pathology. During inpatient treatment, and subsequently in outpatient mode, the patient received complex anti-inflammatory, infusion-detoxification, supportive cofactor enzyme therapy, and specialized nutritional mixtures were selected that were suitable for the patient's clinical and laboratory phenotype.

After 3 months of observation, the therapy resulted in stabilization of laboratory parameters of neuroinflammation (NSE and c100 are normal), stabilization of the immune status (ANF is normal, ECP is normal, arabinthol and arabinose are negative), hormonal status, and the patient's metabolic profile with a significant improvement in fatty acid metabolism. Against the background of the described therapy, the child gained weight, began to focus his gaze, emotional swings and stereotypical limb movements were completely eliminated, the boy began to pay attention to adults, a complex of revival towards mother and father and differentiation of "friend or foe" appeared

Despite significant progress achieved through comprehensive anti-inflammatory therapy, the child's psychomotor developmental delay remained severe, leading a panel of doctors to recommend that the child be included in the study and undergo a stem cell transplant. After official approval and inclusion in the study, the child underwent preparatory infusion therapy with hepatoprotective drugs; antihistamines were administered in a single dose 2 hours before the start of the stem cell infusion. Stem cell transplantation at a dose of 1 billion cells was performed slowly intravenously through a peripheral catheter over 30 minutes under the supervision of the physician on duty, followed by three days of inpatient observation. Donor hematopoietic stem cells from umbilical cord blood were used for the administration. Despite significant progress achieved through comprehensive anti-inflammatory therapy, the child's psychomotor developmental delay remained severe, leading a panel of doctors to recommend that the child be included in the study and undergo a stem cell transplant.

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vision of the physician on duty, followed by three days of inpatient observation. Donor hematopoietic stem cells from umbilical cord blood were used for the administration. After post-transplantation observation, during which no adverse events were identified, child A. was discharged home for outpatient observation.

Within a month after the stem cell transplant procedure, the child significantly strengthened his motor skills, learned to independently roll over from his back to his stomach and back, crawl, and also stand up with support on his hands. His psychoverbal characteristics also changed significantly, a boy began to pay attention to those around him, take an interest in toys, began to coo and develop emotional reactions commensurate with the situation and context.

Thus, bringing stem cells into use to a child with already compensated immunological dysfunction led to significant progress in those functions that were largely unanticipated due to the established genetic syndrome. The child continues to be monitored and receives supplemental support for mitochondrial and immune status. A plan to recur stem cell transplantation three months after the initial procedure is drawn up.

Case Study 2. Child M., 8 years old. The anamnesis shows a successful physiological pregnancy, natural delivery at term. Early psychophysiological development was unremarkable until the age of nine months, after which a decrease in the rate of acquisition of new skills was observed. At the age of 8.5 months, the child suffered from an acute respiratory viral infection, subsequently a hyperthermic reaction to a prophylactic vaccination was noted, subsequently the child began to get sick frequently (2-3 times a month). It should be noted that after nine months, manifestations of atopic dermatitis were observed during breastfeeding with typical rashes on the cheeks and buttocks, without dynamics against the background of correction of the mother's diet. Despite the general pediatric, neurological and rehabilitation work, the child did not walk until the age of two years, and pronounced ataxia was noted. From the age of 1.5 years, the onset of destruction of tooth enamel was detected. From this age, the child was constantly monitored by a neurologist and immunologist, and received courses of antiviral and supportive therapy. He was also monitored by an ophthalmologist for strabismus.

At the age of five, the child was consulted by a geneticist based on the results of a genetic study and thus a clinical diagnosis of Angelman syndrome was made. By the age of 6, the motor delay remained, an obvious psychomotor delay was observed in the form of a poor vocabulary (no more than 20 words that cannot be combined into phrases), communication mainly with gestures, and limited understanding and execution of simple everyday instructions. Many years of psychological, pedagogical, neuropsychological, speech therapy and defectological work did

not bring about any significant changes in the child's psychomotor status. Upon admission, the child looks younger than his age, there is a deficit in weight and muscle mass. The skin is dry, rough, multiple excoriations are noted. Breathing is mainly through the mouth, the mouth is slightly open, salivation is observed. No facial dysmorphisms characteristic of genetic syndromes are detected. Auscultation reveals harsh breathing with isolated dry wheezing; the abdomen is painless and moderately distended. The boy is rapidly exhausted as a result of both physical and cognitive stress. Against the background of exhaustion, undesirable behavioral patterns appear in the form of stereotypical movements, vocalizations, motor disinhibition with periods of aggression and autoaggression.

According to laboratory tests, a moderate increase in neurospecific markers (mainly NSE), a high concentration of antistreptolysin O (422), a high concentration of IL8-94.8, large circulating immune complexes (CIC) increased to 41 U, medium CIC increased to 118, small CIC increased to 278, the sum of CIC is 437. Large CIC decreased by 9%, medium CIC decreased by 27%, small CIC increased by 64%. CMV in saliva - 3.9 × 10 in², HSV type 6 - 5.1 × 10 in³. CMV in scraping from the oropharynx 3.0 × 10 in², HSV type 6 - 7.3 × 10 in². Blood: CMV is not detected, EBV is not detected. In the complete blood count, hematocrit is 40.3, elevated (normal up to 39.8), erythrocyte heterogeneity by volume is 14.7, elevated (normal up to 14.40). Antinuclear factor is1:640.

Based on the results of metabolonal studies, M. found a moderate increase in the concentration of lactate in the blood with a construntial increase in lactic acid excretion with urine, a decrease in pyrovinic acid and metabolists of the cycle of tricarbon acids against the background of a significant increase in the concentration of 3-hydroxylic acid to 477.8 and acetouxus acid, acutexic acid that corresponded to a pronounced Keocidotic status, which, most likely, proceeded in a child in a chronic form, without reaching crisis meanings. A significant increase in glycerin 14.7 (norm up to 8), spare 236.8 (norm up to 50) of acids was accompanied by an increase in concentrations of citric, coffee and wine acids, which corresponded to fungal invasion and secondary excess oxalates. It should be noted the knowledgeable excess of concentrations of medium-aged fatty acids (sebacin, adipi-new, suberin) and meglutol, which is characteristic of mitochondrial dysfunction and violation of the beta-oxidation of fatty acids and is the ways to develop energy designs, especially among children with a systemic inflammatory process to be chronically current.

The results of the conducted EEG monitoring of nocturnal sleep revealed: the frequency characteristics of the cortical rhythms of wakefulness are formed within the age norm, zonal differences are correct. Sleep and wakefulness are differentiated, the stages of sleep are determined. Physiological patterns of sleep are formed correctly, they are sufficiently expressed. Against this background, regional ep-

ileptiform activity was recorded during sleep, represented by single, less often grouped regional sharp waves, often in combination with a slow wave (morphologically corresponding to DERD) of low amplitude with a focus in the left parietal-central region (P3 C3), rarely spreading to the vertex region. The index of regional epileptiform activity during sleep is low, varying from 0 to 10% of the analysis epoch. In wakefulness, pathological local, paroxysmal and epileptiform activity was not registered. According to MRI of the brain, ventriculomegaly, dysplastic phenotype of the left precentral cortex, delayed myelination of the periventricular white matter of the parietal lobes were revealed. The midline structures are not displaced. CSF dynamics is compensated. Subarachnoid spaces are defined satisfactorily. The hippocampi are symmetrical, of normal shape, there are no abnormalities of MR signals. No evidence of vascular malformations or neoplastic formations was obtained. The pituitary-hypothalamic region is without areas of altered MR signal and additional formations. The corpus callosum is formed correctly. The brainstem and cerebellum are without peculiarities. The craniovertebral junction is formed correctly. In a hospital setting, M. underwent a course of anti-inflammatory, infusion-detoxification therapy, as well as a course of mitochondrial rehabilitation with a comprehensive implementation of interval hypoxic therapy, hyperbaric oxygenation and ozone therapy. Against the background of the therapy, the condition showed positive dynamics in the form of improved sleep, improved endurance, and a marked reduction in stereotypical behavior.

During outpatient treatment, positive dynamics continued to increase: compensation of laboratory parameters of immune and mitochondrial status was observed, there were no more acidotic episodes, ASLO and systemic inflammation indicators decreased. The boy's clinical picture also changed significantly: he began to show cards, his understanding and interaction with others improved, imitation appeared, he imitates people, actively interacts with people, cognitive interest is also expressed. However, difficulties in gross and fine motor skills remained, there was a paucity of contact with peers, and everyday understanding with pronounced stereotypes and rigidity. Due to the child's age and the remaining relevant delay in psychomotor development, a decision to introduce cell therapy into the complex of the ongoing treatment was made.

Official permission was obtained, after which the child was included in the study; after preparatory therapy, a transplant of donor hematopoietic cord blood stem cells at a dose of 1 billion cells was performed intravenously through a peripheral catheter. As in clinical case 1, after a three-day observation, due to the absence of adverse reactions, M. was discharged from the hospital. Over the past three months after the stem cell transplantation, pronounced dynamics in the child's psychomotor development have been revealed in the form of significant stabilization of gross and fine motor skills, mastery of hygiene skills and self-

care skills (he began to eat, dress, and undress independently). His vocabulary has significantly increased and the first phrasal links have appeared. Significant improvement in the child's sociocommunicative abilities in the form of interaction with relatives, his brother, and children on the street is noteworthy. He became interested in games and toys, and developed an interest in mastering academic skills. Thus, the stem cell transplantation became the trigger for the development of the most complex skills, both psychomotor and motor. It should be noted that the boy became significantly less sick after the transplantation, making it possible to reduce the need for constant immune system support. At the time of writing this clinical observation, the boy is undergoing preparation for a recurring stem cell transplantation.

Discussion

For both patients discussed, in addition to a verified genetic syndrome, significant changes in the immune, hormonal and mitochondrial status were found, work with which led to a significant improvement in psychoemotional and motor development, but stem cell transplantation led to progress due to the activation of regenerative potential. It should be noted that both children described at the time of the onset treatment were in a state of hypercatabolic-hypermetabolic status with a significant deficit in weight and muscle mass due to a violation of the systemic inflammatory process.

When introducing stem cells, a complex effect on the body is achieved, which is realized through several mechanisms. First of all, the regenerative effect is ensured by the paracrine action of stem cells and their impact on neurosteroidogenesis [5, 14]. The effect on the metabolism of steroid hormones leads to a neuroprotective effect, which, in its turn, will lead to the stimulation of adaptation, regeneration and repair of neuronal tissue [15]. Secondly, after stem cell transplantation, stimulation of endogenous stem and progenitor cells of those tissues affected by the introduced donor cells occurs. Among the patients with psychoneurological pathology, due to the introduction of stem cells, an effect on endogenous tissue-specific neuronal stem cells of the subventricular zone of the lateral ventricles of the brain, hippocampus, dentate gyrus and olfactory region occurs. The regenerative effect is achieved simultaneously by stimulating the patient's own cells, as well as by directly influencing damaged and susceptible (in our case, as a result of a chronic inflammatory process) tissue elements by inhibiting neurocyte apoptosis. The systemic effect of stem cell administration ensures stabilization of the patient's summative compensatory potential and, consequently, prevention of further inflammatory processes. All the described mechanisms of the therapeutic effect of stem cells are characteristic of all types of stem cells; however, the greatest safety and effectiveness have led to the use of umbilical cord blood stem cells [16].

As noted in the first part of our article, over the past twenty years there have been numerous scientific studies and clinical trials on stem cell transplantation for various diseases.

Among these studies, those that showed significant positive effects of the cell therapy were published [17], however, a review of clinical studies also reveals observations with conflicting results and a lack of proven effectiveness [18].

In our opinion, the ambiguity of the results of many scientific studies on the effectiveness of stem cells in genetic diseases and psychoneurological pathology is largely due to the lack of proper preparation of the patient for the regenerative stage of treatment, as well as post-transplant patient management. In our clinical practice, the accuracy of diagnosis alongside with the verification of dysfunctions of the key regulatory mechanisms of the human body (immune, hormonal and mitochondrial functions) are considerably taken into account. Stem cells largely exert their effects through paracrine and systemic effects, which can only be demonstrated in a prepared patient with properly functioning regular mechanisms. A strict stage-by-stage therapeutic strategy allows for planned preparation of the patient's body for stem cell transplantation and the achievement of maximum therapeutic effect, as in the clinical cases described in the article.

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胰腺恶性肿瘤的危险因素
RISK FACTORS FOR MALIGNANT NEOPLASMS OF THE PANCREAS

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摘要：在不久的将来，胰腺癌将在欧盟国家超过乳腺癌，成为癌症相关死亡的第三大原因，就像北美大陆已经发生的那样。这引发了对癌症风险因素的大量研究，这些风险因素多种多样：遗传因素、肥胖、糖尿病、慢性胰腺炎、酗酒、吸烟、慢性肝炎、乳腺癌和非息肉性结直肠癌等也会增加胰腺癌的风险。然而，该疾病的确切病因仍然未知。由于缺乏早期临床表现，这种致命疾病通常在晚期才被诊断出来，并且经常伴有转移。这需要对胰腺癌的风险因素和发病机制进行进一步研究。

关键词：胰腺，癌症，风险因素在全球范围内，胰腺癌是男性第十二大常见癌症，女性第十一大常见癌症，也是癌症死亡的第七大原因[1]。胰腺癌多发于老年患者，通常发病年龄在 60 岁以后，男性发病率略高于女性 [2]。根据国际癌症研究机构 (IARC) 的癌症发病率和死亡率估计，2022 年胰腺癌新诊断病例为 510,566 例，死亡病例为 467,005 例，分别占所有新诊断癌症病例和所有癌症死亡病例的 2.6% 和 4.8% [2]。鉴于胰腺癌的低存活率，发病率和死亡率几乎相同。根据全球统计数据，2018 年胰腺癌的发病率和死亡率分别为每 100,000 人 4.8 例和 4.4 例。近几十年来，胰腺癌的发病率有所上升，预计还将继续上升。

Abstract*. In the near future, pancreatic cancer will surpass breast cancer in the countries of the European Union and become the third leading cause of cancer-related deaths, as has already happened on the North American continent. This has led to a number of studies on the risk factors for cancer, which are diverse: hereditary factors, obesity, diabetes mellitus, chronic pancreatitis, alcohol abuse, smoking, chronic hepatitis, breast cancer, and non-polypous colorectal cancer can also increase the risk of pancreatic cancer, among other factors. However, the exact etiology of the disease remains unknown. This fatal disease is usually diagnosed at an advanced stage, often with metastases, due to the lack of early clinical manifestations. This requires further research on the risk factors and pathogenesis of pancreatic cancer.*

Keywords: *pancreas, cancer, risk factorsGlobally, pancreatic cancer is the twelfth most common cancer in men, the eleventh most common cancer in women, and the seventh leading cause of cancer death [1]. Pancreatic cancer occurs more frequently in older patients, usually after 60 years of age, and the incidence rate in men is slightly higher than in women [2]. According to the International Agency for Research on Cancer (IARC) Cancer Incidence and Mortality Estimates, the incidence of pancreatic cancer was 510,566 newly diagnosed cases and 467,005 deaths from this nosology in 2022, corresponding to 2.6% of all new cancer diagnoses and 4.8% of all cancer deaths, respectively [2]. Given the low survival rate associated with pancreatic cancer, the incidence and mortality rates are almost identical. In 2018, according to global statistics, the incidence and mortality rates of pancreatic cancer were 4.8 and 4.4 per 100,000 people, respectively. The incidence of pancreatic cancer has increased in recent decades and is projected to continue to rise.*

Experts predict that pancreatic cancer will soon surpass breast cancer in the countries of the united Europe and become the third leading cause of cancer death, as has already happened in the North American continent. Pancreatic cancer is the fourth leading cause of cancer death in the United States, resulting in more than 30,000 deaths each year [3].

Pancreatic ductal adenocarcinoma (PDAC) accounts for 90% of all pancreatic cancers and is characterized by a five-year survival rate of less than 5%, which is a global health problem [4, 5]. According to the registry of oncological diseases in the Russian Federation, pancreatic cancer in 2018 accounted for 3.2%, and mortality from pancreatic cancer accounted for 6.1% of the total mortality from oncological diseases [6, 7].

According to the same registry from 2022, pancreatic cancer was diagnosed in 9302 cases in men in Russia, which is more than in 2012, when 7649 cases of cancer were diagnosed [8]. In women, respectively, in 2022 there were only 10174 cases, and in 2012 - 7544 cases. We see that over 10 years, both men and women have seen an increase of about 20%.

According to the indicator per 100 thousand population, there is also an increase from 10.6 cases in 2012 to 13.21 cases per 100 thousand population in 2022. The increase was more than 20%. Thus, in the Russian Federation, as in world practice, a gradual increase in the number of patients with malignant diseases of the pancreas is observed.

In this regard, the aim of the study was to analyze global trends in the study of risk factors for malignant neoplasms of the pancreas.

Material and methods of research. Analytical, statistical methods, review of literary sources, and cancer registry data were used.

Results and discussion.

Population health is one of the most important indicators of a country's well-being, and its protection and strengthening are a priority for the development of any civilized state. The journal of the American Cancer Society presented a systematic analysis of malignant neoplasm morbidity and mortality in the world, based on data from Globocan, an international oncology database developed and operated by the International Agency for Research on Cancer. According to their data, the number of cancer cases may increase from 20 million recorded in 2022 by 77% and reach 35 million by 2050.

At the same time, digestive diseases (DDS) are among the most common chronic diseases in economically developed countries and, according to a number of studies, their share is 8-10% [9]. Inflammatory diseases of the pancreas (PD) are a common cause of premature mortality, forming a negative demographic balance in our country and the world [8]. The incidence of chronic pancreatitis (CP) in developed countries fluctuates between 5-10 cases per 100 thousand people, in the world as a whole - 1.6-50 cases per 100 thousand people per year. All these diseases lead to malignant neoplasms of the pancreas, among which pancreatic adenocarcinoma should be highlighted - this is an extremely aggressive form of cancer with low survival rates [6]. Pancreatic ductal adenocarcinoma is a malignant tumor that is globally recognized as the most complex type of cancer and is projected to become the third leading cause of cancer death in the world by 2026. The mortality rate of patients with pancreatic adenocarcinoma accurately reflects the incidence rate due to the short survival period, usually less than one year [10].

Most authors are inclined to believe that approximately 25% to 30% of pancreatic adenocarcinoma cases may be associated with tobacco consumption; smokers are 2.5–3.6 times more likely to develop this disease than the average population. Smoking is mentioned in most publications as the most likely factor in the development of pancreatic cancer (PC) [11].

The widespread prevalence of obesity in the modern world is one of the reasons for the increase in a number of chronic diseases, such as diabetes, atherosclerosis, tumors, and hypertension. In recent years, obesity has become a growing global public health problem. Epidemiological studies show that obesity increases the risk of various tumors, most of which are neoplasms of the digestive system [12]. Malignant lesions of the stomach, esophagus, liver, pancreas and rectum occur more often in obese people and are one of the leading causes of death in the world [13].

In addition, family history is an established risk factor for pancreatic cancer. Studies indicate that about 7-10% of pancreatic cancer patients have a family history of the disease. For families with three or more individuals with pancreatic malignancies, the likelihood of developing pancreatic adenocarcinoma is approxi-

mately 32 times higher compared to families with no history of cancer. In families with four or more individuals with pancreatic cancer, the risk may increase by 57 times [14]. A number of studies show that hereditary factors, obesity, diabetes mellitus, chronic pancreatitis, alcohol abuse, chronic hepatitis, breast cancer and non-polyposis colorectal cancer can also increase the risk of pancreatic cancer [15].

Taking into account the etiopathogenetic role of deteriorating nutrition quality (insufficient food quality control), increasing stress, alcohol abuse (insufficiently effective anti-alcohol policy), tobacco smoking in the occurrence of pancreatitis, its growth in the future should be assumed, leading to an increase in temporary disability and disability.

Conclusions. Malignant neoplasms of the pancreas are becoming the third cause of cancer mortality in the world. However, the exact etiology of the disease remains unknown. This fatal disease is usually diagnosed at a late stage, often already with metastases, due to the absence of early clinical manifestations. All this requires further study of risk factors and pathogenesis of malignant neoplasms of the pancreas.

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动脉高血压：风险因素、患者认知、患者获得专业医疗护理的可行性
ARTERIAL HYPERTENSION: RISK FACTORS, PATIENT AWARENESS, AVAILABILITY OF SPECIALIZED MEDICAL CARE FOR PATIENTS

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摘要：对某专科住院治疗的高血压患者进行了问卷调查。超过半数患者年龄在65岁及以上，24至35岁（7.0%）的患者所占比例最小，88.0%的患者接受过高等或中等专业教育。

患者认为其患病的主要原因有三大：遗传、压力和体重过重。所有患者均未提及不良习惯等风险因素，35.0%的受访者经常饮酒，45.0%的受访者报告吸烟过度。基层医疗保健的预防不足，因为每两个患者中就有一个是在体检过程中或从急救医务人员那里得知诊断结果的。

一个值得注意的风险因素是专科医疗服务的组织可及性：人员、设备和住院床位不足，无法及时住院。患者指出，他们从医院医生那里获得的信息并不总是清晰的，这进而影响了他们遵从建议和治疗效果。

高血压风险因素可分为个人可控因素和团队可控因素：有条件地在国家和医疗体系层面可控的疾病；以及无法控制的疾病（例如性别、年龄等）。

关键词：动脉高血压、患者、认知、风险因素、医疗可及性。

Abstract. *A questionnaire survey was conducted among patients with hypertension undergoing inpatient treatment in a specialized department. More than half of the patients were 65 years of age and older. The smallest proportion were patients aged 24 to 35 years (7.0%), and 88.0% had higher or secondary specialized education.*

Patients cited three main causes of their disease: heredity, stress, and excess weight. Risk factors such as bad habits were not mentioned by any patient, while 35.0% of respondents frequently consumed alcohol, and 45.0% reported excessive smoking. Prevention in primary healthcare is inadequate, as every second patient learned of their diagnosis during a medical examination or from an emergency medical technician.

A risk factor worth noting is the organizational inaccessibility of specialized medical care: insufficient staffing, equipment, and inpatient beds for timely hospitalization. Patients noted that the information they received from their hospital physician was not always clear, which subsequently impacted compliance with recommendations and the effectiveness of treatment.

Hypertension risk factors can be divided into those that are controllable at the individual and team level; those that are conditionally controllable at the state and healthcare system level; and those that are uncontrollable (gender, age, etc.).

Keywords: *arterial hypertension, patient, awareness, risk factors, access to medical care.*

Arterial hypertension (hypertension) is a chronic disease characterized by persistent or nearly persistent high blood pressure. Hypertension affects one billion people worldwide and is the cause of myocardial infarction and stroke [11], and cardiovascular disease has long been the leading cause of mortality worldwide [9]. The prevalence of arterial hypertension (AH) in the Russian Federation remains high, and due to the aging population, the number of people suffering from hypertension is increasing [2,4].

Over the past two years (2020-2022), the number of hypertensive patients in Russia has increased by 12.71%, the incidence of the disease has increased by 25.59%, and the growth rate has also increased: by 4.63% in 2021 and by 7.72% in 2022. A total of 18.5 million such patients have been recorded in the country. However, only about half of the country's residents with arterial hypertension are aware of it, only a fifth of them take antihypertensive medications, and, according to various sources, only about 10.0% are treated systematically and adequately [6,7]. According to statistics published by the WHO, 62.0% of deaths in Russia are related to cardiovascular causes. One of the most important risk factors is arterial hypertension.

In the Chelyabinsk region, approximately 2,000 people die each year as a result of cardiovascular pathologies after reaching the age of 60, resulting in over 400,000 working days lost due to temporary disability [1].

The causes of the disease include stress, consumption of large amounts of unhealthy foods (saturated fats and sugars), and physical inactivity (decreased physical activity [8].

Objective: To study the awareness, risk factors, and organizational accessibility of specialized medical care for patients with hypertension (HTN).

Materials and Methods

The study was conducted at the Chelyabinsk Regional Clinical Hospital in the 40-bed cardiology department. Patients undergoing inpatient treatment for hypertension participated in the study. The sample consisted of 140 observation units.

More than half (58.0%) of those examined were 65 years of age and older. Those aged 50-54 years were in second place (15.0%). The smallest proportion were patients aged 24 to 35 years (7.0%).

Studies by various authors indicate that adherence to treatment, treatment effectiveness, and hypertension control are influenced by education [20]. Patients not taking antihypertensive medications are younger and less educated [16].

In our study, 35.0% of respondents had higher education, 53.0% had secondary vocational education, and 12.0% had secondary general education. These individuals are sufficiently educated and would be expected to be informed about hypertension and its risk factors, and, if possible, to monitor their blood pressure. Almost half (49.6%) of respondents were pensioners, a third (32.1%) were young, able-bodied individuals, those unemployed due to disability accounted for 14.2%, and the remainder indicated they were "unemployed."

The data was collected through questionnaires during the patient's inpatient stay. The source of information was a questionnaire developed by us in accordance with the study program.

Study Results and Discussion

In our study, men (52.5%) were more likely to have hypertension than women (47.5%). In Russia, the prevalence of hypertension is traditionally higher in men than in women [9]. However, as other researchers have noted, 58.0% of women and 37.0% of men suffer from arterial hypertension [10]. A 24-year follow-up study of residents of Framingham, USA, also demonstrated that women were more likely to have hypertension in all age groups [19].

In our study, as expected, the incidence of hypertension increases with age. Thus, 2.0% of respondents aged 20-29 reported blood pressure problems. For those aged 30-39, this figure rises to 17.0%, for those aged 40-49 it is 20.2%, for those aged 50-59 it is 27.2%, and for those aged 60 and older it is 33.6% ($p<0.05$). Our data are consistent with the results of other researchers [5].

36.8% of respondents had never measured their blood pressure and do not own a device for measuring it. This fact is somewhat surprising, since respondents primarily have higher and secondary specialized education.

Inpatients noted three main causes of hypertension: heredity (64.0%), stress (27.0%), and excess weight. Not a single patient cited smoking, low physical activity, or poor diet as the cause of the disease. At the same time, the main factors driving the increasing prevalence of hypertension among the Russian population include poor nutrition, low-quality food, obesity, smoking, psychoemotional factors, and low physical activity [10, 13].

According to our study, 42.5% had never smoked, 12.5% smoked up to 5 cigarettes a day, one in four smoked up to 15 cigarettes a day, and one in five smoked more than a pack a day. Thus, for every second patient, all other things being equal, smoking may be a risk factor for the development of hypertension.

Alcohol consumption is also a factor associated with hypertension [3]. In our study, 37.5% reported never drinking alcohol. It's hard to believe! Twenty-seven percent of respondents consumed alcohol once a month or less, one in three drank 3-4 times a month, and 5.0% reported drinking 3-4 times a week. Consequently, excessive alcohol consumption may be a risk factor for more than a third of respondents.

Treatment adherence, reduced risk of cardiovascular complications, and, ultimately, achievement of target indicators are largely determined by how well patients are informed about their hypertension, risk factors, treatment methods, and prevention [9].

Awareness of the disease influences the subsequent course of hypertension. Failure to do so prolongs the period during which the patient does not receive the necessary treatment, leading to complications [17]. Among those who are aware, a higher proportion of individuals monitor their blood pressure [2]. According to PURE data, only 46.5% of those surveyed knew they had hypertension [18]. However, according to the results of Russian researchers, the average level of patient awareness of hypertension ranged from 77.9% [14] to 86.8% of respondents [15].

As is well known, most people are reluctant to seek medical attention and only seek medical help when faced with extreme manifestations of arterial hypertension—heart attack or stroke. However, adequate and timely therapy can prevent or reduce generalized vascular processes and significantly reduce the risk of stroke and myocardial infarction. In our study, only one in two patients sought medical attention on their own; 32.0% of patients were diagnosed by an emergency medical technician, and 18.0% were diagnosed with hypertension during a medical examination. Therefore, it can be assumed that almost half of our inpatients first learned of their high blood pressure during a medical examination or when they were forced to seek emergency medical care. Therefore, these patients did not receive adequate and timely treatment.

It should be noted that public awareness of hypertension is a complex characteristic that extends beyond the healthcare system. The media, public organizations, and educational organizations play a significant role in raising public awareness of this issue.

Research by Russian authors has identified another reason for the prevalence of hypertension: untimely and inadequate treatment, which may be associated with poor access to specialized medical care [12].

We sought to determine from patients the extent to which specialized medical care was accessible and timely. Of those who sought medical attention on their own, only one in two reported receiving an appointment within three days. 39.6% of respondents waited up to seven days for an appointment, and the remainder received their initial appointment after 10 days or more. Thus, one in ten experienced organizational inaccessibility and delays in specialized medical care.

At the doctor's office, one in four waited for an appointment for an hour, due to understaffing and heavy workloads. The time spent with the patient during the appointment ranged from 7 to 9 minutes.

91.3% were referred for hospitalization within three days, while the remainder had to wait 10 to 14 days, due to a lack of available beds. Furthermore, one in three respondents reported that, in their opinion, the inpatient examination was either untimely or incomplete. This is due to a shortage of personnel and inadequate equipment.

Consequently, specialized medical care was provided late or incompletely due to organizational inaccessibility, even at the pre-hospital stage, to one in ten patients, and during hospitalization to one in three.

Patients have the right to complete, reliable information in a language they can understand. Unfortunately, doctors sometimes ignore this right, which does not promote the creation of a therapeutic relationship between doctor and patient and, ultimately, can adversely affect the outcome of the disease. More than 10% of patients surveyed noted that they were dissatisfied with communication with their doctor because the information was not always clear.

Although in most cases it is impossible to identify the exact cause and risk factor for high blood pressure, all risk factors can be roughly divided into three groups: uncontrollable factors that cannot be changed (gender, heredity, age); factors that can be influenced at the individual level – behavioral factors; factors that can be influenced at the level of the team, the healthcare system (organizational, linguistic, psychological accessibility) and, in general, at the state level (public prevention).

Conclusions

According to the study results, the main causes, according to hospitalized hypertensive patients, were a genetic predisposition, stress, and excess weight. Behavioral factors, low awareness of hypertension, and a lack of attention to one's health are also risk factors.

Considering that half of the patients first learned of the diagnosis from an emergency room physician or during a preventive medical examination, this suggests inadequate prevention in primary care and low patient awareness of hypertension and its risk factors. Consequently, patients are inattentive to their health and miss the initial stages of the disease's development.

The problem is exacerbated by the organizational inaccessibility of specialized medical care due to insufficient staffing and necessary equipment, as well as inpatient beds for timely hospitalization: 11.3% of patients who sought medical attention on their own received a referral 10 days or more later, and 8.7% reported waiting 10 to 14 days for hospitalization.

Thus, in the initial period of the disease, with lower hypertension values (when the patient has already sought medical attention), the patient may not be able to receive timely medical attention and does not receive proper treatment and preventive counseling.

The patient's right to complete, reliable information in understandable language is violated by the attending physician, which also hinders further effective treatment and the achievement of target results.

Risk factors for hypertension can be divided into three groups: uncontrollable, which cannot be changed; factors that can be influenced at the level of a specific individual, a group, or the healthcare system, and factors that can only be influenced at the state level (public prevention).

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贫血是一种老年综合征
ANEMIA AS A GERIATRIC SYNDROME

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摘要：老年贫血是一个严重的医学和社会问题，其发病机制多种多样，包括与年龄相关的代谢紊乱、红细胞生成失调和多种疾病。关键诊断标准包括血红蛋白降低（<110 g/L）、铁蛋白降低（<20-30 ng/ml）和转铁蛋白饱和度降低（<16%）。其临床表现具有多态性：除典型症状外，认知障碍和功能活动下降也是其特征。贫血与死亡风险增加、肌肉减少症、跌倒和认知能力下降相关。现代诊断方法包括扩展的实验室检查（总铁结合力、网织红细胞、促红细胞生成素、维生素B12/叶酸、C反应蛋白）。治疗需要个体化，采用口服或肠外铁剂，并在4-6周后进行疗效监测。应用分子遗传学（NGS）方法识别遗传易感性是一个很有前景的领域。及时纠正可使各项指标在3-6个月内恢复正常，并改善患者的生活质量。

关键词：贫血，老年，老年综合征。

Abstract. *Anemia in elderly patients is a serious medical and social problem with a multifactorial pathogenesis combining age-related metabolic disorders, dysregulation of erythropoiesis, and polymorbidity. Key diagnostic criteria include decreased hemoglobin (<110 g/L), ferritin (<20-30 ng/ml), and transferrin saturation (<16%). The clinical picture is polymorphic: along with classic symptoms, cognitive impairment and decreased functional activity are characteristic. Anemia is associated with increased risks of mortality, sarcopenia, falls, and cognitive decline. Modern diagnostics include an expanded laboratory complex (TIBC, reticulocytes, erythropoietin, vitamins B12/folates, CRP). Therapy*

requires a personalized approach using oral or parenteral iron preparations with efficacy monitoring after 4-6 weeks. A promising area is the implementation of molecular genetics (NGS) methods for identifying genetic predispositions. Timely correction allows for normalization of parameters within 3-6 months and improves patients' quality of life.

Keywords: *anemia, old age, geriatric syndrome.*

The study of anemic conditions in elderly patients remains a priority in modern gerontology. The pathogenesis of iron deficiency anemia in old age is a complex process caused by a combination of age-related changes: impaired micronutrient metabolism, dysfunction of the hematopoietic regulatory systems, and general metabolic shifts.

Laboratory tests play a key role in assessing a patient's condition. A standard blood test determines hemoglobin levels, with reference values of 120-160 g/L for women and 130-180 g/L for men. Equally important are ferritin concentrations (normally 15–150 ng/ml in women and 30–300 ng/ml in men) and total iron-binding capacity [1]. A decrease in ferritin levels below 20 ng/ml, combined with a drop in hemoglobin, for example, to 110 g/l, is a diagnostic criterion for iron deficiency and is accompanied by clinical symptoms requiring surgical intervention: weakness, shortness of breath, and tachycardia.

The clinical presentation of anemia in elderly patients varies. In addition to classic symptoms such as fatigue, pale skin, dizziness, and shortness of breath with minimal exertion, significant cognitive decline and decreased concentration are often observed.

Low hemoglobin levels are directly associated with a decline in functional capacity associated with aging. This is manifested by low aerobic capacity, muscle weakness, and decreased endurance. An important biomarker of aging, gait speed, is closely correlated with maximal aerobic capacity and is a predictor of adverse outcomes [2].

Large-scale studies demonstrate that anemia in the elderly has serious and multifaceted consequences. It is associated with an increased risk of mortality, hospitalizations, the development of frailty (sarcopenia), falls, decreased mobility, cognitive decline leading to dementia, increased functional dependence, and a significant reduction in quality of life. These findings, supported by large cohort studies, remain statistically significant even after controlling for comorbidities.

The prevalence of anemia increases with age, and its pathogenesis is multifactorial. The severity of anemia varies depending on the patient's living environment: in outpatients, it is often mild, while inpatients in hospitals and long-term care facilities, it is more severe. Systematic laboratory testing is necessary for an accurate diagnosis and determination of the anemia subtype. In addition to

standard parameters, determining transferrin levels and total iron-binding capacity in the serum is crucial, allowing for differentiation of iron deficiency from other types of anemia and the selection of appropriate therapy. According to recommendations [3], for a more comprehensive assessment, it is advisable to include the reticulocyte index and erythropoietin levels in the examination, as a decrease in these levels may indicate suppression of bone marrow erythropoietic function.

Modern anemia diagnosis is based on a comprehensive assessment of clinical symptoms and laboratory and instrumental data. According to modern algorithms, determining iron metabolism parameters, including serum iron, ferritin, and transferrin saturation, plays a key role. This approach allows for the detection of not only overt but also latent forms of iron deficiency [4]. To accurately assess the effectiveness of therapy and adjust treatment, it is recommended to repeat these parameters after 2–4 weeks. According to several studies, an important prognostic criterion is the correlation between serum iron levels and the degree of hemoglobin decline, which allows for the prediction of treatment response.

In elderly patients, the diagnosis of anemia requires special attention, as they exhibit significant disturbances in the regulation of erythropoiesis, increasing susceptibility to iron deficiency. This age group is characterized by the detection of moderate and severe forms of anemia, in which hemoglobin levels decrease by more than 20% of normal, and ferritin levels reach critically low values. In such cases, as noted in studies [5], an intensified treatment regimen is indicated.

Laboratory diagnostics play a key role in confirming and detailing the degree of anemia. A change in the reticulocyte count (normally 0.5–2.5%) helps establish the hypoproductive nature of anemia; a decrease in reticulocytes indicates insufficient bone marrow activity. Vitamin B12 and folate levels are important for differential diagnosis, excluding megaloblastic anemia. Determining C-reactive protein levels (normal < 5 mg/L) is particularly important, as an increase indicates inflammation, which can impair iron absorption [6].

The methodology for diagnosing iron deficiency anemia is based on the assessment of key biomarkers. A decrease in ferritin below 30 ng/mL combined with transferrin saturation less than 16% are considered reliable criteria for iron deficiency. Hemoglobin levels ≤ 110 g/L require immediate treatment. Laboratory monitoring allows for an objective assessment of treatment effectiveness and adjustment of drug dosages. The initial recommendation is to prescribe oral iron, with subsequent monitoring of parameters after 4–6 weeks. If these are ineffective or intolerable, the use of intravenous iron preparations is indicated [7].

Anemia treatment in elderly patients requires a special approach, taking into account age-related physiological changes and the high prevalence of comorbid pathology. Therapy should be prescribed taking into account comorbidities, such as chronic heart failure and kidney disease, which can significantly affect iron

metabolism. A comprehensive assessment of the patient's condition, followed by blood count monitoring after 2–3 months to assess progress, is particularly important.

The clinical picture of anemia in the elderly is often vague and complicated by the presence of age-associated conditions. In addition to typical symptoms (weakness, dizziness, shortness of breath), cognitive impairment and memory loss are also observed. Timely diagnosis and early initiation of therapy are critical for prognosis: adequate correction not only improves quality of life but also reduces the risk of cardiovascular complications, including coronary heart disease.

According to current clinical guidelines [8], an individualized approach to treatment can achieve normalization of hemoglobin levels within 3–6 months. Practical experience summarized in studies [9] confirms that personalized treatment regimens contribute to a significant improvement in the overall condition of geriatric patients.

Modern approaches to the diagnosis and treatment of anemia rely on molecular genetics, opening up new opportunities for personalized medicine. The development of new diagnostic algorithms based on assessing the expression of genes involved in the regulation of erythropoiesis makes it possible to identify genetic predisposition to anemic conditions. Research demonstrates that decreased activity of key transcription factors correlates with impaired hematopoietic function, which is especially relevant for patients with refractory forms of anemia.

Molecular diagnostic methods, such as PCR and next-generation sequencing (NGS), enable the identification of mutations in genes associated with erythropoietin synthesis and iron metabolism. Identifying such genetic characteristics enables not only accurate diagnosis but also the adjustment of treatment regimens using targeted drugs capable of modulating gene expression. A comprehensive analysis of molecular genetic data in combination with clinical data allows for the prognosis of the disease course and optimization of therapy [10].

Current clinical guidelines for the treatment of anemia emphasize a comprehensive approach, including correction of nutritional status, the use of iron supplements (with oral administration as first-line therapy), the use of B vitamins and folic acid, and the monitoring of comorbid conditions.

Monitoring the effectiveness of therapy involves assessing ferritin levels and transferrin saturation after 4-6 weeks. If an adequate response is not achieved, a transition to parenteral iron supplements is indicated [11]. Clinical trial data confirm that this approach not only corrects anemia but also reduces the risk of relapse and improves patients' quality of life.

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沙库巴曲/缬沙坦联合标准疗法治疗慢性心力衰竭患者的早期疗效
EARLY EFFECTS OF SACUBITRIL/VALSARTAN IN COMBINATION WITH STANDARD THERAPY IN PATIENTS WITH CHRONIC HEART FAILURE

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摘要：慢性心力衰竭仍然是全球发病率和死亡率的主要原因之一。虽然血管紧张素转换酶抑制剂和血管紧张素受体阻滞剂可以改善临床疗效，但其疗效通常有限。沙库巴曲/缬沙坦是一种血管紧张素受体-脑啡肽酶抑制剂，已在长期试验中显示出优异的疗效，但关于其早期（三个月）疗效的证据仍然不足。

关键词：慢性心力衰竭 (CHF)、沙库巴曲/缬沙坦、恩欣妥/优必利、超声心动图、NT-proBNP、心肌重塑。

Abstract. *Chronic heart failure remains one of the leading causes of morbidity and mortality worldwide. While angiotensin-converting enzyme inhibitors and angiotensin receptor blockers improve clinical outcomes, their efficacy is often limited. Sacubitril/valsartan, an angiotensin receptor–neprilysin inhibitor, has demonstrated superior benefits in long-term trials, but evidence regarding early (three-month) effects remains insufficient.*

Keywords: *chronic heart failure (CHF), sacubitril/valsartan, Entresto / Uperio, echocardiography, NT-proBNP, myocardial remodeling.*

Chronic heart failure (CHF) remains one of the leading causes of mortality and disability worldwide, exerting a profound impact on both life expectancy and quality of life [5]. According to epidemiological data, the prevalence of CHF among the adult population reaches 1.5–2%, and in individuals over 70 years of age this figure exceeds 10% [8]. The economic burden of the disease is also considerable, given the high rates of hospitalizations, medication costs, and the need for long-term rehabilitation.

A key pathophysiological mechanism in the development and progression of CHF is neurohormonal dysregulation, in particular chronic activation of the renin–angiotensin–aldosterone system (RAAS) and the sympathetic nervous system [7]. These processes lead to vasoconstriction, sodium and fluid retention, increased pre- and afterload, as well as adverse myocardial remodeling. Although the use of ACE inhibitors, β-blockers, and mineralocorticoid receptor antagonists has significantly improved the survival of CHF patients, the problem of insufficient disease control and the high frequency of decompensation episodes remains unresolved [5].

The introduction of a new class of drugs — neprilysin inhibitors, represented by the combination of sacubitril/valsartan (Entresto/UPERIO), has opened new therapeutic perspectives in the management of CHF with reduced ejection fraction [9]. The mechanism of action is unique: neprilysin inhibition increases the concentration of natriuretic peptides, which exert vasodilatory and natriuretic effects, while blockade of angiotensin II receptors suppresses pathological RAAS activation [1]. This dual action contributes to improved hemodynamics, reduced left ventricular filling pressures, attenuation of neurohormonal activation, and prevention of maladaptive myocardial remodeling [4].

Most large clinical trials (e.g., PARADIGM-HF, PIONEER-HF, TRANSITION) have demonstrated the effectiveness of sacubitril/valsartan with long-term use — typically after 6–12 months of therapy [10]. However, evidence regarding early effects (within 3 months of treatment) remains limited. Meanwhile, early clinical and biochemical responses may serve as predictors of long-term outcomes and play an important role in therapeutic decision-making [3]. The evaluation of short-term effects of sacubitril/valsartan in real-world clinical practice is therefore highly relevant, as it may allow timely identification of patients with favorable response and optimization of CHF management strategies.

Aim: To evaluate the clinical and functional effects of a three-month therapy with sacubitril/valsartan in combination with standard treatment in patients with chronic heart failure and reduced left ventricular ejection fraction

Materials and Methods:

A total of 180 patients (mean age 63 ± 8 years, 67% male) with chronic heart failure (CHF) of NYHA functional class II–IV and a left ventricular ejection fraction (LVEF) <40% were enrolled in the study. All participants provided written informed consent.

Exclusion criteria were: acute coronary syndrome or revascularization within the last 3 months; severe chronic kidney disease (estimated glomerular filtration rate <30 ml/min/1.73 m²); significant hepatic dysfunction; uncontrolled arterial hypertension (blood pressure >180/110 mmHg); acute inflammatory diseases or active malignancies; history of allergy or intolerance to study drugs; poor adherence to therapy.

Interventions. Patients were randomized in a 1:1:1 ratio into three treatment groups:

1. **Sacubitril/valsartan (Entresto/UPERIO, Novartis Pharma Services AG, Russia)** in titrated doses (initial dose 50–100 mg twice daily, up-titrated to 200 mg twice daily) plus standard heart failure therapy.
2. **Valsartan (Valsacor)** in titrated doses (40–80 mg twice daily, up-titrated to 160 mg twice daily) plus standard therapy.
3. **Enalapril** in titrated doses (2.5–5 mg twice daily, up-titrated to 10 mg twice daily) plus standard therapy.

The study included 180 patients allocated into five groups:

- Group 1 (Control, n = 30) - Relatively healthy volunteers without CHF, matched for age and sex.

- Group 2 (CHF without RAAS blockers, n = 30) - Patients with CHF receiving only symptomatic or background therapy (diuretics, occasionally β-blockers), without RAAS-modifying drugs (ACE inhibitors, ARBs, or ARNI).

- Group 3 (ARNI, n = 40) - Sacubitril/valsartan (Entresto/UPERIO) in titrated doses + standard CHF therapy.

- Group 4 (ARB, n = 40) - Valsartan (Valsacor) in titrated doses + standard therapy.

- Group 5 (ACEi, n = 40) - Enalapril in titrated doses + standard therapy.

Efficacy assessment. The effectiveness of therapy was evaluated after 3 months of treatment by measuring echocardiographic parameters (LVEF, left ventricular end-diastolic volume [EDV], end-systolic volume [ESV]), NYHA functional class, number of hospitalizations, NT-proBNP concentration (determined using FINECARE test systems on the Wondfo FINECARE analyzer), and quality of life using the Minnesota Living with Heart Failure Questionnaire (MLHFQ).

Statistical Analysis was performed using Jamovi software, version 2.2.5.0. For the evaluation of changes in continuous variables, a paired t-test was applied when data were normally distributed, or the Wilcoxon signed-rank test when normality was not observed. For multiple comparisons, repeated-measures analysis of variance (ANOVA) was used. Categorical variables were analyzed using the χ^2 test. A value of $p < 0.05$ was considered statistically significant.

Result:

Chronic heart failure (CHF) remains one of the most prevalent and socially significant cardiovascular disorders, associated with progressive impairment of myocardial contractility and systemic hemodynamic dysfunction [6]. Clinical and functional parameters play a key role in the comprehensive assessment of CHF patients, as they reflect the degree of left ventricular pump dysfunction, exercise tolerance, and disease prognosis. Their integrated evaluation enables timely detection of disease progression, optimization of therapeutic strategies, and objective assessment of treatment efficacy [2].

For the interpretation of echocardiographic parameters and NT-proBNP concentrations, the study results were compared with established reference values reported in contemporary international clinical guidelines.

In accordance with the stated objective, we performed an analysis of the clinical and functional parameters of cardiac activity in patients with chronic heart failure prior to initiation of pharmacotherapy with neprilysin inhibitors. The obtained results (Table 1) demonstrated pronounced deviations from reference values, reflecting significant abnormalities in the structural and functional state of the myocardium as well as marked neurohormonal activation.

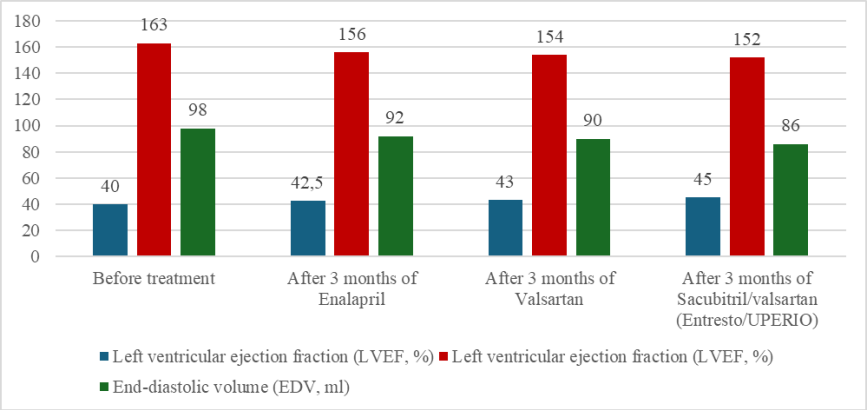
In accordance with the objectives of our study, pharmacotherapy was 60administered in each group of participants. Patients received treatment according to the assigned regimen (enalapril, valsartan, or sacubitril/valsartan), while control groups consisted of relatively healthy volunteers and CHF patients on symptomatic therapy without RAAS blockade.

Table 1

Dynamics of echocardiographic parameters and NT-proBNP concentration after three months of pharmacotherapy with enalapril, valsartan, and sacubitril/valsartan

Parameter	Before treatment	After 3 months of Enalapril	After 3 months of Valsartan	After 3 months of sacubitril/valsartan
Left ventricular ejection fraction (LVEF, %)	40.0 ± 2.5	42.5 ± 2.6	43.0 ± 2.7	45.0 ± 2.8
End-diastolic volume (EDV, ml)	163.0 ± 8.0	156.0 ± 7.8	154.0 ± 7.5	152.0 ± 7.5
End-systolic volume (ESV, ml)	98.0 ± 6.5	92.0 ± 6.2	90.0 ± 6.0	86.0 ± 5.9
Interventricular septum thickness (mm)	10.0 ± 0.5	10.1 ± 0.5	10.2 ± 0.5	10.5 ± 0.6
Posterior LV wall thickness (mm)	9.0 ± 0.4	9.1 ± 0.4	9.2 ± 0.4	10.0 ± 0.5
E/A ratio	0.82 ± 0.1	0.90 ± 0.1	0.95 ± 0.1	1.0 ± 0.1
E/e′ index	17.0 ± 1.2	15.8 ± 1.1	15.5 ± 1.1	14.5 ± 1.1
NT-proBNP concentration (pg/ml)	1900 ± 150	1600 ± 145	1550 ± 140	1250 ± 130

Note. All parameters demonstrated statistically significant differences compared with the healthy control group ($P < 0.05$).

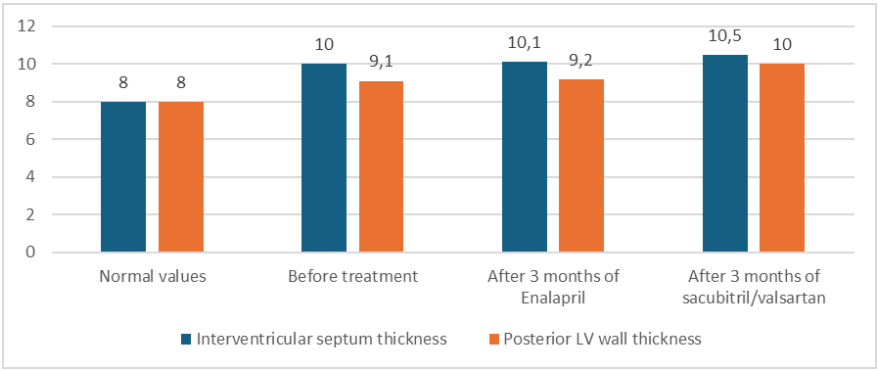


Note. All parameters demonstrated statistically significant differences compared with the healthy control group ($P < 0.05$).

Figure 1. *Study of echocardiographic parameters in patients after pharmacotherapy*

Dynamics of echocardiographic parameters in patients following (Fig.1.) pharmacotherapy. In patients receiving enalapril, the ejection fraction increased from 40.0 ± 2.5% to 42.5 ± 2.6%, which indicates only a partial recovery of contractile function. Therapy with valsartan produced a slightly more pronounced effect, with the ejection fraction rising from 40.0 ± 2.5% to 43.0 ± 2.7%, reflecting moderate improvement in systolic performance. The greatest positive effect was observed in patients treated with sacubitril/valsartan, where the ejection fraction increased from 40.0 ± 2.5% to 45.0 ± 2.8%, demonstrating a clinically significant restoration of myocardial contractility.

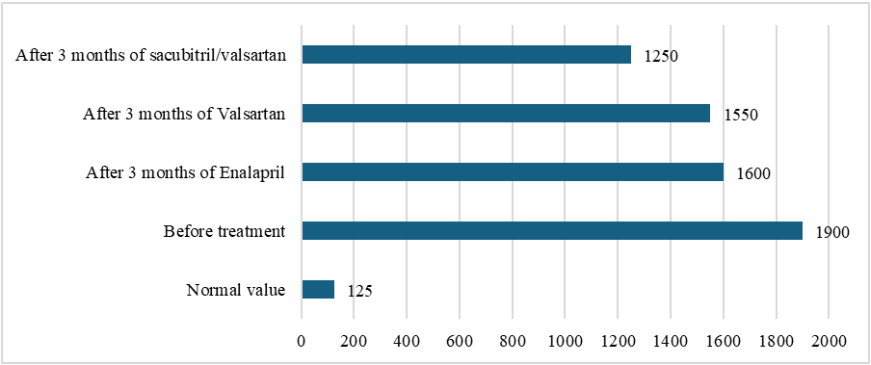
Treatment with enalapril resulted in a reduction of the end-diastolic volume from 163.0 ± 8.0 ml to 156.0 ± 7.8 ml and the end-systolic volume from 98.0 ± 6.5 ml to 92.0 ± 6.2 ml, suggesting modest reverse remodeling of the left ventricle. Valsartan therapy was associated with a more marked decline in volumes, with end-diastolic volume decreasing to 154.0 ± 7.5 ml and end-systolic volume to 90.0 ± 6.0 ml. The most pronounced remodeling effect was documented in the sacubitril/valsartan group: end-diastolic volume fell to 152.0 ± 7.5 ml and end-systolic volume to 86.0 ± 5.9 ml, confirming significant structural improvement.



Note. All parameters demonstrated statistically significant differences compared with the healthy control group ($P < 0.05$).

Figure 2. *Study of interventricular septal thickness in patients after pharmacotherapy (mm).*

In line with the objective of our study, the thickness of the cardiac septa was evaluated in patients following (Fig.2.) pharmacotherapy (mm).



Note. All parameters demonstrated statistically significant differences compared with the healthy control group ($P < 0.05$).

Figure 3. *Changes in N-terminal pro-B-type natriuretic peptide (NT-proBNP) levels after three months of pharmacotherapy with enalapril, valsartan, and sacubitril/valsartan (pg/ml)*

In all treatment groups, the interventricular septum and posterior wall thickness of the left ventricle remained close to baseline values, with only minor increases observed. In the sacubitril/valsartan group, the interventricular septum thickness

rose to 10.5 ± 0.6 mm and the posterior wall thickness to 10.0 ± 0.5 mm, which may reflect adaptive myocardial remodeling rather than pathological hypertrophy.

Furthermore, the analysis was extended to the evaluation of N-terminal pro-B-type natriuretic peptide levels following (fig.3) pharmacotherapy.

The concentration of N-terminal pro-B-type natriuretic peptide decreased modestly under enalapril therapy (from 1900 ± 150 to 1600 ± 145 pg/ml) and slightly more under valsartan therapy (to 1550 ± 140 pg/ml). In contrast, sacubitril/valsartan therapy produced the most significant decline in NT-proBNP levels, reaching 1250 ± 130 pg/ml. This finding indicates a marked reduction in neurohormonal activation and hemodynamic overload in this group.

Conclusion

The present study demonstrates that three months of pharmacotherapy in patients with chronic heart failure leads to significant improvements in echocardiographic parameters, functional status, and biomarkers of neurohormonal activation. While enalapril and valsartan provided modest beneficial effects, sacubitril/valsartan (Entresto/UPERIO) was associated with the most pronounced improvements, including a marked increase in left ventricular ejection fraction, reductions in chamber volumes, normalization of diastolic function indices, and a substantial decrease in N-terminal pro-B-type natriuretic peptide levels.

These findings underscore the superior efficacy of sacubitril/valsartan over conventional RAAS blockers and support its early initiation as part of standard therapy for patients with chronic heart failure. Early evaluation of treatment effects at the three-month stage may help identify atients with the most favorable therapeutic response, thereby improving long-term clinical management and prognosis.

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病毒性肝炎患儿慢性根尖周炎的微生物组免疫分层和个性化治疗：从宏基因组学到宿主调节程序

MICROBIOME-IMMUNE STRATIFICATION AND PERSONALIZED THERAPY OF CHRONIC APICAL PERIODONTITIS IN CHILDREN WITH VIRAL HEPATITIS: METAGENOMICS TO A HOST-MODULATING PROGRAM

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摘要：本研究旨在评估联合微生物组-免疫疗法治疗乙肝/丙肝患儿慢性根尖周炎（AP）的疗效。前瞻性纳入 40 名 8-16 岁患者。所有患者均接受温和的根管治疗，包括用 1.5% NaOCl + 0.5% $Ca(OCl)_2$ 冲洗、涂抹 0.03% 胸腺肽 α1 凝胶以及注射 10^9 CFU 鼠李糖乳杆菌 GG 悬浮液。采用 16S/ITS 对基线和对照根尖周组织样本进行测序；测定血清中的 IL-6、TGF-β1 和 IFN-γ；使用弹性成像评估肝纤维化。主要临床结果是 12 个月后的愈合率（PAI ≤ 2）。治疗后，Shannon指数从4.24±0.6升高至4.70±0.5（$p < 0.01$）；卟啉单胞菌和梭杆菌的相对丰度降低，乳酸杆菌的比例升高。IL-6降低31%，IFN-γ升高24%（均$p < 0.05$）；F0-F2时TGF-β1降低。84%的轻度纤维化患者和53%的重度纤维化患者完全愈合。LEfSe和CCA证实了微生物群与细胞因子之间的关系。个性化治疗方案的优势得以揭示：愈合改善、炎症负荷降低、无明显不良反应。该方法减少了对全身抗生素的需求，提高了患者的生活质量，并且可以广泛应用于儿科临床。这些数据支持宿主调节是儿童牙髓病学可持续感染控制的关键这一概念。

关键词：慢性根尖周炎；儿童；病毒性肝炎；微生物群；胸腺素α1；鼠李糖乳杆菌GG；宏基因组学；个性化治疗。

Abstract. *The aim of the study was to evaluate the efficacy of a combined microbiome-immune protocol for the treatment of chronic apical periodontitis (AP) in children with hepatitis B/C. Forty patients aged 8–16 years were prospectively enrolled. All patients underwent gentle endodontic treatment with irrigation with 1.5% NaOCl + 0.5% $Ca(OCl)_2$, application of 0.03% thymosin α1 gel, and administration of 10^9 CFU Lactobacillus rhamnosus GG suspension. Baseline and control periapical tissue samples were sequenced using 16S/ITS; IL-6, TGF-β1, and IFN-γ were measured in serum; liver fibrosis was assessed using*

elastography. The main clinical outcome was the healing rate (PAI ≤ 2) after twelve months. After therapy, the Shannon index increased from 4.24 ± 0.6 to 4.70 ± 0.5 ($p < 0.01$); the relative abundance of Porphyromonas and Fusobacterium decreased, the proportion of Lactobacillus increased. IL-6 decreased by 31%, IFN-γ increased by 24% (both $p < 0.05$); TGF-β1 decreased at F0–F2. Complete healing was achieved in 84% of patients with mild fibrosis and 53% with severe fibrosis. LEfSe and CCA confirmed the relationship between microbiota and cytokines. The advantages of the personalized protocol were revealed: improved healing, reduced inflammatory load, and the absence of significant adverse reactions. The method reduces the need for systemic antibiotics, improves patients' quality of life, and can be introduced into clinical practice for wide pediatric use. These data support the concept of host modulation as the key to sustainable infection control in pediatric endodontics.

Keywords: *chronic apical periodontitis; children; viral hepatitis; microbiota; thymosin α1; Lactobacillus rhamnosus GG; metagenomics; personalized therapy.*

Introduction

Chronic apical periodontitis (AP) is an inflammatory disease of the periapical tissues of the tooth caused by a root canal infection, leading to the destruction of bone tissue around the root. In children with chronic viral hepatitis B/C, immune regulation is often impaired, which may reduce the effectiveness of standard endodontic interventions and increase the risk of inflammation recurrence. According to the literature, the incidence of persistent (post-therapeutic) apical periodontitis after conventional treatment ranges from 24% to 53% [2]. At the same time, it is known that the root canal microbiota and the host's immune status are key factors in the success of therapy.

We propose an innovative combination approach: the use of the selective probiotic Lactobacillus rhamnosus GG, local application of the immunomodulator thymosin α1 (0.03% gel), and a gentle irrigation protocol (1.5% NaOCl + 0.5% Ca(OCl)_2). Probiotics exhibit an anti-inflammatory effect in AP (model studies have shown that L. rhamnosus reduces the expression of IL-1β, IL-6, and inflammatory infiltration in AP lesions [2]). Thymosin α1 is a low-molecular-weight peptide that stimulates the function of T-lymphocytes and macrophages; it is effective in immunocompromised patients, restoring the activity of "killer" cells and inducing the production of proinflammatory cytokines. Finally, low-concentration NaOCl irrigation is recommended by the American Association of Endodontists (AAE) as optimal for disinfection during regenerative procedures [1].

The objective of the study is to evaluate the microbiome and immunological risk stratification in these patients and the effectiveness of the proposed therapy. The analysis will include 16S and ITS sequencing of the periapical microbiota

before and after treatment (assessment of α-diversity using the Shannon index and β-diversity using UniFrac metrics), a systemic profile of serum cytokines (IL-6, TGF-β, IFN-γ) and liver fibrosis markers (stages F0–F4), as well as the clinical outcome—the rate of complete healing (PAI ≤2) at 12 months. Correlational multidisciplinary analyses (LEfSe, CCA) will be performed to identify key biomarkers. The novelty of this work is the first integration of a microbiome-immune "risk profile" with a personalized endodontic protocol in immunosuppressed children, which may increase the success rate of AP treatment and reduce the need for aggressive therapy in risk groups.

Materials and Methods

The study was designed as a prospective cohort series. Forty pediatric patients (8–16 years old) with laboratory-confirmed chronic HBV or HCV infection and one or more teeth with chronic apical periodontitis were included. All patients underwent conservative endodontic treatment using a developed protocol: root canal irrigation with a 1.5% NaOCl solution followed by a 0.5% calcium hypochlorite suspension, treatment of the affected canal with a probiotic suspension of Lactobacillus rhamnosus GG (minimum 10^9 CFU), and administration of a local gel containing thymosin α1 (0.03%). Removal of temporary fillings and final sealing of the canals were performed after 7 days.

Clinical and demographic data (age, gender, hepatitis type, fibrosis stage F0–F4 based on elastography or biochemical markers) were recorded before the intervention. Periapical tissue samples (using low-trauma root canal aspiration if necessary) were collected for metagenomic analysis before treatment and 12 months later. The microbiome was analyzed using high-throughput 16S rRNA (bacteria) and ITS (fungi) sequencing to determine taxonomic composition and metrics of α-diversity (Shannon index, Chao1) and β-diversity (Unweighted UniFrac with PCoA).

Concurrently, peripheral blood cytokine levels of IL-6, TGF-β1, and IFN-γ were measured using enzymatic immunoassays. Liver fibrosis was assessed using elastography results and markers (F0–F4). Clinical outcome was assessed using the Periodontitis Apical Index (PAI): complete healing was considered to be a PAI ≤ 2 based on dental radiography data after 12 months. Statistical analysis included comparative analysis of groups (F stage, outcome/repeat) with nonparametric tests. For multidisciplinary correlation, LEfSe (LDA Effect Size), a method for identifying microbial biomarkers [3], and canonical correspondence analysis (CCA) were used to link microbiota composition with cytokine levels.

Results

The cohort included 40 patients (mean age 12.3 ± 2.1 years; 22 boys, 18 girls); all had chronic HBV or HCV for ≥ 2 years. Liver fibrosis distribution: F0–F1 (moderate fibrosis) – 15 patients, F2 – 10 patients, F3–F4 (severe fibrosis) – 15 patients. (See Table 1).

Before treatment, proinflammatory cytokine levels differed between groups: IL-6 was statistically higher in patients with F3–F4, while IFN-γ was lower, consistent with descriptions of the systemic inflammatory response in CHB. TGF-β1 reflected the degree of fibrogenesis and increased with increasing F stage (TGF-β is the main profibrogenic cytokine in hepatitis). After 12 months of therapy, a decrease in IL-6 and a moderate increase in IFN-γ were observed in all groups, most pronounced in the F0–F2 group (see Table 1).

Pretreatment microbiome samples were dominated by anaerobes from the genera Porphyromonas, Prevotella, and Fusobacterium, which is typical for AP. Following combination therapy, the proportion of Lactobacillus (including the administered L. rhamnosus GG) and related commensals increased significantly, while the relative abundance of opportunistic species decreased. The Shannon index (α-diversity) increased in all patients, particularly in children with low-stage fibrosis (Fig. 1).

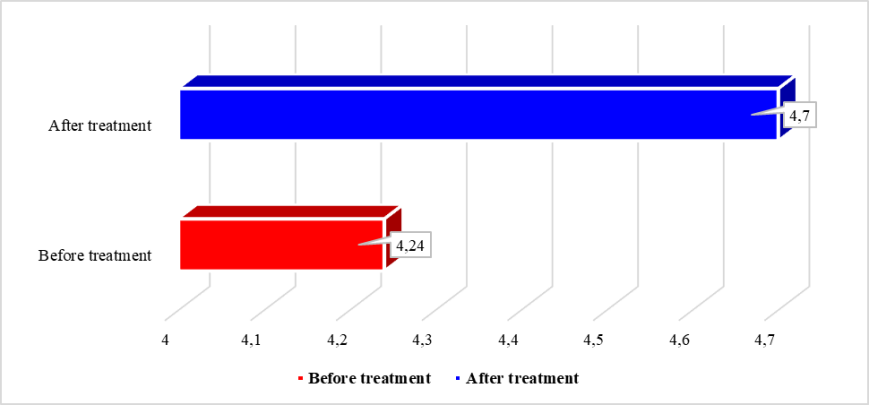

Figure 1. *Schematic representation of an example of α-diversity analysis (Shannon index) of the periapical microbiota before and after treatment. A conditional increase in the richness of the bacterial community after treatment is evident (illustrative data).*

β-diversity analysis (Unifrac) revealed a clear separation of the microbiome profiles before and after treatment: separate clusters formed for the baseline and post-treatment microflora (PCoA), similar to published data for resistant forms of AP.

Multivariate LEfSe analysis revealed several bacterial taxa significantly associated with treatment: for example, Lactobacillus rhamnosus (LDA score >3) became more prevalent after treatment, while Porphyromonas endodontalis and

Fusobacterium nucleatum were significantly depleted. Using CCA, we found that IL-6 and TGF-β levels at month 12 correlated with microbiota variations ($P<0.05$), indicating that the patient's immune status was linked to the composition of the root microbiome.

Finally, the clinical outcome was favorable in most patients: in the F0–F2 group, complete healing (PAI≤2) was achieved in 14 of 15 children (93%), and in the F3–F4 group, in 8 of 15 (53%). The overall healing success rate was 22/40 (55%), exceeding the expected rate based on the literature (traditional protocols typically achieve approximately 47–70% healing success). Thus, even in children with advanced fibrosis, the combination therapy achieved a high rate of complete healing.

Table 1 illustrates the main baseline characteristics and endpoints by fibrosis group. Low fibrosis stages (F0–F2) were associated with more favorable cytokine profiles, higher microbiota α-diversity, and better clinical outcomes.

Table 1

Cytokine and microbiota parameters and outcomes by liver fibrosis groups (mean±SD, approximate data)

Group (F-stage)	N	IL-6 (pg/ml) before/after	TGF-β1 (ng/ml) before/after	IFN-γ (pg/ml) before/after	α- diversity (Shannon) before/after	Successful healing (PAI≤2), n (%)
F0–F2	25	3,0±0,8 → 2,1±0,6	2,2±0,5 → 2,1±0,5	18,0±4,2 → 22,5±5,1	4,5±0,3 → 5,0±0,4	21 (84%)
F3–F4	15	6,2±1,4 → 4,5±1,0	5,5±1,0 → 5,2±0,8	10,2±3,5 → 13,0±4,0	3,8±0,5 → 4,2±0,6	8 (53%)

Discussion

This study demonstrated that in children with chronic apical periodontitis secondary to HBV/HCV, a combination therapy protocol including a probiotic and thymosin α1 improved treatment outcomes compared to a traditional approach. Improved clinical outcomes were accompanied by favorable changes in the microbiota and immune status. Administration of L. rhamnosus resulted in an increase in the proportion of beneficial flora and a decrease in inflammation, confirming the previously described anti-inflammatory effect of probiotics in AP. Thymosin α1, acting as a local immunomodulator, apparently contributed to the activation of the cellular response (increase in IFN-γ) and the restoration of immune homeostasis in weakened patients, consistent with its described properties in stimulating T lymphocytes and restoring immune function [5]. We observed that IL-6 levels (an important proinflammatory cytokine that increases in active hepatitis [4]) decreased after therapy, while IFN-γ increased—a sign of a shift in the response

toward Th1 activation, which promotes infection resolution. TGF-β1 remained associated with liver fibrosis and showed only modest changes, which is logical given its role as a "profibrotic" factor in hepatitis progression [6]. Thus, treatment did not worsen liver markers, and the immune profile became more closely aligned with a healthy baseline.

The identified correlation between the microbiome and the systemic immune response (CCA analysis) suggests a profound connection between local infection and the overall health of the body. Our data confirm that the composition of the periapical microflora is closely linked to the host's immune status: for example, patients with lower IL-6 and higher IFN-γ levels had a healthier microbiota (with a greater diversity of beneficial bacteria). This is consistent with the idea of the need to consider microbiome and immune "risk profiles" when planning therapy.

Importantly, the combined approach achieved a high rate of complete cure (PAI≤2) even in the severe fibrosis group (53% success rate), significantly exceeding the literature-reported rates of chronic AP after standard treatment. The inclusion of microbiome-targeted agents (probiotic) and immune system (thymosin α1), along with gentle irrigation, appears to have reduced the need for systemic antibiotics and generalized medication. The results suggest that combining conventional endodontic treatment with microbiome-immune correction is a promising approach.

Our data are consistent with the concepts of microbiome-targeted therapy discussed in periodontology: for example, it has been shown that the use of probiotics and other microbiome-targeted methods can improve outcomes in inflammatory oral diseases. The use of modern analytical methods (LEfSe for biomarker detection) and integrative statistical models confirmed the validity of the selected biomarkers (Lactobacillus, cytokines) and demonstrated their significant association with outcome.

A limitation of the study is the relatively small sample size and the lack of a "classical treatment" randomization group as a control. However, the results suggest that immuno-microbiome stratification of patients with AP secondary to HBV/HCV infection could form the basis for personalized protocols. Further studies with larger N and long-term follow-up may clarify optimal drug dosages and therapy duration.

In conclusion, this study demonstrates for the first time that combining metagenomic analysis of periapical microflora and immune profiling with tailored endodontic intervention significantly improves the treatment efficacy of chronic apical periodontitis in children with viral hepatitis. This approach reduces relapses and avoids aggressive drug therapy in patients with weakened hepatitis-related immunity, which has important practical implications for pediatric dentistry.

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用于诊断粘膜免疫疾病的通用多环境系统：牙科的发展和前景
A UNIVERSAL MULTI-ENVIRONMENT SYSTEM FOR DIAGNOSING MUCOSAL IMMUNITY DISORDERS: DEVELOPMENT AND PROSPECTS FOR DENTISTRY

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摘要：黏膜局部（黏膜）免疫在预防感染和维持微生物群落方面发挥着关键作用。分泌型免疫球蛋白A（sIgA）及其相关局部防御因子的减少与黏膜慢性炎症性疾病相关（lvrach.ru）。本研究旨在开发一种通用的免疫学检测方法，用于评估不同生物环境（口腔、阴道等）的黏膜免疫状态。

材料与方法：基于临床免疫学和微生物学原理，开发了一种多学科方法，包括定量测定黏膜分泌物样本中的sIgA和其他局部免疫防御标志物（免疫球蛋白和先天免疫因子，如溶菌酶）。一项妇科先导临床研究对该系统进行了测试：分析了患有各种感染性和炎症性疾病（需氧菌性阴道炎、细菌性阴道病、滴虫性阴道炎）的患者组和健康女性（对照组）的阴道分泌物样本 (dermatology.ru)。结果：检测结果显示，患者的免疫参数存在显著差异。与健康对照组相比，患者阴道分泌物中sIgA浓度显著下降（p < 0.01）：需氧菌性阴道炎组约为15.68 mg/L，对照组为33.95 mg/L；细菌性阴道病和滴虫性阴道炎组约为9-10 mg/L (dermatology.ru)。相比之下，溶菌酶活性因病原体而异：阴道病患者溶菌酶活性降低（平均6.69 μg/ml，正常值为10.0 μg/ml），滴虫病患者溶菌酶活性急剧升高（约71.6 μg/ml）（dermatology.ru）。该诊断系统显示出检测局部黏膜免疫缺陷的能力。讨论：所得数据证实了所开发的检测方法在识别黏膜免疫疾病方面的临床有效性。跨学科方法（结合微生物病因的免疫学分析）确保了该技术的多功能性，适用于妇科和牙科。口腔中类似的免疫失衡（例如，慢性复发性口疮性口炎（dentalmagazine.ru）或牙周炎（dental-press.ru）唾液中sIgA和溶菌酶减少）表明该测试有可能用于牙科实践中，以诊断牙龈炎、牙周炎和其他免疫介导的粘膜病变。结论：已经开发出一种用于评估局部粘膜免疫的通用免疫诊断系统，并在妇科中成功测试。其在识别粘膜免疫缺陷方面的信息价值已被证实。这种方法为在牙科中广泛应用以早期诊断和监测口腔粘膜疾病开辟了前景。

关键词：粘膜免疫、免疫学分析、口腔粘膜疾病的早期诊断和监测。

Abstract. *Local (mucosal) immunity of the mucous membranes plays a key role in protecting against infections and maintaining the microbiome. A decrease in secretory immunoglobulin A (sIgA) and associated local defense factors correlates*

with chronic inflammatory diseases of the mucous membranes (lvrach.ru). This study focuses on the development of a universal immunological test for assessing the state of mucosal immunity in various biotopes (oral cavity, vagina, etc.).

Materials and Methods: *A multidisciplinary methodology based on the principles of clinical immunology and microbiology was developed, including the quantitative determination of sIgA and other markers of local immune defense (immunoglobulins and innate immunity factors, such as lysozyme) in mucosal secretion samples. A pilot clinical study in gynecology tested the system: vaginal secretion samples were analyzed from groups of patients with various infectious and inflammatory diseases (aerobic vaginitis, bacterial vaginosis, trichomoniasis) and from healthy women (control) (dermatology.ru). Results: The test revealed significant deviations in immune parameters in patients. Patients showed a significant decrease in the concentration of sIgA in vaginal secretion compared to healthy controls ($p < 0.01$): ~15.68 mg/L in aerobic vaginitis versus 33.95 mg/L in the control; ~9–10 mg/L in bacterial vaginosis and trichomonas colpitis (dermatology.ru). Lysozyme activity, in contrast, varied depending on the pathogen: it decreased in vaginosis (on average 6.69 μg/ml versus 10.0 μg/ml in the norm) and increased sharply in trichomoniasis (~71.6 μg/ml) (dermatology.ru). The diagnostic system demonstrated the ability to detect local mucosal immunity deficiency. Discussion: The data obtained confirm the clinical efficacy of the developed test in identifying mucosal immune disorders. The interdisciplinary approach (immunological analysis taking into account the microbiological etiology) ensures the versatility of the technique, suitable for both gynecology and dentistry. Similar immune imbalances in the oral cavity (for example, decreased sIgA and lysozyme in saliva in chronic recurrent aphthous stomatitis (dentalmagazine.ru) or periodontitis (dental-press.ru) indicate the potential for this test to be used in dental practice for the diagnosis of gingivitis, periodontitis, and other immune-mediated mucosal pathologies. Conclusions: A universal immunodiagnostic system for assessing local mucosal immunity has been developed and successfully tested in gynecology. Its informative value in identifying mucosal immunodeficiency has been demonstrated. This approach opens up prospects for expanded application in dentistry for the early diagnosis and monitoring of oral mucosal diseases.*

Keywords: *mucosal immunity, immunological analysis, early diagnosis and monitoring of oral mucosal diseases.*

Introduction

Mucous membranes (oral cavity, vagina, nasopharynx, etc.) are the first barrier to infection, possessing a local immune system. One of the main humoral factors of this system is secretory immunoglobulin A (sIgA), which binds to the epi-

thelium and provides immunological protection to the mucosa (abstract.sciencereview.ru). Optimal levels of immunoglobulins (sIgA, as well as IgG, IgM, etc.) in secretions support local antibacterial immunity (lvrach.ru). Disruption of local immune homeostasis—in particular, sIgA deficiency—is associated with increased susceptibility to infections and chronic inflammatory and destructive lesions of the mucous membranes (lvrach.ru). However, in clinical practice, diagnosis of local immune disorders is rare and is hampered by the lack of universal methods for assessing immunity directly at the mucosal level. Hypothesis and objective of the study: We hypothesized that a multisystem approach to immunodiagnostics based on measuring key factors of local immunity would enable the detection of latent mucosal immune dysfunction in various organs. To this end, a universal multimedia immunoassay was developed, initially designed to diagnose mucosal immune dysfunction in any location (unified for various types of biological fluids, including saliva and vaginal secretions). The aim of this study was to describe the development of such a system and evaluate its clinical efficacy during pilot application in reproductive medicine. We also aimed to discuss the potential of this method for implementation in dental diagnostics.

Materials and Methods

Immunological Test Development: The developed diagnostic system represents a set of immunological methods for the quantitative assessment of mucosal immunity markers. The primary analytical parameters selected were secretory IgA (as a key component of specific mucosal defense), as well as additional immunological markers, including other classes of immunoglobulins and nonspecific antimicrobial factors (e.g., lysozyme). Concentrations were determined using enzyme-linked immunosorbent assays (ELISA) using standardized reagent kits for each analyte. The methodology was standardized for different sample types: oral fluid (saliva), cervicovaginal secretions, nasal contents, etc. To ensure comparability of results across different environments, sample collection and preparation standards were developed: for example, for saliva, collection was performed on an empty stomach without stimulating salivary flow, and for vaginal secretions, collection was performed with a swab from the vaginal vault before performing hygiene procedures.

Pilot study design: Preliminary clinical testing of the developed system was conducted in a gynecological practice. A group of women of reproductive age with diagnoses of infectious and inflammatory diseases of the vagina were examined: aerobic vaginitis (AV), bacterial vaginosis (BV), and trichomonas colpitis (TC). Diagnoses were established based on the clinical picture and microbiological methods (microscopy of smears, cultures, PCR). The control group consisted of apparently healthy women with no signs of vaginal infection. Vaginal discharge samples were obtained from all subjects using a standard method. A total of 46

samples were selected for lysozyme analysis, and 133 samples of vaginal secretions were selected for sIgA analysis (dermatology.ru). The content of secretory IgA and other immunoglobulins was determined by enzyme-linked immunosorbent assay; lysozyme concentration was determined colorimetrically (based on the ability to lyse a microbial suspension of a standardized strain). The measurement results were compared between the patient groups and the control group. Statistical data processing was performed using the Student's t-test; differences were considered significant at $p < 0.05$.

Ethical aspects: The study was observational in nature during the pilot testing of the methodology; all subjects provided informed consent. The work was conducted within the framework of the institution's local bioethics regulations.

Results

Immunological indicators of local immunity in the vagina (pilot testing): Comparative analysis revealed significant differences in the levels of mucosal immune markers between healthy women and patients with vaginal infections. The most significant changes concerned secretory IgA: in all patient groups, the concentration of sIgA in vaginal secretions was significantly lower than control values ($p < 0.01$). As shown in Table 1, in patients with aerobic vaginitis, the average sIgA level was 15.68 mg/L, which is approximately 2 times lower than in healthy women (33.95 mg/L). In bacterial vaginosis, the decrease was more than threefold (to 9.93 mg/L), while in trichomonas colpitis, it was down to 8.11 mg/L (dermatology.ru). Thus, in all the infection cases examined, a deficiency of local IgA in the vaginal mucosa compared to normal was observed.

Furthermore, significant changes in the activity of lysozyme, an enzyme in tear fluid that reflects the state of the innate antimicrobial defense mechanism, were noted. In the group of patients with bacterial vaginosis, the amount of lysozyme in vaginal secretions was reduced to 6.69 μg/ml versus 10.0 μg/ml in healthy subjects (i.e., approximately 33% below normal). In contrast, with Trichomonas infection, a sharp increase in lysozyme levels was recorded – an average of 71.62 μg/ml, which is many times higher than the levels in both the control group and other groups (dermatology.ru). In aerobic vaginitis, lysozyme levels were close to normal (≈12.3 μg/ml, slightly higher than the control). Statistical analysis confirmed a significant difference between the groups for each of the measured parameters ($p \leq 0.01$). The data are summarized in the table. Table 1. Average concentration of secretory IgA and lysozyme in vaginal secretions in healthy women and patients with various vaginal infections (M±m)

Group	sIgA, mg/L	Lysozyme, μg/ml
Healthy (control)	33,95 ± 2,1	10,0 ± 0,5
Aerobic vaginitis (AV)	15,68 ± 1,3*	12,28 ± 1,1
Bacterial vaginosis (BV)	9,93 ± 0,8*	6,69 ± 0,6*
Trichomonas colpitis (TC)	8,11 ± 0,7*	71,62 ± 5,4*

Note: Statistically significant differences compared to the control group ($p<0.01$) are marked with an asterisk. In all patient groups, sIgA was significantly reduced relative to normal; lysozyme levels were significantly lower than normal in BV and higher than normal in TC ($p=0.001$).

Clinical observations: The developed test demonstrated significant utility in diagnosing immune disorders. Patients with vaginosis and minimal subjective symptoms showed significantly reduced sIgA levels, indicating severe local immunodeficiency even with a meager clinical picture. In contrast, in trichomoniasis, extremely high lysozyme activity indicated an intense inflammatory response of the mucosa. Thus, the use of a panel immunoassay allowed for a more detailed characterization of local vaginal immunity for different etiologies of vaginitis. These data are potentially valuable for treatment selection: for example, if sIgA deficiency is detected, the use of immunomodulatory agents is advisable. The pilot study only assessed the diagnostic capabilities of the method, without influencing treatment decisions; however, even at this stage, the informative value of the proposed system is evident.

Discussion

An interdisciplinary approach to diagnosing mucosal immunity: The results of the pilot study confirmed that the proposed multi-media immunodiagnostic system is capable of detecting pathological changes in local mucosal immunity. In gynecological practice, the test has demonstrated clinical value, detecting severe secretory IgA deficiency and imbalances of innate defense factors in patients with vaginal infections, which were not diagnosed by standard methods. These data are consistent with the idea that local immunity plays a crucial role in maintaining mucosal homeostasis. Thus, in infectious vaginitis, abnormalities in the local defense system are observed (decreased sIgA, altered lysozyme levels, etc.), leading to impaired colonization resistance and disease development (dermatology.rudermatology.ru). The developed system was initially created as a universal tool combining immunological and microbiological approaches. The immunological component—quantitative analysis of secretory immune factors—provides a direct assessment of the mucosal defense reserves. At the same time, reliance on microbiological principles (pathogen identification, consideration of normal flora composition) allows for the interpretation of immunological test results in relation to the etiology of the disease. This interdisciplinary design enhances the versatility

of the method: essentially, the same set of test parameters can be used by various specialists (immunologists, gynecologists, dentists), adapting to a specific biotope through appropriate reference values and sampling algorithms.

Comparison with existing studies and summary of results: Our data on decreased sIgA in bacterial vaginosis and other vaginitis confirm the results of previous studies on local immunity of the female reproductive tract (dermatology.ru). It is known that in healthy women, high levels of sIgA in vaginal secretions prevent the adhesion and overgrowth of pathogenic flora, while decreased sIgA is associated with recurrent infections (lvrach.ru). A pilot trial demonstrated that our test effectively detects these immune deficiencies. It is interesting to note the different dynamics of lysozyme: a decrease in bacterial vaginosis and a significant increase in trichomoniasis. This variation is explained by the different nature of the pathogens and the nature of the inflammatory response: Trichomonas induces an acute reaction with neutrophil activation and lysozyme release, while in dysbiosis (BV), the local immune response is rather suppressed. Nevertheless, in both cases, deviations from normal parameters are observed, confirming the general concept that infectious processes are accompanied by an imbalance in local vaginal immunity (dermatology.rudermatology.ru).

Potential for dental application: The system, originally conceived as a universal system, holds great promise for dental practice. The oral mucosa, like the vaginal mucosa, has a local immune system, and a number of dental diseases are associated with its disruption. For example, chronic recurrent aphthous stomatitis is characterized by a significant decrease in sIgA secretion and lysozyme activity in saliva (dentalmagazine.ru), indicating a deficiency in local immune defense and predisposing to frequent ulcerative lesions. Inflammatory and destructive periodontal diseases (periodontitis) also reveal an imbalance in humoral defense factors: sIgA concentrations in patients' saliva decrease (in severe cases, up to two times the normal level) and lysozyme levels fluctuate (dental-press.ru). Interestingly, in the early stages of periodontitis, a compensatory increase in lysozyme activity is possible, followed by depletion as the disease progresses (dental-press.ru). These findings demonstrate that measuring local immune markers in the oral cavity can provide valuable information about the extent and nature of immune dysfunction in gingival and mucosal diseases. Our proposed universal test system, after appropriate adaptation, could be implemented for screening local immunity in dentistry. For example, regular monitoring of sIgA and lysozyme levels in the oral fluid of patients with gingivitis and early periodontitis could identify individuals with severe mucosal immune deficiency requiring more intensive prophylaxis or immunomodulatory therapy. Furthermore, this system could be used in scientific research to objectively evaluate the effectiveness of new treatments aimed at enhancing local immunity (e.g., vaccines against cariogenic bacteria, lysozyme preparations, etc.).

Limitations and further research: This pilot study is limited in sample size and focuses only on gynecological diseases. Although the obtained results demonstrate the feasibility of the method, further studies are required for widespread implementation. Clinical trials in dentistry are planned, specifically to study the correlation between our immunological test parameters and clinical manifestations of gingivitis and periodontitis, as well as to evaluate the dynamics of these parameters during treatment. Additionally, the inclusion of new markers (e.g., secretory component, cytokines IL-1, IL-6, etc.) in the test panel should be considered, which could increase diagnostic sensitivity. The interdisciplinary nature of the technology will ensure the integration of knowledge: further collaboration between immunologists, microbiologists, and dentists will optimize the interpretation of results and develop standards for various fields of medicine.

Conclusion

A new multi-environment immunological test system for the diagnosis of mucosal immune disorders has been developed. Pilot use in gynecological practice confirmed its clinical significance: characteristic immune abnormalities (sIgA deficiency, lysozyme activity imbalance) were identified in patients with vaginal infections, demonstrating the method's ability to recognize mucosal immunodeficiency in vivo. The technology is interdisciplinary in nature, integrating immunological and microbiological principles, making it versatile and suitable for use in various fields of medicine. This system has particular potential in dentistry, for diagnosing and monitoring oral diseases associated with impaired local immunity (periodontitis, gingivitis, stomatitis, etc.). Implementation of this approach will facilitate earlier detection of immune dysfunctions, personalized prevention and treatment, and the collaboration of specialists from various fields around the issue of mucosal immunity. Thus, this immunodiagnostic tool opens up new possibilities for advanced clinical diagnostics and interdisciplinary research in the field of mucosal diseases.

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男性不育症的现代诊断方法
MODERN APPROACHES TO DIAGNOSTICS OF MALE INFERTILITY

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摘要：男性不育的早期诊断有助于发现和治疗影响生育能力和患者整体健康的疾病。根据现有数据，在过去40年中，全球范围内，尤其是发达国家和工业化国家，精子质量（由精子浓度和精子数量等因素决定）平均下降了50%至60%。精子分析仍然是评估男性不育的基石，提供有关精子数量、活力和形态的重要信息。同时，激素水平分析对于识别可能影响精子发生和整体生殖健康的下丘脑-垂体-性腺轴疾病至关重要；基因检测可以检测染色体异常、Y染色体微缺失以及影响生育能力的基因突变；影像学检查包括超声和磁共振成像。因此，对男性不育的全面诊断评估需要采用多模式方法。

关键词：男性不育，男性不育诊断。

Abstract. *Early diagnosis of male infertility helps in the detection and treatment of diseases that affect not only fertility, but also the overall health of patients. According to current data, over the past 40 years, sperm quality, which is determined by factors such as sperm concentration and sperm count, has decreased by an average of 50-60% worldwide, particularly in developed and industrialized countries. Sperm analysis remains a cornerstone in the assessment of male infertility, providing important information about sperm count, motility, and morphology. At the same time, hormonal profiling is crucial for identifying disorders of the hypothalamic-pituitary-gonadal axis that can affect spermatogenesis and overall reproductive health; genetic testing can detect chromosomal abnormalities, Y-chromosome microdeletions, and mutations in genes that affect fertility; imaging methods include ultrasound and magnetic resonance imaging. Therefore, a comprehensive diagnostic assessment of male infertility involves a multimodal approach.*

Keywords: *male infertility, male infertility diagnosis.*

Relevance. Early diagnosis of male infertility helps in the detection and treatment of diseases that affect not only fertility but also the general health of patients.

Semen analysis remains the cornerstone of male infertility assessment, providing important information on sperm count, motility and morphology. Free radical generation caused by various lifestyle factors and reproductive toxins may be associated with deterioration in sperm quality, which has also been identified as changes in the antioxidant enzyme system and increased sperm DNA damage. Thus, according to current data, over the past 40 years, sperm quality, determined in particular by sperm concentration and sperm count parameters, has decreased by an average of 50-60% worldwide, especially in developed and industrialized countries [1]. Thus, semen analysis remains the cornerstone of male infertility assessment, providing important information on sperm count, motility and morphology. At the same time, hormonal profiling is crucial for identifying hypothalamic-pituitary-gonadal axis disorders that may affect spermatogenesis and overall reproductive health, while genetic testing can identify chromosomal abnormalities, Y-chromosome microdeletions and mutations in genes that affect fertility. Visualization methods, such as ultrasound and magnetic resonance imaging, are also an important aid in diagnosing male infertility.

The aim of the study is to analyze the available arsenal of methods for diagnosing male infertility at the current stage of urological care development.

Material and methods of the study. Material and methods of the study. The analytical method was used to study the literature sources in the Scopus, Web of Science, MedLine, The Cochrane Library, CyberLeninka, eLibrary.ru, and Russian Science Citation Index databases for the last 10 years.

Results and discussion. Semen analysis remains the cornerstone of male infertility assessment, providing important information on sperm count, motility, and morphology [2]. There is a positive relationship between sperm motility and fertilization success; in turn, decreased expression of the testicular isoform of angiotensin-converting enzyme, which is involved in sperm maturation, negatively affects sperm motility and male fertility [3]. Azoospermia, oligozoospermia, asthenozoospermia, teratozoospermia, and oligoasthenoteratozoospermia are abnormal sperm parameters that cause male infertility. Semen analysis is the mainstay of male infertility evaluation and can be useful both to investigate male fertility status and to monitor spermatogenesis during and after male fertility interventions. In addition, advanced diagnostic tests to investigate semen quality are gaining popularity and can improve diagnosis and treatment. Parameters such as semen volume, sperm concentration, total sperm count, viability, and morphology are assessed according to World Health Organization (WHO) criteria. Abnormal results may indicate problems with spermatogenesis, obstruction, or ejaculation and require further investigation [4].

Mitochondrial activity is a reliable indicator of sperm fertilization capacity [5, 6]. Mitochondrial dysfunction, especially due to increased ROS production,

is often associated with impaired sperm function/quality. Over the decades, various methods and approaches have been developed to assess mitochondrial characteristics that may correlate with sperm functionality. Recently, mitochondria-targeted compounds have been at the forefront of both assessment and therapeutic approaches [7].

WHO guidelines recommend using strict criteria to identify normal sperm. According to the 2010 WHO spermogram, ejaculate volumes of 2 ml or less are classified as microspermia; in the case of ejaculate volumes greater than 5 ml, the risk of developing an inflammatory process in the prostate gland, seminal vesicles, or Cooper's glands is considered. Measurement of semen volume by weight is preferably performed at the time of sample collection and before liquefaction.

The normal color of ejaculate is also established - grayish. In case of brown or red color of ejaculate, the presence of blood cells in the ejaculate is determined, which may be a sign of tumors or stones in the prostate gland. Yellow color may be a sign of jaundice or occur as a result of taking certain vitamin preparations.

The acidity of the ejaculate depends on the relative contribution of acidic prostatic secretion and alkaline seminal vesicular secretion. The clinical interest of pH of the ejaculate is a low value. If it is necessary to assess the pH, this should be done at the same time, preferably 30 minutes after collection, but in any case within 1 hour after ejaculation. For normal samples, pH test strips in the range of 6.0-10.0 should be used. If the pH decreases, the question of the presence of inflammatory processes in the germ cells is considered. The sperm liquefaction time is considered fundamental when performing a spermogram and should be approximately 60 minutes in total. Liquefaction of the ejaculate is performed in an incubator at a temperature of 37 °C and, if possible, on an orbital mixing platform to facilitate liquefaction and mixing of the sample. An increase in the sperm liquefaction time is a sign of enzymatic deficiency or the presence of prolonged inflammatory processes in the prostate gland, seminal vesicles.

Sperm viscosity is measured in centimeters of the ejaculate thread, at which the latter forms a drop and separates from the pipette. According to WHO standards, individual small drops should separate. In case of increased viscosity, with the formation of a thread longer than 2 cm, a possible enzymatic deficiency or prolonged inflammatory processes in the seminal vesicles, prostate is diagnosed.

Another spermogram indicator that characterizes the ability of spermatozoa to actively move is sperm motility, which is assessed in 4 groups, the relative content of each of the groups is standardized:

- group A - spermatozoa actively move along a straight-line trajectory (should be more than 25%);

- group B - spermatozoa are poorly mobile, their trajectory of movement is straight (in combination with spermatozoa of group A should be more than 50% 1 hour after ejaculation);

- group C - spermatozoa are poorly mobile, their trajectory of movement is rotational;

- group D - spermatozoa are immobile.

It is preferable that the assessment begin within 30 minutes after collection and no later than 60 minutes after collection.

The morphology of spermatozoa is also determined: spermatozoa of normal structure should be more than 15%. The number of live spermatozoa should be at least 50%.

In secretory forms of infertility, spermatogenase cells are found in the ejaculate. Agglutination of spermatozoa may also be observed, which, as a rule, indicates the presence of significant disturbances in the immune system. Only motile spermatozoa are capable of agglutination, sticking to each other head to head, tail to tail, or in a mixed manner. Motility is often vigorous, with a frantic trembling movement, but sometimes the spermatozoa are so agglutinated that their movement is limited. Any motile spermatozoa that stick to each other with their heads, tails, or middle parts should be noted during analysis.

Since the ejaculate may contain dangerous infectious agents (HIV, herpes simplex virus, hepatitis viruses), it is necessary to strictly observe safety regulations.

The presence of leukocytes in the ejaculate should normally be 1 x 106. If this indicator increases, the development of an inflammatory process in the genital area (prostatitis, vesiculitis, urethritis, orchitis) is noted. There should be no erythrocytes in the ejaculate; the presence of erythrocytes may be due to injuries, tumors, vesiculitis [8].

Hormonal profiling is also critical to identify hypothalamic-pituitary-gonadal axis disorders that may impact spermatogenesis and overall reproductive health. Measurements typically include FSH, LH, testosterone, and prolactin levels. Abnormal levels may indicate hypogonadism, hyperprolactinemia, or other endocrine disorders that require targeted treatment [9].

In men with severe problems with sperm production or certain clinical manifestations (such as azoospermia), genetic testing can identify chromosomal abnormalities, Y chromosome microdeletions, and mutations in genes that affect fertility. Such tests help counsel couples about their reproductive options, including the use of donor sperm or the risks of passing on genetic diseases to offspring [10]. The examination for the identification of the causes of male infertility should begin with imaging methods: ultrasound (US), magnetic resonance imaging (MRI)) [11].

Conclusions. A comprehensive diagnostic assessment of male infertility includes a multimodal approach, including sperm analysis, hormonal profiling, genetic testing and imaging to identify the underlying causes of infertility. This allows for the development of a targeted treatment plan to address specific problems and increase the chances of successful conception.

Male infertility can be caused by a complex of genetic, immunological, pathophysiological and functional causes, the consideration of which requires theoretical analysis and further practical research to understand the mechanism of male infertility development and the development of possible measures for its correction.

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关于钢纤维增强混凝土混合结构涂层构件技术经济性能的确定方法
ABOUT THE METHOD FOR DETERMINING THE TECHNICAL AND ECONOMIC PERFORMANCE OF ELEMENTS OF HYBRID STRUCTURAL COATINGS BASED ON STEEL FIBER-REINFORCED CONCRETE

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摘要：本文介绍了钢纤维增强混凝土（包括混合结构）空间结构涂层的信息，以及基于平面尺寸、临时荷载和所用材料计算其技术和经济性能指标的方法。本文还简要概述了已知的结构涂层方案，并探讨了利用BIM技术和Revit软件评估结构构件技术和经济性能的可行性，并结合为此开发的计算表进行了分析。

关键词：钢筋水泥、钢纤维增强混凝土、钢纤维增强混凝土结构、混合结构、结构涂层构件、金字塔、加劲板、BIM技术。

Abstract. *This article presents information on spatial structural coatings using steel fiber reinforced concrete, including hybrid ones, and a methodology for calculating their technical and economic performance indicators based on plan dimensions, temporary loads, and the materials used. It also provides a brief overview of known structural coating options and the feasibility of using BIM technology and Revit software to evaluate the technical and economic performance of structural elements using calculation tables developed for this purpose.*

Keywords: *reinforced cement, steel fiber reinforced concrete, steel fiber reinforced concrete structures, hybrid structures, structural coating elements, pyramids, stiffening slabs, BIM technologies.*

STRUCTURAL COATINGS OF CIVIL BUILDINGS BASED ON STEEL FIBER CONCRETE

In modern construction practice, three main structural coating design solutions are widely used: metal, reinforced cement, and steel fiber reinforced concrete [1, 2, 3]. The first spatial metal rod systems were developed between 1847 and 1922 by the American scientist and inventor Alexander H. Bell. In recent decades, domestic structural coatings such as “Kislovodsk,” “Berlin,” and “TsNIISK” have

been used in construction practice. According to experts, these coatings were up to 40% more cost-effective than existing metal structures in the mid-20th century [4].

Experts attribute the emergence of reinforced cement structural coatings to the Italian engineer and architect Pier Luigi Nervi, who in 1948-49 built the world's first thin-walled vault made of reinforced cement elements for the exhibition hall in Turin.

In the USSR, the first reinforced cement structures appeared in 1957 [2]. The use of reinforced cement structural pavements (Fig. 1), compared to traditional reinforced concrete, allows for cost savings of up to 40% [4].

The use of steel fiber-reinforced concrete in thin-walled structural pavement elements, due to its high corrosion resistance, tensile strength, crack resistance, and deformability, ensures high operational reliability of the pavement elements [2]. When creating structures using steel fiber-reinforced concrete, depending on the stress-strain state of the elements, it is rational to use fiber or combined reinforcement, which includes reinforcement with steel fiber and rod or wire reinforcement [5, 6]. The spatial structure of the public building pavement – a structural steel fiber-reinforced concrete slab made of pyramidal elements and stiffeners – does not require additional finishing or the installation of a suspended ceiling. The multifaceted surface of the structural coating serves to increase the level of sound absorption in the hall and provides architectural expressiveness to the interior in the rooms and foyer.

a) b)

Figure 1. *Structural pavement made of reinforced concrete elements: a) pavement of the Proletarskaya metro station lobby in St. Petersburg; b) BIM model of the pavement structure*

Steel fiber concrete structural pavements with a regular structure consist of pyramidal elements with their apexes upward and stiffening slabs (Fig. 1). Moreover, the pyramidal elements in the slab have a beneficial psychophysiological effect on people [7]. This design allows the pavement to be used in halls with various floor plans (Fig. 1).

In addition to the regular structural pavement, a combined (hybrid) pavement version has been developed using pyramidal elements with their apexes downward (pyramids with reinforced concrete bases and steel pipes in the tension zone). (Fig. 2). The lower chord of the hybrid roof, constructed from individual metal rods (e.g., Ø 114 x 5.5 mm pipes), forms a diagonal lattice (compared to the orthogonal upper chord).

Calculations have shown that this structural system is not only efficient in terms of material consumption, but also, when staggered, allows for the placement of skylights at intervals, improving room illumination and introducing unique design features. It is also suitable for covering tall halls and atriums.

According to the analysis, the hybrid structural roof is less material-intensive than a regular structural roof in terms of key performance indicators. However, the height of the hybrid roof, according to calculations, is almost twice that of a regular steel fiber reinforced concrete structure.

GENERAL INFORMATION

The subject of this study is a hybrid structural roof comprising pyramids with steel fiber concrete faces facing downwards, a reinforced concrete base (Figs. 2, 3), and a stretched steel pipe chord.

a) b)

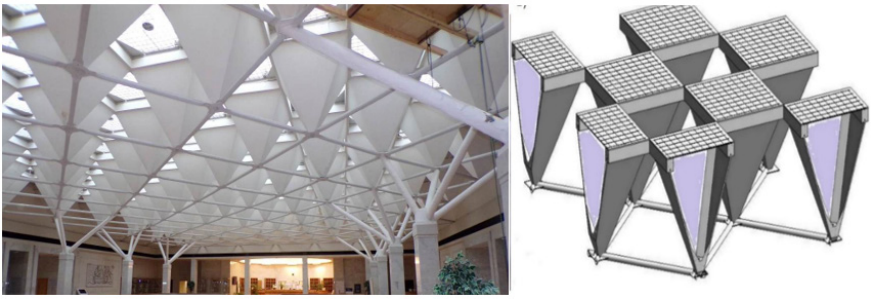


Figure 2. *Hybrid structural roof with pyramidal elements with steel fiber concrete faces and reinforced concrete bases attached to a tension chord: a) roof for the building of the Russian National Library in St. Petersburg; b) BIM model of the hybrid roof structure.*

The use of BIM technologies (Building Information Modeling) is of particular importance in the design of structures with complex geometry [8], such as structural roofs (Figs. 1, 2). Using the structural information model (Fig. 3), a calculation model was created that took into account the roof structure geometry. This made it possible to evaluate the technical and economic performance of each structural element of the roof (Fig. 4), using the results of static (performed using SCAD) and structural calculations using a computer program (Certificate)

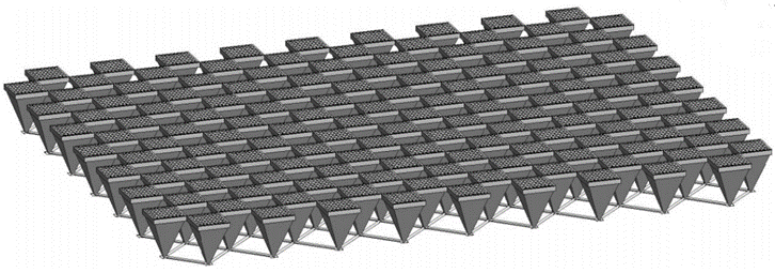


Figure 3. *Information model of a structural roof with pyramidal elements facing downwards and a stretched steel pipe belt*

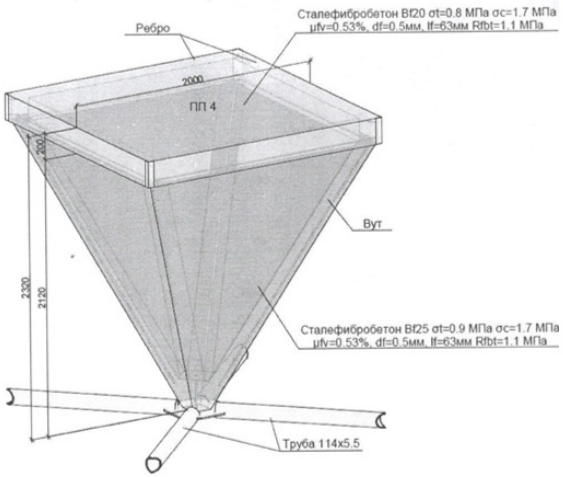


Figure 4. *Pyramidal element of a hybrid structural pavement with geometric and fiber reinforcement parameters*

(State Registration of Computer Program No. 2012619865 dated October 31, 2012). Based on the results of the static calculation, the structural elements are divided into unification groups (Figure 5).

ASSESSMENT METHOD

The purpose of assessing the technical and economic indicators for a given pavement size and configuration is to determine the most efficient (in terms of geometry and material consumption) cross-section and dimensions of the structural elements.

To obtain the technical and economic indicators, an information model of the structural element was created using Revit software. To simplify the workflow

and make adjustments to element sizes and material properties, parameters are assigned to the model. Changing these parameters changes the geometry, followed by recalculation of the technical and economic indicators. The parameters of the information model are shown in Figure 6.

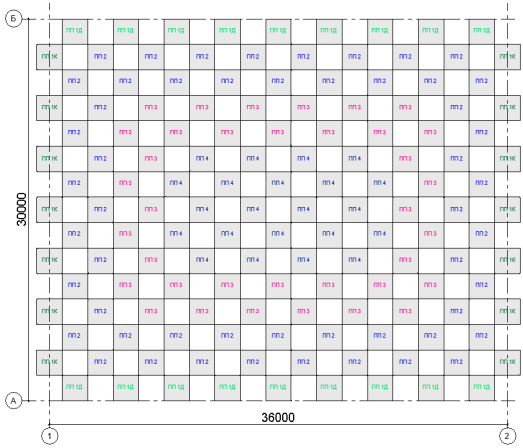
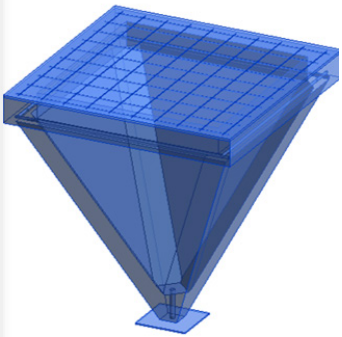


Figure 5. *Layout plan of pyramidal elements of a hybrid structural coating based on steel fiber concrete in axes 1-2/AB*

Параметр	
Размеры	
Размер структурног элемента в плане, мм	2000.0
Высота структурного элемента, мм	2200.0
Толщина боковых граней структурного элемента, мм	30.0
Высота сечения плиты, мм	20.0
Длина продольной и поперечной арматуры в плите, мм	1880.0
Диаметр продольной и поперечной арматуры в плите, мм	5.0
Шаг поперечной и продольной арматуры в плите, мм	200.0
Длина выпусков продольной и поперечной арматуры в плите, мм	40.0
Высота сечения ребра в сжатой зоне структурного элемента, мм	240.0
Ширина сечения ребра в сжатой зоне структурного элемента, мм	200.0
Размер выступа ребра относительно грани структурного элемента, мм	75.0
Диаметр арматуры в ребре структурного элемента, мм	22.0
Длина арматуры в ребре структурного элемента, мм	1880.0
Растояние от оси арматуры до внешней стороны ребра, мм	30.0
Высота вута в вершине пирамидального структурного элемента, мм	250.0
Ширина вута в вершине пирамидального структурного элемента, мм	150.0
Высота сечения вута между боковыми гранями структурного элемента, мм	100.0
Диаметр арматуры в вуте между боковыми гранями структурного элемента, мм	10.0
Размер закладной детали в вершине структурного элемента в плане, мм	440.0
Толщина закладной детали в вершине структурного элемента, мм	10.0
Диаметр стержня закладной детали в вершине структурного элемента, мм	36.0
Размер скоса закладной детали в вершине структурного элемента, мм	100.0
Ширина уголка в сжатом поясе структурного элемента, мм	63.0
Толщина уголка в сжатом поясе структурного элемента, мм	6.0
Длина анкера уголка в сжатом поясе структурного элемента, мм	100.0
Диаметр анкера уголка в сжатом поясе структурного элемента, мм	6.0



a) *b)*

Figure 6. *User-defined parametric model of a structural element (a), generated using Revit software; (b) pyramidal roof element*

After creating the structural element information model, the entire roof geometry was loaded into the project and laid out (Fig. 6), and standard sizes were created according to calculations. All standard sizes were assigned the required calculated volumetric percentage of fiber reinforcement.

Table 1.

Technical and economic indicators of the standardization groups of steel-fiber-reinforced concrete elements of a hybrid structural roof

Element brand		Number of elements per coating pcs..	Maximum tensile stress σ_t MPa	MMaximum compressive stress σ_cMPa	Volumetric percentage of reinforcement %	Mass t		Concrete consumption m³		Steel consumption kg				
										per element				on the entire surface
						one element	on the entire surface	on the element	on the entire surface	fiber	reinforcement	mortgages	total	
PP-1D	pyramid	18	3.7	8.1	4.1	0.7012	12.6	0.3	5.5	96.3	25.5	21.7	170.9	3076.2
	slab		1.9	2.2	1.4	0.6093	11	0.25	4.6	27.4				
PP-1K	pyramid	14	2.3	6.2	2	0.7012	9.8	0.3	4.3	47	5.9	21.7	126	1764
	slab		2.4	1.6	2.7	0.7281	10.2	0.3	4.2	51.4				
PP-2	pyramid	52	1.6	5	1	0.6841	35.6	0.3	15.5	22.9	25.6	21.7	81.9	4258.8
	slab		0.9	3.2	0.57	0.6405	33.3	0.27	13.9	11.7				
PP-3	pyramid	36	1.1	2.5	0.53	0.6444	23.2	0.28	10.1	11.4	11.7	21.7	57.9	2084.4
	slab		0.3	2	0.61	0.671	24.2	0.28	10.1	13.1				
PP-4	pyramid	22	0.9	1.7	0.53	0.817	18	0.36	7.8	13.7	7.3	21.7	54.1	1190.2
	slab		0.8	1.7	0.53	0.5813	12.8	0.24	5.3	11.4				
Pipes 114×3.8		144	-	-	-	0.026	3.8	-	-	-	-	-	-	3795

Pipes 114×5.5	108	-	-	-	0.037	4.0	-	-	'	'	'	'	4033
Corner of the overhead	-				0.001	0.24	-	-	'	'	'	'	192
Totally	**394**					198.7		81.2					19665

To obtain the quantity of materials consumed, a specification of structural elements was created and configured according to the table necessary for obtaining technical and economic indicators. 1.

a) b)

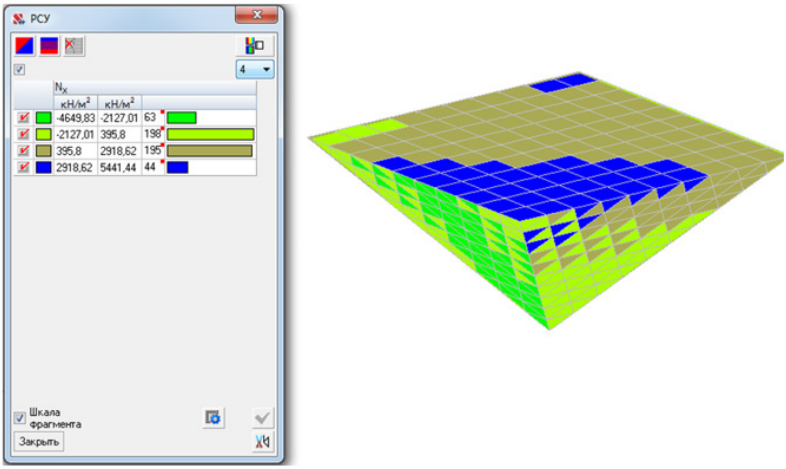


Figure 7. *- Stress field pattern Nx in the most loaded pyramidal element of size PP-1*

DETERMINING FIBER REINFORCEMENT PARAMETERS USING MICROSOFT EXCEL

The fiber reinforcement parameters were determined based on an analysis of the stress fields obtained from a static analysis using the SCAD software (Fig. 7).

The calculated stress values obtained from the static analysis are entered into the software package (Certificate of State Registration of Computer Program No. 2012619865 dated October 31, 2012), along with data on the dimensions of the design cross-section, fiber type, and type of original concrete. The calculation results generate data on the fiber diameter and length, the calculated resistances of the concrete matrix, the percentage of fiber reinforcement, and the calculated resistances of the resulting steel fiber reinforced concrete.

A comparative analysis of the thermal performance characteristics of a structural pavement made of regular steel-fiber concrete slabs (option 1) and a hybrid steel-fiber-reinforced concrete pavement (option 2) allowed us to estimate that the indicators of the first option are lower than similar indicators of the second option: concrete consumption per 1 m2 of pavement by 13%, steel consumption per 1 m2 by 26%, the tare weight of the pavement by 7%, and the number of elements in the pavement is 57% less.

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不同小麦品种蛋白质消化率的研究

RESEARCH ON THE DIGESTIBILITY OF PROTEINS OF DIFFERENT WHEAT VARIETIES

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摘要：小麦因其高营养价值和优良的工艺性能而在粮食作物中占据主导地位。确定小麦品种特性，例如蛋白质消化率及其生物学价值，对于提高食品质量至关重要。本研究旨在比较评估不同小麦品种的蛋白质消化率。研究对象：1号小麦品种“叶尔马克”（对照），2号小麦品种“纪念科诺瓦洛夫”。谷物蛋白质的消化率是在体内测定的（使用尾草履虫纤毛虫）。结果发现，新品种紫粒小麦“纪念科诺瓦洛夫”的生物潜能值和标准化相对生物学价值更高，表明其蛋白质消化率更高。

关键词：小麦“纪念科诺瓦洛夫”，品种，蛋白质，消化率，纤毛虫。

Abstract. *Wheat occupies a leading position among grain crops due to its high nutritional value and technological properties. Determining wheat varietal characteristics, such as protein digestibility and its biological value, is essential for improving food quality. The aim of this study was to comparatively evaluate the protein digestibility of different wheat varieties. Subjects of study: No. 1 – wheat variety "Ermak" (control), No. 2 – wheat variety "In Memory of Konovalov." Grain protein digestibility was determined in vivo (using Paramecium Caudatum ciliates). It was found that the biotic potential and standardized relative biological value were higher in the new purple-grained wheat variety "In Memory of Konovalov," indicating better protein digestibility.*

Keywords: *wheat "In Memory of Konovalov," variety, proteins, digestibility, ciliates.*

Wheat is the most widely used cereal grain in the world due to its nutritional and organoleptic properties, as well as its exceptional versatility in the production

of all types of flour products. These unique technological properties are primarily due to its proteins, which comprise 80% gliadin and glutenin [1].

However, beyond their technological role in shaping the texture and structure of foods, wheat proteins are fundamental to human nutrition. Their value is determined not only by their composition but also by their digestibility—the body's ability to effectively break down these proteins into amino acids and absorb them. Protein digestibility directly impacts the bioavailability of nutrients, determining how well wheat-based products can meet human needs [2, 3].

Poor digestibility leads to incomplete absorption of essential amino acids, which can lead to nutrient deficiencies, especially lysine, which is low in wheat protein. High digestibility, on the other hand, promotes greater satiety, maintains muscle mass, and improves overall health, reducing the risk of disease [4]. In the context of global grain consumption, this necessitates research on the digestibility of cereal proteins, including in the new purple-grained wheat variety "In Memory of Konovalov."

Therefore, the aim of the study was to comparatively evaluate the protein digestibility of different wheat varieties. The subjects of the study were common wheat varieties: No. 1 – "Ermak" (control), No. 2 – "In Memory of Konovalov."

Wheat protein digestibility was assessed based on the biotic potential (BP) of the P. caudatum population and the standardized relative biological value (SRBV). RBV is an indicator used to assess the digestibility of proteins in raw materials (products). These indicators were also determined at stages when the BP of the P. caudatum population was at its highest [5].

The digestibility of grain samples was assessed using egg white (standard), which was used at concentrations of 1, 2, and 4 mg/cm³. Distilled water served as the solvent. No additional micronutrients, macronutrients, or vitamins were added to the ciliate culture substrate. Therefore, the standard excluded the influence of non-protein components on protein digestibility.

Monitoring the status of the P. caudatum population growing in experimental substrates with protein concentrations of 1, 2, and 4 mg/cm³ revealed no biocidal effect on ciliates. Counting the number of ciliates cultured on the substrate containing the test samples relative to the egg white-based substrate revealed lower reproductive function at all experimental points at the studied protein concentrations (Table 1).

Table 1

Population size and biotic potential of P. caudatum cultured in egg white-based medium and wheat grain samples (P < 0.05)

Sample	Protein content, mg/cm ^{3}		
	1,0	**2,0**	**4,0**
1	2	3	4
Egg white	26197±1010* 0,27**	36668±1001* 0,38**	44557±1120* 0,47**
№ 1	9708±789* 0,101**	13846±966* 0,144**	15624±963* 0,163**
№ 2	11089±808* 0,115**	15763±991* 0,164**	16412±874* 0,171**
In % to egg white			
№ 1	62,9	62,2	64,9
№ 2	57,7	57,0	63,2
* The numerator represents the population size; ** The denominator represents the biotic potential.			

The digestibility and biological value of the test samples were calculated after 48 hours of incubation at a protein level of 4 mg/cm³ in the culture medium, as this is when the biotic potential reached its maximum.

It was found that the biotic potential of P. caudatum grown on a substrate containing the new purple-grained wheat variety was higher than that of P. caudatum grown on a substrate containing the 'Ermak' variety of grain throughout their entire lifespan.

The standardized relative biological value of the test samples was calculated relative to egg white (Table 2).

Table 2

Biological value of the test samples based on the results of assessment for P. caudatum (P < 0.05)

Sample	Standardized relative biological value, %
Egg white	100
№ 1	35,07
№ 2	36,83

The study found that the new "Memory of Konovalov" wheat variety had a higher SOBC value, indicating improved protein digestibility. This should be taken into account when developing new healthy flour products.

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铁路设计人工智能基础
FUNDAMENTALS OF ARTIFICIAL INTELLIGENCE FOR RAILWAY DESIGN

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摘要：本文介绍了开发人工智能（AI）用于新建和改建铁路设计的基本原理。开发人工智能的必要性在于新建铁路设计和建设地区极具挑战性的自然条件。现有的自动化系统依赖于设计师和个人计算机的交互操作，这引入了相当大的主观性，最终无法确保技术上和经济上合理的设计方案。

关键词：结构识别、泛化、设计分解、多准则问题、帕累托原则。

Abstract. *This article presents the fundamentals of developing artificial intelligence (AI) for the design of new and reconstructed railways. The relevance of developing AI is determined by the extremely challenging natural conditions in areas where new railways are being designed and built. Existing automated systems rely on the interactive operation of the designer and a personal computer, which introduces a significant degree of subjectivity and, ultimately, does not ensure technically and economically sound design solutions.*

Keywords: *Structure recognition, generalization, design decomposition, multi-criteria problem, Pareto principle.*

Developing artificial intelligence (AI) is a structured process that includes several distinct stages, a summary of which is presented below.

Stage 1. Defining AI Goals and Objectives

The first stage is identifying the problems that determine the appropriate architecture and approach for developing AI railway design. This includes two problems:

- AI design of the plan and profile of new railways;
- AI design of the plan and profile of reconstructed railways.

Based on these problems, a universal artificial intelligence for railway design will be created. The results obtained by the AI must comply with general design

principles developed over more than 150 years of experience in designing new and reconstructed railways.

Stage 2. Collection and Preparation of Initial Data

The input data for designing the plan and profile of new and reconstructed railways, which are the baselines, include models of the main line (MLO) and the ground profile along the route plan in the form of X, Y coordinates of points; a 3D model of the track axis in the form of X, Y, Z coordinates of points, which is mathematically processed to bring the plan and profile of the operating railway to the correct geometric outline; digital terrain models (DTMs) and other natural conditions are represented by piecewise linear functions.

Stage 3. Selecting a Model Architecture.

The choice of model architecture depends on the problems identified in Stage 1.

It should be noted that existing architectures, such as speech and face recognition AI, and other similar architectures, are not applicable to AI-based railway design. The architecture of the AI system for designing the plan and profile of new and reconstructed railways is based on a general model and method developed by the author and includes the following blocks [1]:

Block I. Recognition of the structure (element boundaries) of the plan and profile of new and reconstructed railways based on the analysis of baselines.

Block II. Generalization (combination) of plan and profile elements of new and reconstructed railways with parameters of the same sign (curvature or slope).

Block III. Calculation of the position of plan and profile elements of new and reconstructed railways within designated boundaries based on a set of main criteria using the Pareto principle with the formation of gaps (decomposition) along the element boundaries.

Block IV. Conjugation of discontinuous plan and profile elements of new and reconstructed railways to eliminate gaps along the element boundaries.

Block V. Adjustment of the associated plan and profile of new and reconstructed railways based on a variety of other criteria corresponding to the standards of SP [2].

The theoretical foundations of each block of the AI for automated design of the plan and profile of new and reconstructed railways are described below.

Block I. Recognition of the structure (element boundaries) of the plan and profile of new and reconstructed railways.

The AI recognizes the structure (element boundaries) of design lines: the plan and profile of new and reconstructed railways, based on an analysis of the original lines, taking into account traditional design principles, according to which the main properties (signs) of the boundaries of design line elements are a change in the sign or magnitude of the curvature (slope) of the plan (profile) elements of new and reconstructed railways.

The general method for recognizing the boundaries of design line elements based on an analysis of the original lines is presented as follows:

1. Recognition of “watersheds” and “thalwegs” (1)

$$\begin{aligned} Z(i-1) \le Z(i) \ge Z(i+1) \to \max \\ Z(i-1) \ge Z(i) \le Z(i+1) \to \min \end{aligned} \quad \text{i=2, N-1,1.} \tag{1}$$

2. Recognition of global “watersheds” and “thalwegs” (2)

$$\begin{cases} Z^{vt}_{jl} < Z^{vt}_{j} > Z^{vt}_{jp} \\ Z^{vt}_{jl} > Z^{vt}_{j} < Z^{vt}_{jp} \end{cases} \quad \text{j = 3, M-2,1.} \tag{2}$$

3. Recognition of regional “watersheds” and “thalwegs” provided (3)

$$i_G = \frac{[Z_G(m+1) - Z_G(m)]}{[S_G(m+1) - S_G(m)]} \le i_p - i_{\text{экв}} \tag{3}$$

is carried out by decomposing the conditional profiles of “watersheds - v” and “thalwegs - t” into “BACKGROUND” and “RESIDUAL” [3]. Then the “RESIDUAL” is determined by the formulas (4)

$$\begin{aligned} \Delta Z_v = Z(i) - [Z_G(m) + i_G \cdot (S_c(i) - S_G(m))] \\ \Delta Z_t = Z(i+1) - [Z_G(m) + i_G \cdot (S_c(i+1) - S_G(m))] \end{aligned} \tag{4}$$

Regional “watersheds” and “thalwegs” occur when the following condition is met: (5)

$$\begin{aligned} \Delta Z_v(i-2) < \Delta Z_v(i) > \Delta Z_v(i+2) \to max \\ \Delta Z_t(i-2) > \Delta Z_t(i) < \Delta Z_t(i+2) \to min \end{aligned} \tag{5}$$

4. Recognition of the boundaries of design line elements based on the magnitude of curvature (slope) in sections between global or regional watersheds or thalwegs, as well as between each two adjacent “watersheds” and “thalwegs” (the average curvature (slope) between which is less than the limit), is carried out based on the decomposition of the original lines into “BACKGROUND” and “RESIDENT.” The simplest way to identify the “BACKGROUND” is averaging. Then, the magnitude of the average natural slope, for example, icp, corresponding to the “BACKGROUND” will be equal to the formula (6)

$$i_{cp} = [Z_c(j+1) - Z_c(j)] / [S_c(j+1) - S_c(j)], \le i_{cp} \tag{6}$$

where $Z_c(j), Z_c(j+1), S_c(j), S_c(j+1)$ – respectively, the ordinates and stationing of the adjacent thalweg and watershed.

The value of the "REMAIN" is determined by the formula (7)

$$\Delta Z(j) = Z(j) - [\, Z(i) + i_{cp} * (S_c(j) - S_c(i))] \quad (7)$$

where j is the number of the baseline point between i and i+1—the thalweg and watershed in the section between two adjacent global or regional watersheds and thalwegs.

Boundaries of design line elements based on the curvature (slope) of the elements occur when one of the following conditions is met

$$\begin{aligned} \Delta Z(j-1) > \Delta Z(j) < \Delta Z(j+1) \\ \Delta Z(j-1) < \Delta Z(j) > \Delta Z(j+1) \end{aligned} \quad (8)$$

Thus, by recognizing the structure of design lines (plan and profile) based on an analysis of the initial lines in steps 1–4, the boundaries of design line elements will be assigned in accordance with traditional design principles for both new and reconstructed railways.

To meet the requirements of SP [2] for the design of elements of the maximum possible length, it is necessary to generalize (combine) elements with the same curvature (slope) sign.

Block II. Generalization (combination) of plan and profile elements of new and reconstructed railways.

The AI generalizes (combines) elements with the same ρ (i) sign, located between every two adjacent watersheds and thalwegs, the average curvature (slope) between which is less than ρ_{ogp} (iorp), which, in turn, are located between global or regional watersheds and thalwegs, the average curvature (slope) between which is also less than ρ_{ogp} (i_{ogp}). The generalization criterion is ensuring standardized deviations (shifts, increases/decreases) of the generalized element from the original ones at each point.

Generalization is performed using the "tube" method, which consists of the following [1]. Let "upper" and "lower" constraints be defined on a set of elements of the original line, in the section between the watershed and the thalweg, the curvature (slope) between which is less than ρorp (iorp), to ensure standardized deviations at each point.

The "upper" constraint is the upper bound, the "lower" constraint is the lower bound, and are denoted, respectively, by $Z^{sup}(S)$ and $Z^{inf}(S)$. They form a "tube of constraints," which represents an infinite set of positions of the generalized element, the analysis of which is performed by dividing it into four subsets with the parameters listed in Table 1.

Table 1

Parameters of subsets of positions of the generalized element (design) line

Subset	Restriction parameters	
	ordinate	slope
M1	$Z_G(j) = Z^{inf}(j)$	$i_G = \left[Z^{inf}(j+1) - Z^{inf}(j)\right] / \left[S(j+1) - S(j)\right]$
M2	$Z_G(j) = Z^{inf}(j)$	$i_G = \left[Z^{sup}(j+1) - Z^{inf}(j)\right] / \left[S(j+1) - S(j)\right]$
M3	$Z_G(j) = Z^{sup}(j)$	$i_G = \left[Z^{inf}(j+1) - Z^{sup}(j)\right] / \left[S(j+1) - S(j)\right]$
M4	$Z_G(j) = Z^{sup}(j)$	$i_G = \left[Z^{sup}(j+1) - Z^{sup}(j)\right] / \left[S(j+1) - S(j)\right]$

Having determined the parameters of each subset and calculated the difference between the elements of the original lines and the graphs of the functions $Z^{sup}(S)$, $Z^{inf}(S)$ – we will get two arrays of numbers $\delta_m^{sup}(i)$, $\delta_m^{inf}(i)$, determined by formulas (9)

$$\begin{aligned} \delta_m^{sup}(i) &= Z^{sup}(i) - (Z_G(j) + i_G(S(i) - S(j))) \\ \delta_m^{inf}(i) &= Z^{inf}(i) - (Z_G(j) + i_G(S(i) - S(j))) \end{aligned} \quad (9)$$

where $i \in j, j+1$ – internal point number;

m is the number of the subset of positions of the generalized element, m = 1, 4.

If for any point $i \in j, j+1$ the inequality is satisfied (10)

$$\delta_m^{sup}(i) * \delta_m^{inf}(i) \geq 0, \quad (10)$$

then the section of the approximated line between the points $j, j+1$ is generalized by one element.

Otherwise, the **generalization** of the section of the original line between the points $j, j+1$ If this is impossible, the "tube" method will yield the initial boundaries of elements based on criteria I and II.

Block III. Calculation of design line elements based on multiple principal criteria.

The calculation of each element is performed based on the principle of decomposition of complex systems, i.e., regardless of the position of adjacent elements to the left and right, which eliminates design difficulties associated with the presence of pre- and posthistory and solution uncertainty. The AI performs the calculation using the Pareto principle [4], according to which, a conditionally optimal solution is first found based on one or more criteria: criterion K1 – the curvature (slope) of each element must be less than or equal to ρorp (i_{ocp}) (11) and criterion

Ko – the minimum profile volume of excavation work (sum of shifts) (12), which will serve as the principal criteria.

$$\rho(j) \le \rho_{\text{пред}} \quad \text{или} \quad i(j) \le i_{\text{пред}} \quad , \tag{11}$$

$$\int_{l1}^{l2} [Z_p(l) - Z_c(l)]dl \rightarrow \min \tag{12}$$

In general, the design of each element according to the Ko criterion in areas with the maximum curvature (slope) is carried out using an iterative method based on the following assumptions:

1. At $Z_p(j) = Z_c(j)$, the volume of excavation work (sum of shifts) is equal to max.

2. Function $Q_{\text{проф}}(Z_p(k, j))$ has one extremum at $Q_{\text{нас}} = Q_{\text{выем}}$.

Let the profile of the initial line (for example, the profile of the earth) within the j-element have the form shown in Fig. 1. We accept the initial position of the design line element corresponding to the point, the value of the efficiency criterion $Q_{\text{проф}}(n)$, $n = 1$ in which has a maximum value. With a step of Δh we change the value of h_j and thus $Q_{\text{проф}}$, which will tend to the min point.

We continue the procedure until the condition is met. (13).

$$Q_{\text{проф}}(k+1) > Q_{\text{проф}}(k) \tag{13}$$

where $Q_{\text{проф}}(k+1)$, $Q_{\text{проф}}(k)$ – accordingly, the volume of excavation work on $k+1$ and k interation.

The design position of the element at the *k+1* iteration will correspond to the minimum value of the efficiency criterion.

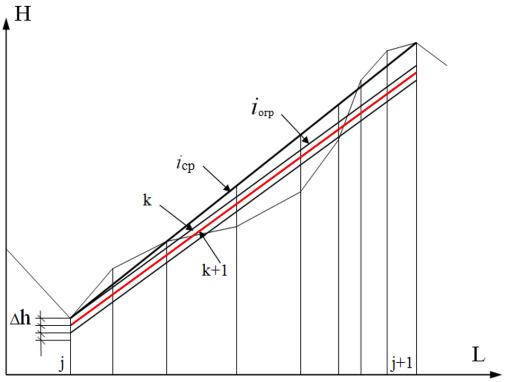

Figure 1. *Determining the rational position of a design line element with a maximum curvature (slope)*

Similarly, by designing each element within the designated boundaries, we obtain a design line with discontinuities along the element boundaries, indicating the presence of pre- and post-history in the design of the plan and profile of new and reconstructed railways.

Block IV. Connecting Elements of Discontinuous Lines.

Connecting elements of a discontinuous plan or profile of new or reconstructed railways is performed by AI between every two elements, one of which is the last element of the connected plan (profile), and the other is the next element of the discontinuous plan (profile), by solving a system of two linear equations with two unknowns, represented by formulas (14).

$$\begin{cases} a_1 S(l) + b_1 H(l) + c_1 = 0 \\ a_2 S(l) + b_2 H(l) + c_2 = 0 \end{cases} \quad (14)$$

where $S(l)$, $H(l)$ – accordingly, the chainage and the design elevation l are the points of the conjugate approximating line

The coefficients of the equations a_1, b_1, c_1 are determined by the formulas (15)

$$a_1 = \frac{1}{S(j) - S(l-1)}; b_1 = -\frac{1}{H(j) - H(l-1)}; c_1 = \frac{H(l)}{H(j) - H(l-1)} - \frac{S(l)}{S(j) - S(l-1)} \quad (15)$$

Similarly, the coefficients of the equations a_1, b_1, c_1 are determined.

The solution of the system *S(l), H(l)* for the l-point of intersection of the elements can be found, for example, by the **Gauss method**, using the formulas (16).

$$S_{(l)} = \frac{\Delta S}{\Delta}; \quad H_{(l)} = \frac{\Delta h}{\Delta}; \quad (16)$$

where ΔS, Δh, Δ– particular determinants of the system with respect to *S(l)* and *H(l)* and the general determinants of the system (14).

The solution of the system must satisfy condition (16), which corresponds to the requirement of finding the intersection point within the mating elements.

$$S(j-1) \le S(l) \le S(j+1) \quad (16)$$

If condition (16) is not satisfied, then conjugation must be sought between *l* and *j+1* elements if *S(l+1) > S(j+1)* and between j and l-1 elements if *S(l) < S(l-1)*.

Conjugation of a discontinuous line leads to an increase in the efficiency criterion. $\min Q_{зр}^{проф}$ ($min\sum\Delta i$) by the minimum required value. The conjugate line has no discontinuities between elements, and the curvature (slope) of each element is less than or equal to ρorp ($i_{огр}$), but other requirements of the SP [2] for the plan (profile) of new or reconstructed railways may be violated.

Thus, a conditionally optimal conjugate line, designed according to a set of main criteria, must be adjusted according to a set of remaining criteria (Block V) that comply with the standards and requirements of the SP [2].

Block V. Adjustment of elements of the conjugate plan and profile of new and reconstructed railways.

The theoretical foundations for adjusting the elements of the conjugate approximating line are presented in two aspects.

The first aspect. Calculation of the new position of each element of the conjugate line within the new boundaries from the condition $Q_{зр}^{проф} \Longrightarrow \min$ or $\sum_{1}^{N} \Delta_i \Rightarrow 0$ and a constant value of the element's curvature (slope).

As a result, a new discontinuous line will be obtained, the magnitudes of the discontinuities and the changes in the element boundaries along which will be significantly smaller than in the initial calculation. Obviously, with each such cycle, the magnitudes of the discontinuities and changes in the element boundaries will tend toward 0. The process ends if the magnitudes of the discontinuities along the boundaries of each element at any step are less than the predetermined accuracy.

The second aspect is related to the adjustment of the elements of the conjugate line, adjusted by the min objective function, according to a set of other criteria that correspond to the norms and requirements of SP [2]. Adjustment of the elements of the conjugate line is performed based on the criteria of length and the difference in slopes of adjacent elements and consists of rotating the j element relative to its midpoint by a certain angle δi (Fig. 2).

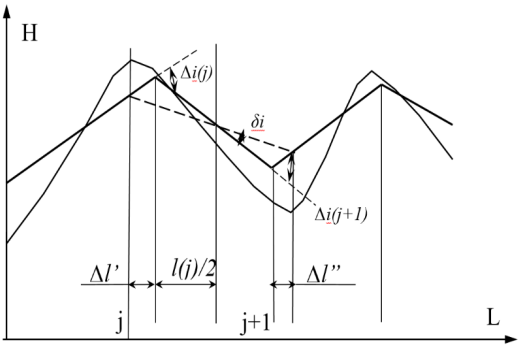

Figure 2. *Adjusting design line breaks based on length and slope differences between adjacent elements*

When turning the j element by an angle δi, simultaneously due to a decrease in the slope of the j element and a decrease in the values of the algebraic differences

in the slopes of adjacent profile elements at j and j+1 fractures, an increase in its length occurs, determined by the formula (17).

$$l(j) = l_1^{'} + l_2^{''} = 0{,}5R^b(j)(\Delta i(j) - \delta i) + 0{,}5R^b(j+1)(\Delta i(j+1) - \delta i) \quad (17)$$

From triangles, according to the law of sines, we obtain (18).

$$\frac{l'_1}{l_1} = \frac{\sin(\pi - \Delta i(j))}{\sin(\Delta i(j) - \delta i)}; \frac{l''_1}{l'_1} = \frac{\sin(\pi - \Delta i(j+1))}{\sin(\Delta i(j+1) - \delta i)} \quad (18)$$

where $l_1 = l(j)/2$.

Using the reduction formulas and moving from proportions to equations, taking into account that for small angles $sin\delta i \approx tg\delta i \approx \delta i$ we obtain (19).

$$l_1 \frac{\Delta i_{(j)}}{\Delta i_{(j)} - \delta i} + l_1 \frac{\Delta i_{(j+1)}}{\Delta i_{(j+1)} - \delta i} = 0{,}5R^B(\Delta i(j) + \Delta i(j+1) - 2\delta i). \quad (19)$$

By performing algebraic transformations of formula (19), we obtain a polynomial of degree 3, from which it is necessary to find *i* formula (20).

$$A\delta i^3 + B\delta i^2 + C\delta i + D = 0, \quad (20)$$

where $A = R_в$;

$B = -1{,}5R_в\ (\Delta i_{(j)} + \Delta i_{(j+1)})$;

$C = -(0{,}5R_в\ (\Delta i_{(j)} + \Delta i_{(j+1)}))^2 + R_в\ \Delta i_{(j)}\Delta i_{(j+1)} - l_1(\Delta i_{(j)} + \Delta i_{(j+1)})$;

$D = \Delta i_{(j)}\Delta i_{(j+1)}(2l_1 - 0{,}5R_в(\Delta i_{(j)} + \Delta i_{(j+1)}))$

Polynomials, starting with degree 3, are solved using approximate methods (chords, tangents) [5].

Stage 4, Stage 5. Training, testing, and evaluation of the model architecture.

Stages 4 and 5 are critical stages determining the system's readiness for use. They were completed through experimental design of the plan and longitudinal profile of new and reconstructed railways. The results of the design of the route plan for the new AI railway – "New Railways" – are shown (Fig. 3).

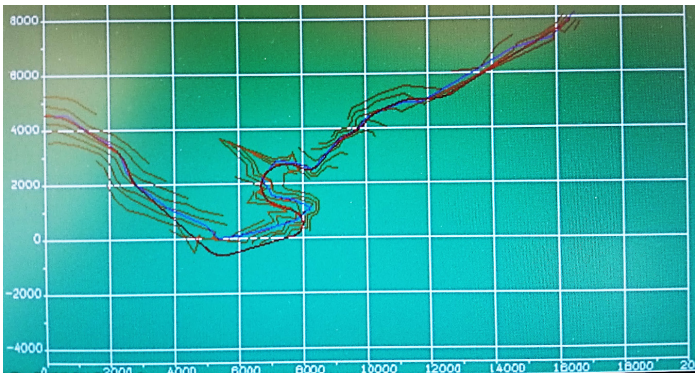

Figure 3. *Route plan of a new railway designed by AI*

Monitoring or tracking the quality of the new railway route plan design by AI is performed through a comparative analysis of its compliance with classical design principles. The results of the analysis show that the route plan of the planned section, designed by AI, does not contradict classical design principles.

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容错控制
FAULT-TOLERANT CONTROL

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摘要：本文以周期性多阶段工艺过程的自动控制系统和专用自动化数字控制系统为例，探讨了构建各种过程容错控制系统的方法，并列举了改进系统以实现容错能力的方法。

关键词：容错控制、容错性、硬件和软件干预、反馈、诊断对象、计算机、冗余。

Abstract. *The article discusses approaches to building fault-tolerant control systems for various processes, using the examples of automated control systems for cyclic multi-stage technological processes and specialized automated digital control systems; methods for improving systems to achieve their fault tolerance are listed.*

Keywords: *fault-tolerant control, fault tolerance, hardware and software interventions, feedback, diagnostic object, computers, redundancy.*

INTRODUCTION

A promising direction in the development of modern automatic control theory is the creation of fault-tolerant control systems (FTCS) or systems tolerant to faults. A system malfunction is typically defined as unexpected changes in physical parameters that go beyond permissible limits, which are temporary in nature, and failures, if they are permanent (1, 3). In turn, the goal of fault-tolerant control is to temporarily maintain system functionality in case of malfunctions, preventing the situation from developing into failures and accidents (2).

The relevance of fault-tolerant control systems is extremely high today for several reasons:

1. Development of autonomous systems - systems operating without constant human involvement require autonomous resolution of malfunctions.

2. Industries with high safety requirements - in industries such as medicine, nuclear power, etc., the occurrence of emergency situations is unacceptable (as they lead to disasters).

3. Economic losses arising from system malfunctions are undesirable for production.

The goal of fault-tolerant control is to create control that ensures continuous performance of their intended functions by objects in the presence of malfunctions.

Fulfillment of the minimum requirements for a control system, such as maintaining quality indicators at a given level, safety, environmental friendliness, economic benefit, is mandatory but, under modern conditions of technical development, is no longer sufficient. FTCS are required to perform the following tasks (4):

1. Collect information about the system state and compare it with the normal operating mode to detect deviations.

2. Neutralize the effect of these malfunctions by reconfiguring faulty systems.

3. If it is impossible to restore faulty systems and the situation develops critically, correctly terminate the control process to prevent an impending failure.

DESIGN APPROACHES

The property of control systems known as fault tolerance can be achieved by improving the quality and reliability of their components, design quality, manufacturing technology, testing, etc. Although these areas are constantly developing, practice shows that they are insufficient for building FTCS due to the high complexity and critical application conditions of such systems. The solution to this problem is the introduction of redundancy into system components and parameters (e.g., temporal, hardware, algorithmic, informational redundancy) (3). Two types of redundancy are distinguished (1, 3):

1. Static redundancy, ensuring only the correctness of the output information of the designed FTCS when allowable sets of information occur.

2. Dynamic redundancy, which enables a longer period of operability for the FTCS and the object it controls.

Thus, the design of FTCS is carried out using either an “external” or an “internal” approach. The first approach implies hardware intervention, and the second – software intervention.

The essence of the first approach is that the design stage is divided into two stages. At the first stage, a nominal control system is developed assuming no faults, and at the second stage – a “new” system, coordinated with the nominal system and taking into account possible faults. The task of ensuring tolerance is solved by “external” means – by encompassing the diagnostic object (DO) with feedback. In this case, “signal” influences are applied to the system (2). A faulty control system is interpreted as a technical object that has lost qualitative process indicators, for

example, part of the stability margin or even become unstable. Here, there is no need to localize the fault – it is sufficient to have the result of current identification indicating unsatisfactory system dynamics (5).

The second approach to building control systems is based on the concept of ensuring fault tolerance by "internal" means, i.e., by adjusting subsystems or components, switching, and removing existing connections (5). This approach is implemented as follows: systemic influences of various ranks are applied to the faulty diagnostic object: parametric, operator, or topological. If tolerance can be achieved by parameter adjustment, such systems are classified as adaptive. In cases where correcting the diagnostic object requires measures whose adequate modeling involves changing the structures of component operators (preferably algorithms implemented in software), we speak of tolerant systems (2).

APPLICATION OF THE "EXTERNAL" APPROACH

Automated control systems for cyclic multi-stage technological processes (ACS CMTP) were selected for analysis. The relevance of developing such control systems lies in the fact that a multi-stage technological process implies a set of various equipment groups, which entails a flow of malfunctions that increases the risk of failure as the entire process is executed. Also, during repeated reproduction of the technological process, the development of individual malfunctions may occur, which repeat from cycle to cycle with a tendency towards failure (4, 6).

Considering the features of the selected system, the following requirements form the basis for designing a fault-tolerant ACS CMTP (6):

1. A malfunction of a functional device or subsystem at the main stage of the process is considered a failure of the entire system, as it will cause irreversible consequences.

2. Malfunctions at other stages can be detected as incipient with their quantitative assessment or as already occurred. To ensure tolerance to such malfunctions, it is necessary to provide the possibility of reconfiguring the control system, and in case of failure to meet stage requirements – stopping the process before the start of the main stage.

3. The cyclical nature of the process increases the cost of the final product and exacerbates the consequences of failure at the main stage of the next cycle, which requires accumulating diagnostic information from each cycle to analyze the nature of development of incipient malfunctions and forming control actions on the system considering the cost of a potential failure.

Articles (4, 6) describe an innovative method for ensuring fault tolerance of ACS CMTP. The construction of the final control system is carried out in 3 stages: 1 – control system for a multi-stage nominal TP assuming no faults, 2 – fault-tolerant control system for a stage of the multi-stage TP, 3 – fault-tolerant control system for a cyclic multi-stage TP. Article (5) presents a general methodology for ensuring fault tolerance of control systems.

The "external" approach is traditional and reflects the informational-algorithmic method of forming new dynamics, accepted in the practice of automatic regulation in technical systems and in process control. Implementing the approach involves solving a number of tasks related to forming structures of information links and algorithms for processing current information in real time. These include: selecting output variables of the DO that ensure observability of state variables, i.e., measurement points; selecting inputs that ensure controllability, i.e., points for introducing "signal" influences; synthesis of stabilization algorithms (2).

In the general case, a single feedback loop is not capable of correcting all sets of faulty systems. Then the task of system decomposition/decentralization is solved, which consists of optimally partitioning the set of potentially faulty systems into groups, for each of which its own correction subsystem is created (5).

APPLICATION OF THE "INTERNAL" APPROACH

As an example of an FTCS using the second approach, specialized automated digital control systems (ADCS SN) are chosen. These systems are distributed multi-computer computing systems of network structure that parallelly execute many interacting target tasks (3). The relevance of developing fault-tolerant control for computers is obvious – their malfunctions entail economic losses, delays in task execution, and slowing down the development of science and technology as a whole.

When designing a fault-tolerant ADCS SN, the following requirements must be considered (1, 3):

1. Computational integrity, defining the possibility of an error in calculations or an unacceptable delay (in the systems under consideration, calculation errors or their delay during the occurrence of allowable malfunctions are not permitted).

2. Fault coverage, defining the measure of good performance of the used fault tolerance mechanisms and meaning the conditional probability of correct recovery of the ADCS SN upon the occurrence of a malfunction.

Article (3) presents a unified method for ensuring fault and failure tolerance in distributed ADCS SN. Generalized models of the upper, architectural level of the design process for diagnostics, fault and failure tolerance subsystems of such multitasking systems and methods for their construction are proposed. It is shown that the design of such a diagnostics, fault and failure tolerance subsystem for a multitasking system should begin at the very top, architectural level of the design process of this system, be controlled and evaluated at all lower design levels.

The implementation of the "internal" approach, besides diagnostic problems, is also associated with tasks of forming structures of information links and decision-making algorithms. These include: 1 – ordering malfunctions by the degree of their influence on system dynamics; 2 – ranking components and connections by the degree of influence on dynamics; 3 – synthesis of algorithms for adjust-

ing parameters, changing structures of component operators of the faulty system, or reconfiguring topology (2). Besides, with an increase in the number of digital computers in the system, the level of redundancy introduced into each of these machines must grow to maintain a constant level of reliability of the ADCS SN. Therefore, for the considered systems, the first approach is not optimal (3).

CONCLUSION

The article discusses two fundamentally different methods for ensuring fault tolerance of control systems, the first of which is implemented through hardware intervention, and the second – through software. The approach "external" to the diagnostic object implies "signal" influences, while the "internal" one implies systemic influences of parametric, structural, or topological ranks. In tolerant systems, the diagnostic device delivers information about the technical state of the diagnostic object to the higher, supervisory control level, which adjusts parameters or reconfigures the structure of the object (2).

The creation of fault-tolerant control systems must be based on the use of strict scientifically and practically justified models of both individual hardware-software elements of such systems and the entire system as a whole.

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使用模糊神经网络识别医学专家行为以自动评估实践技能的方法

METHODS OF RECOGNITION OF ACTIONS OF MEDICAL SPECIALISTS FOR AUTOMATED ASSESSMENT OF PRACTICAL SKILLS USING FUZZY NEURAL NETWORKS

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摘要：本文致力于开发和分析基于模糊神经网络和计算机视觉技术的混合系统，用于医学专科医生实践技能的自动评估方法。文中考虑了诸如动作多变性、数据噪声以及结果可解释性等关键问题。文中介绍了集成YOLOv8算法的软硬件综合体“LUCH”，用于评估学生的实践技能。文中特别关注了各种现代方法的比较，包括传统方法、时空模型和深度学习，并重点介绍了它们在模拟训练中的适用性。研究结果证明了混合系统在最小化数据噪声和提高专科医生自动化评估效率方面的潜力。

关键词：自动化评估、实践技能、模糊神经网络、模糊逻辑、计算机视觉、YOLOv8、混合系统、模拟学习、动作识别。

Abstract. *The article is devoted to the development and analysis of methods for automated assessment of practical skills of medical specialists using hybrid systems combining fuzzy neural networks and computer vision technologies. Key issues such as variability of actions, noisy data and the need for interpretability of results are considered. The hardware and software complex «LUCH» is presented, integrating YOLOv8 algorithms for assessing practical skills of students. Particular attention is paid to the comparison of modern approaches, including traditional methods, spatio-temporal models and deep learning, with an emphasis on their applicability in simulation training. The results demonstrate the potential of hybrid systems to minimize data noise and improve the efficiency of automated assessment of specialists.*

Keywords: *automated assessment, practical skills, fuzzy neural networks, fuzzy logic, computer vision, YOLOv8, hybrid systems, simulation learning, action recognition.*

Introduction. Simulation technologies play a key role in the professional training of medical specialists, enabling the development of clinical competen-

cies in a controlled learning environment. Their use helps minimize potential risks to patients during the acquisition of practical skills. In the context of modern medical education, accurate and objective methods for assessing clinical skills are particularly important, given their direct impact on the quality of medical care. Classic assessment methods based on expert observations have significant limitations, such as subjective interpretations, significant time requirements, and a lack of scalability. In this context, the importance of automated assessment systems using computer vision technologies and artificial intelligence algorithms is growing. A key challenge in developing such systems remains the handling of variability and uncertainty in the actions of medical personnel. Even when performing standardized clinical procedures, individual deviations in technique are observed, and external factors (spatial organization of the work area, lighting parameters, etc.) are subject to dynamic change. A promising solution to these problems is the development and implementation of hybrid models combining fuzzy logic methods with deep neural networks.

Fuzzy neural networks (FNNs) combine the advantages of both approaches: the ability of fuzzy systems to handle imprecise data and the power of neural network algorithms to recognize complex patterns. This makes them particularly suitable for analyzing practical skills, where both the accuracy and interpretability of results are critical.

The current state of the problem of pattern recognition using artificial intelligence. Recently, artificial intelligence (AI) technologies have been actively implemented in education for processing statistical data, analyzing educational materials, and assessing practical actions. Particular attention is being paid to teaching sports skills using virtual reality (VR) and augmented reality (AR). Methods based on fuzzy neural networks, which allow for the creation of complex event structures for users and the evaluation of data based on multiple criteria, are also gaining popularity. These criteria include the user's general condition, medical parameters (pulse, temperature, blood pressure, psycho-emotional state), speech recognition, and the accuracy of gesture-based exercises.

However, the number of studies devoted to automated assessment of practical actions using computer vision systems and fuzzy logic remains limited. Most existing studies use fuzzy logic only for image noise suppression or input parameter correction. The bulk of publications focus on classical machine learning methods and statistical approaches to data processing.

In their paper, Amit K. Shukla and Pranab K. Mukhuri [1] propose a new deep belief network (DBN) architecture, "Interval Type-2 Fuzzy DBN (IT2FDBN)," which models weights and biases using IT2 FS. Thus, the algorithm is designed for augmented deep learning, which has the potential to address all the limitations of classical DBN (CDBN) and T1 fuzzy DBN (T1FDBN). The authors apply the

algorithm to accurately recognize noisy and imprecise image data. To demonstrate the algorithm's robustness and capabilities, the researchers use data with additive white Gaussian noise and data with motion blur. The root mean square error (RMSE) and error rate, as well as three datasets, are used to compare the experimental results. IT2FDBN outperforms both T1FDBN and CDBN by all metrics.

In the study [2], the authors apply a method for detecting abnormal student behavior to identify cases of cheating on exams. The method is based on the improved YOLOv8 model, which enables real-time detection even on standard-performance computers. Results showed that the detection accuracy of the improved YOLOv8 model reached 82.71%.

In the paper [3], the researchers proposed an approach based on fuzzy clustering around medoids for analyzing patterns of human activity. The method classifies ordered sequences (paths) that reflect individual behavioral patterns. The authors use fuzzy clustering algorithms to process noisy images to improve recognition quality and implement a partitioning strategy based on medoids. This approach was chosen because, when analyzing behavioral patterns, it is important to represent each cluster using a real, observed prototype (medoid), rather than an artificially created one.

Kaifeng Gao, Gang Mei, and other authors [4] presented an overview of the Julia language's capabilities in the field of machine learning. The Metalhead.jl package, which contains ready-made computer vision models based on the Flux machine learning library, is used for developing image processing applications in Julia. Another important tool is the ImageProjectiveGeometry.jl package, which serves as the basis for creating libraries of projective geometry functions used in computer vision tasks. The Julia language has found widespread application in seven key areas of machine learning, including image recognition, NLP, IoT data analysis, computer vision, autonomous driving, graph analytics, and signal processing.

In [5], researchers Jianpeng Liao, Jun Yan, and their colleagues proposed an innovative multi-view neural network, the Hypergraph Aware Hypergraph Neural Network (MD-HGNN). This model represents a new approach to processing dual connections, uniquely combining the hypergraph structure with representation learning mechanisms within a single architecture. MD-HGNN begins with the use of a multi-view hypergraph learning (MVHL) network to explore the optimal hypergraph structure from multiple views, constrained by a coherence loss proposed to improve its generalization. The new model leverages the potential for exploiting implicit information, such as density, leading to improved performance.

In [6], the authors propose MDSI, a semantic integration methodology for gesture recognition based on a multi-strategy decoupling approach. For IR, a multi-strategy decoupling network (MDN) is presented to accurately separate

pose-motion features and the spatiotemporal channel between modalities. MDSI's pluggable architecture enables seamless integration with various RGB-D-based gesture recognition methods with minimal computational overhead.

Fotini Patrona, Dimitrios Zarpalas, et al. [7] presented a new framework for detecting, recognizing, and evaluating motion capture data in real time. Experimental results on the MSR-Action3D and MSRC12 datasets, as well as a new publicly available one, indicate that the proposed framework outperforms state-of-the-art methods by 0.5–6% on all three datasets, demonstrating that the proposed method can be effectively used for unsupervised gesture/action learning.

Matthew Barnachon, Saida Bouakaz, et al. [8] presented a framework for streaming action recognition using Motion Capture (MoCap) data. The method is based on histograms of action poses extracted from MoCap data, which are computed according to the Hausdorff distance. The histograms are then compared with the Bhattacharyya distance and warped using a dynamic time warping process to achieve optimal alignment. The method enables efficient continuous human action recognition in real time.

In their work [9], Yu.A. Egorov and I.G. Zakharov and colleagues presented the development of a pipeline method for recognizing complex actions performed by an observed object in video recordings. The uniqueness of this work lies in its approach to modeling actions using sequences of elementary actions and a combination of neural networks and stochastic models.

In the article [10], the authors proposed a video preprocessing algorithm to improve the detection accuracy of small-scale images. The algorithm processes a fixed number of video images at specific points in time and extracts new independent motion features from dynamic images based on spatiotemporal processing of the video images. This approach allows for the consideration of motion features in dynamic scenes while preserving the static characteristics of the image. This improves object recognition accuracy, especially in cases where moving elements are present against a static background.

In their work [11], M.V. Aliyev, D.A. Berbentsev, and V.O. Nemykin presented an algorithm for detecting and identifying objects with the ability to determine their relative positions. The algorithm is based on the YOLO neural network model.

Problem Description and Statement. During a practical simulation lesson, a teacher works with a group of 12 students. During one academic hour, the teacher can only conduct an individual assessment of each student's practical skill once. This is because 10 minutes per student are allocated for skill completion and assessment. Students spend the remainder of the lesson practicing their skills independently. The teacher evaluates students' practical skills based on several criteria, including completing assignments based on the provided input data. For ob-

jective assessment, special checklists containing binary ("yes/no") questions are used. Each checklist item has a specific weight, and a penalty point system allows for the calculation of a final grade based on the sum of the results. The instructor visually assesses the student's actions when working with patients, medical records, and medications. Concurrently, an auditory assessment is performed to assess the accuracy of the questions asked and the fulfillment of key skill criteria: checking medication expiration dates, assessing the injection site, and asking the patient about any allergic reactions and their current condition. All responses from the simulated patient are based on the input provided by the instructor.

Research has revealed the ineffectiveness of medical specialist training in mastering practical skills, due to the predominance of independent student work. To address this shortcoming, a multi-agent training system was developed, allowing each student to actively practice practical skills throughout the entire academic hour. The system consists of the "LUCH" hardware and software system, which includes a server with an artificial intelligence core for processing data and storing educational video materials, as well as automated user workstations with a video and audio recording system. When working with the system, students can first watch educational videos on skill performance and then proceed to the exam section. In this section, a virtual patient is displayed on the screen (Fig. 1), who, thanks to the speech recognition and synthesis system, conducts a direct dialogue with the trainee.

Figure 1. *Virtual patient work page (exam mode)*

The system's front-facing and rear-facing cameras recognize the user's face, automatically blocking the testing process if they detect a stranger in the frame. Simultaneously, the system monitors the performance of medical procedures, including proper glove donning and doffing, waste disposal, hand and injection site sanitization, syringe angle maintenance, and other key actions. The system uses

the YOLOv8 motion recognition module, trained on 20,000 iterations of 64 images each. TensorRT software is used to accelerate the system's performance. An Nvidia Quadro RTX A2000 GPU is used. Figure 2 shows a general view of the client workstation. Testing the recognition system revealed several factors that impact user assessments and cause technical errors. These include omitted assessments on checklists due to insufficient lighting (causing noise), unclear actions due to students' uncertainty, and poor speech intelligibility. In such cases, the system skips errors and moves on to the next stage of assessment, leaving the possibility of additional skill verification by the teacher if necessary.

Figure 2. *General view of the client workstation*

To address the problems of noise and fuzzy responses from trainees (such as descriptions of a patient's symptoms and condition using linguistic variables: "high blood pressure," "moderate muscle tone," "injection site unremarkable"), fuzzy models must be used. These models allow for the formalization of expert knowledge and the creation of dynamic scenarios that adapt to trainee actions and lesson conditions.

Review and Analysis of Motion Recognition Methods. Five main approaches to motion recognition were identified during the study.

Traditional Recognition Approach. Before the advent of deep learning and neural networks, human motion recognition was performed using classical computer vision and machine learning methods. These approaches are inferior in accuracy to modern neural network solutions, but offer advantages: simpler implementation, lower computational requirements, and continue to be used in embedded systems based on descriptors [12]. In most modern tasks, neural network methods (YOLOv8, OpenPose, MediaPipe) have replaced classical approaches due to their high accuracy and automated learning. The traditional approach consists of four main stages: detection, tracking, feature extraction, and classification. MOG2 (Gaussian Mixture Models), KNN, and Optical Flow algorithms are used for detection. Their operating principle is based on background subtraction, which allows for the detection of moving objects. The main challenge is sensitivity to illumination and dynamic backgrounds. For tracking, an optical approach, Kalman filter, and Mean-Shift/CAMShift are used. Feature extraction is performed in three ways: analyzing the direction and speed of movement based on optical features, constructing keypoint trajectories, and analyzing periodic movements based on frequency and phase. Motion classification is performed using machine learning methods such as SVM (classification by extracted features), HMM (motion sequence modeling), and DTW (template matching).

Spatio-temporal models. These models will not be discussed in detail in this article, as they are not suitable for solving practical action assessment problems. However, given their application in motion recognition, their existence is worth mentioning. Spatiotemporal models are used for motion recognition, where simultaneous analysis of both spatial characteristics (shape, pose) and temporal parameters (dynamics, sequence) is required. These models process the video stream as 3D data (width, height, time).

Local-binary patterns. LBP is a classic texture analysis method also used for motion recognition. The algorithm works by comparing the brightness of adjacent pixels in a local area and converting the results into a binary code characterizing the image texture. The algorithm works as follows: for each pixel with coordinates (x_c, y_c) and brightness I_c in its value is compared with neighboring pixels. If a neighboring pixel is brighter than the central one, it is assigned a value of 1; otherwise, it is assigned a value of 0. This produces an 8-bit code (range 0-255) describing the local texture of the image. The function is represented as follows:

$$LBP(x_c, y_c) = \sum_{p=0}^{7} s(I_p - I_c) * 2^p, \quad s(x) = \begin{cases} 1, & \text{если } x \geq 0 \\ 0, & \text{иначе} \end{cases}$$

A locally binary pattern-based action recognition method combined with appearance invariance and patch matching [13] was tested on various public datasets

and the multivariate INSIA Xmas Motion Acquisition Sequences (IXMAS) dataset. It achieved a recognition rate of 80.55%.

Fuzzy Logic Approach. This approach is used in situations where it is difficult to scale methods for processing data dominated by uncertainty and complexity, typical of various real-world events. Methods based on fuzzy logic have been developed to solve such problems. Research [14] demonstrates two new approaches using fuzzy logic for human action recognition. The first method combines fuzzy log-polar histograms with temporal self-similarity analysis to represent actions and then applies SVM for classification. Experiments on standard datasets demonstrated the high accuracy and practical applicability of the method. The second approach is based on the analysis of silhouette slices and motion speed characteristics as input parameters to the fuzzy system. A distinctive feature of this method is the use of fuzzy clustering to automatically determine membership functions. Comparative tests have demonstrated the superiority of this approach over traditional (non-fuzzy) methods when working with the same dataset. Some methods based on neuro-fuzzy systems (NFS) have also been proposed for gesture and human action recognition [15]. A promising direction is the development of hybrid systems that combine the advantages of both methods. For example, using YOLO for initial detection followed by fuzzy classification of movements will provide a balance between accuracy and interpretability.

Deep Learning Recognition Methods. Deep learning is an important branch of machine learning (used in computer vision, robotics, video surveillance, VR/AR, and medicine) focused on the study of multi-layered representations and data abstractions. This technology effectively processes speech, images, and text. Modern deep learning-based methods can achieve high accuracy even in complex conditions. Deep learning models are classified into three categories [16]:

1. Generative and unsupervised models. These open up new possibilities for motion analysis and synthesis, especially in settings with limited labeled data. A key area of development is the creation of supervised, interpretable models with physically plausible output. Examples of such models include Deep Boltzmann (DBM), Deep Belief Networks (DBNs), Restricted Boltzmann (RBM), and regularized autoencoders.

2. Discriminative (supervised) models. These models require labeled data, where each input sample (video/frame) corresponds to an action label. The use of such models directly optimizes the boundary between classes, requires large annotated datasets, and demonstrates state-of-the-art results on standard benchmarks. Supervised methods are the gold standard for recognition but require careful design and selection of training data and computational resources. Examples of such models include convolutional neural networks (CNNs), recurrent neural networks (RNNs), and deep neural networks (DNNs).

3. Hybrid models. Hybrid models integrate multiple machine learning paradigms, combining the strengths of supervised and unsupervised learning, as well as heterogeneous architectures (CNNs + RNNs + Transformers) and multimodal data (video, sensors, audio). Key types of hybrid models include neural-symbolic systems, semi-supervised self-training systems (YOLOv8 + pseudo-labeling), and multimodal hybrids. Hybrid models are becoming the new standard, providing a 5-15% increase in accuracy, reduced data requirements, and improved interpretability. For successful implementation, clear definition of interfaces between components, proper balancing of the computational load, and step-by-step validation of each module are recommended.

Table 1 presents a comparison of approaches. Neural network methods such as YOLOv8 are particularly noteworthy. It is a deep convolutional neural network that has high recognition accuracy, speed (when used in conjunction with a GPU), and good noise immunity.

Table 1.

Comparison of motion recognition approaches with the YOLO neural network method

Criteria	Traditional Methods	Local Binary Patterns (LBP)	Fuzzy logic approach	Neural network methods (Yolo)
Accuracy	Low/Medium	Low/Medium	Average, depending on settings, ~60-80% accuracy for simple movements (heavily dependent on manual settings)	High accuracy for complex scenes: 53.9 mAP on COCO
Speed	Fast (on CPU)	Very fast (on CPU)	Fast (on CPU), depending on the complexity of the rules, 30-60 FPS on CPU	Requires a GPU for maximum speed: 150-200 FPS on GPU (NVIDIA RTX 3060)
Noise Resistance	Sensitive	Medium	Average (requires manual settings)	Robust
Flexibility	Hardly tied to features	Hardly tied to features	Hardly tied to features	Automatically trained
Applicability	Simple tasks	Simple tasks	Simple, resource-limited systems with clear logic	Complex tasks

Table 2 presents comparisons of deep convolutional neural networks with each other on a GPU (NVIDIA RTX 3060) under equal conditions.

Table 2.
Comparison of deep convolutional neural networks

Model	Year	Features	Speed (FPS)	Accuracy (mAP)
YOLOv8	2023	Improved backbone (CSPDarknet), Anchor-free	150–200	53.9 (COCO)
YOLOv7	2022	Transformer blocks, reparameterization	160–180	51.4
YOLOv6	2022	Anchor-free, Bi-directional FPN	170–190	52.8
YOLO-NAS	2023	Neural architecture search (AutoML)	140–170	55.6
RT-DETR	2023	Detection via transformer (DETR)	120–150	53.1
Faster R-CNN	2015	Two-stage, regions of interest (RoI)	10–20	37.8
EfficientDet	2020	Scalable (D0-D7), BiFPN	30–60	51.5

Table 2 shows that YOLOv8 remains the best general-purpose solution. A detailed comparison of Faster R-CNN and YOLOv8 revealed that Faster R-CNN provides higher accuracy in object detection and classification, while YOLOv8, although inferior in accuracy, maintains competitive performance. In terms of data processing speed during training, Faster R-CNN requires significantly more computing resources and time, while YOLOv8 demonstrates faster training under similar hardware conditions. During operation, YOLOv8 provides significantly higher processing speed, while Faster R-CNN demonstrates slower task execution. YOLO demonstrates an optimal combination of speed and accuracy, making it the most sought-after solution, while Faster R-CNN maintains leadership in specialized areas that tolerate increased data processing time [11]. A promising direction is the development of hybrid systems that combine the advantages of deep learning and fuzzy logic methods. For example, using YOLO for primary detection followed by fuzzy classification of movements will ensure a balance between accuracy and interpretability. Such hybrid systems effectively compensate for image noise, increasing the overall accuracy of results.

Conclusion. This article provides a comprehensive analysis of methods for recognizing the actions of medical professionals, with a particular focus on automated assessment of practical skills. The focus is on hybrid systems combining fuzzy neural networks and computer vision technologies, such as YOLOv8, which demonstrate an optimal balance between accuracy, processing speed, and interpretability of results. It is found that traditional methods are inferior to neural network approaches in accuracy but remain relevant in resource-constrained environments, whereas deep learning, especially when combined with fuzzy logic, offers

the most promising solutions for processing noisy data and variable conditions. The developed hardware and software system "LUCH" confirms the effectiveness of neural network technologies in simulation-based training, ensuring continuous assessment of skills and adaptation to the individual characteristics of students. However, systemic shortcomings have been identified in the system's operation, including degradation of video stream quality due to suboptimal lighting conditions and the influence of parasitic factors.

Prospects for further research include improving the hybrid architectures of the LUCH hardware and software system and implementing fuzzy logic approaches to ensure the algorithms' resilience to noise distortions in input data.

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审查在现有轧机上按照 GOST 34028-2016 标准生产 A500 级钢筋的方法
REVIEW OF METHODS FOR PRODUCING CLASS A500 REBAR IN ACCORDANCE WITH GOST 34028-2016 ON EXISTING ROLLING MILLS

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摘要：本文回顾了俄罗斯和独联体现有轧机按照GOST 34028-2016标准生产A500级钢筋的方法，并指出了钢筋生产的主要趋势以及实现生产模式现代化的途径。文中重点介绍了类似单位的成功实施方案和实施路径。

关键词：轧制产品、钢筋、轧机、A500。

Abstract. *This review of production methods for grade A500 rebar in accordance with GOST 34028-2016 at existing rolling mills in Russia and the CIS identifies key trends in rebar production and approaches to modernizing production modes. Successful implementation options and implementation paths for similar units are highlighted.*

Keywords: *rolled products, rebar, rolling mill, A500.*

Rebar, used in the construction industry for the production of reinforced concrete, is one of the most widely produced products in the ferrous metallurgy industry.

The most significant properties of rebar used in the production of precast concrete, in addition to strength and deformability, are its adhesion to concrete and weldability. The anchorage length of reinforcement at the supports of precast concrete slabs and beams, the strength of their inclined sections, the moment of crack formation and crack width, the length of anchor rods of embedded parts, etc., depend on the effectiveness of the bond. In prestressed reinforced concrete ele-

ments, the effectiveness and feasibility of using high-strength reinforcement bars of classes higher than A800 depend on the type of reinforcement surface profile and its expansion in the concrete. This is due to the risk of failure of the supporting sections of the elements when high prestress values in the reinforcement are released onto the hardened concrete.

To reduce the cost of rolled reinforcement, the method of thermomechanical strengthening of metal has been widely implemented since 1990 [1]. GOST 10884–94 "Thermomechanically Strengthened Reinforcing Steel for Reinforced Concrete Structures" was developed. This strengthening method allows for high strength properties of reinforcement made from metal with a low alloying content, significantly reducing its cost. Unfortunately, this strengthening method reduces the weldability of the rebar due to the loss of the achieved strength after repeated heat input during welding.

As a result, the introduction of thermomechanically strengthened rebar necessitated adjustments to welding modes and methods, significantly complicating the welding process and reducing its quality both in the factory and on-site. RTM 393–94 [2] and GOST 52544–2006 "Welded Rolled Reinforcing Bars with Die-Section Classes A500C and B500C for Reinforcing Reinforced Concrete Structures" tighten the requirements for flash-butt welding of thermomechanically strengthened rebars. Bath welding with removable overlays and submerged arc welding are not recommended, and the technology for some other types of welded joints has been significantly complicated.

Since 1990, Russian metallurgists have begun mass-producing rebar for export to other countries. In accordance with the recommendations of European standards, adopted by many countries, rebar supplied to the international market is manufactured with the so-called "European" profile. This profile differs from the ring-shaped profile produced in the USSR according to GOST 5781-82, with an open perimeter (without intersections with the longitudinal ribs) and a double-sided (two-row) arrangement of transverse crescent-shaped ribs. To standardize production, rebar with the "European" profile has begun to be widely introduced in Russia, despite the fact that its adhesion properties to concrete are significantly lower than those of the ring-shaped profile according to GOST 5781-82 [4]. The introduction of a new type of reinforcement profile necessitated the harmonization of requirements for adhesion to concrete, crack resistance, and deformability of reinforced concrete in domestic standards with international ones, as defined in SNiP 52-01–2003 and SP 63.13330.2012 "Concrete and Reinforced Concrete Structures." This, in turn, significantly increased (up to 30%) the consumption of reinforcement in reinforced concrete structures [5].

Thus, to summarize the above, the following conclusions can be drawn.

The consumer properties of rebar depend primarily on its manufacturing technology, the chemical composition of the metal, and the surface profile of the reinforcement.

Производство современного арматурного проката осуществляется по технологии, позволяющей значительно снизить его себестоимость за счет непрерывной разливки стали, термоупрочнения металла, увеличения производительности прокатных станов, методом продольного разделения заготовки и применения дешевых исходных металлов, но, к сожалению, в ущерб качеству выпускаемой продукции.

The harmonization of domestic and foreign rebar production and the resulting forced introduction of new requirements for the design of reinforced concrete structures in SP 63.13330.2012 to SNiP 52-01–2003 has increased the consumption of rebar in reinforced concrete by 30% or more, leading to an increase in its cost.

To improve quality and reduce construction costs, it is necessary to develop and implement innovative types of rebar that meet the needs of the Russian metallurgical and construction industries and are competitive in the global market.

Next-generation rebar must be manufactured using modern, high-performance metallurgical production technologies, without complicating process regulations, and with a quality level that meets construction needs. It must meet all requirements of domestic and international standards for the manufacture and use of reinforcement and reinforced concrete structures without any additional costs compared to design results based on standards in effect before 2003.

New-generation domestic rebar must have properties that ensure its patent protection and competitive advantages over all known types of rebar.

Since 2003, the A.A. Gvozdev Research Institute of Reinforced Concrete has been conducting research into rebar that meets the above requirements [5].

As a result, six-row rebar of class A500SP has been introduced and has been in mass production for over 12 years at Evraz ZSMK OJSC (Novokuznetsk). To date, approximately 4 million tons of this rebar have been produced and used in construction.

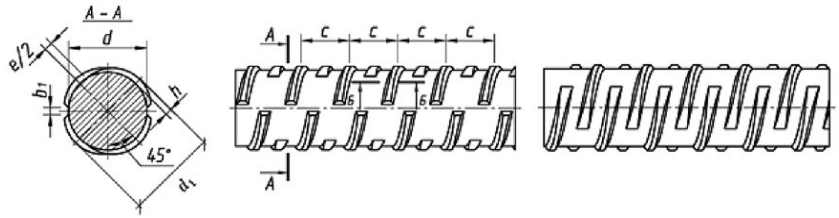
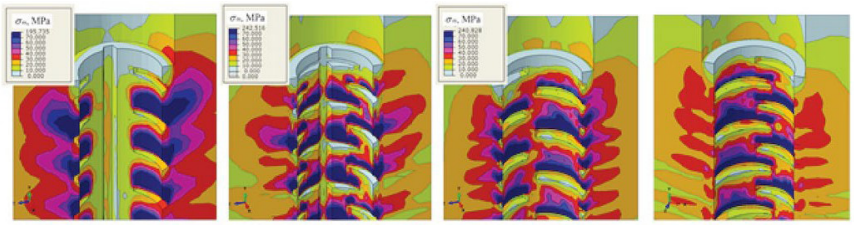


Figure 1. *Design of a four-row helical profile*

Experiments have demonstrated higher bond strength and lower deformability, as well as smaller crack widths, in reinforced concrete with this type of reinforcement. High bond energy capacity has been established for grade A500SP reinforcement after reaching its yield strength, which largely ensures the survivability of the structure under specific types of loads (seismic, explosive, impact, etc.).

These research results are explained by the lower expansion of reinforcement with a multi-row arrangement of transverse crescent-shaped ribs along the bar surface than with a two-row arrangement, as is the case with “European” reinforcement [5].



a) *b)* *c)*

Figure 2. *Comparative computer analysis* of stress distribution at the interface between reinforcement and concrete. Demonstration of uniform distribution of wedging forces from the surface of reinforcement with a multi-row profile: a – double-sided double-row profile; b – six-row A500SP profile; c – four-row Av500P profile*

Effective January 1, 2019, interstate standard GOST 34028-2016 “Rolled Reinforcement Products for Reinforced Concrete Structures. Specifications” came into effect. It replaces GOST R 52544 (regarding class A500C), GOST 10884, and GOST 5781. The new standard introduces a set of additional properties for class A500 rebar to ensure its reliable use in high-rise construction, in areas of high seismicity, in aggressive environments (offshore areas), and in bridge construction (high cyclic loads). At the initiative of JSC Research Center “Construction” and the Federal State Unitary Enterprise “TsNIIChermet” named after I.P. Bardin, a unified interstate standard, GOST 34028–2016 “Reinforcing Steel for Reinforced Concrete Structures. Specifications,” has been developed. This standard unifies all current rebar standards in the CIS and raises the requirements for rebar of 400 MPa and above to the level of European normative documentation (EN 10138).

The innovative idea and the main difference between the new standard and previously used standards is the broad inclusion of indicators responsible for the operational characteristics of the rebar. The standard set of acceptance character-

istics for metal products includes standardized levels of strength, ductility, and geometric parameters. For rebar, operational characteristics are paramount due to the specific nature of its use, which relates to the safety of people and structures, taking into account the interaction of the metal with concrete.

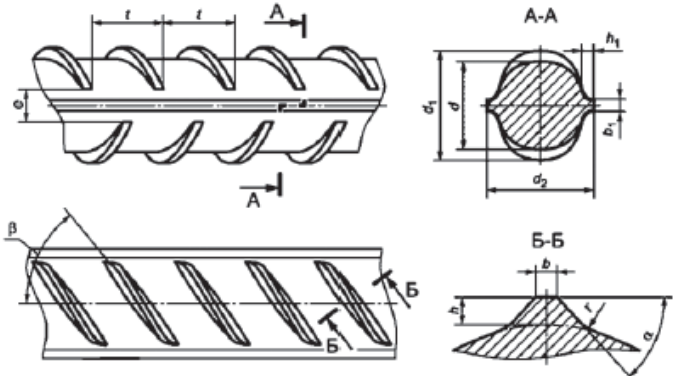


Figure 3. *Configuration of a periodic profile of form 2f according to GOST 34028–2016:*
h, t, β – height, pitch, and inclination angle of the transverse ribs, respectively; e – distance between the ends of the transverse ribs; α – inclination angle of the lateral surface of the transverse rib; r – radius of the mating surface of the transverse ribs with the rod core; b, b1 – width of the transverse and longitudinal ribs, respectively; d – rod diameter; d1, d2 – diameter along the longitudinal and transverse ribs, respectively.

GOST 34028–2016 recommends the use of microalloying with Nb, V, and Mo to ensure the technological properties of rebar. However, alloying steel with even small amounts of carbide- and nitride-forming elements significantly increases the cost of rolled products [9, 10]. Control of the structure, and through it the mechanical and technological properties of rebar, is possible by selecting an effective mode of in-line thermomechanical processing of rolled products using the heat of rolling heating through two-stage cooling of the end of rolling wire mills.

Previously, a set of works was carried out to develop a technology and master the production of rebar of strength class A500C, form 2F, according to the requirements of GOST 34028-2016 [11] in the conditions of the 370/150 mill of OJSC BMZ - the management company of the BMK holding.

Two-stage cooling in the wire rod line of the 370/150 mill (Fig. 4, a) is carried out in the first stage with water in sections No. 1–3 after the 10-stand BGV block and in sections No. 4 and 5 after the 4-stand finishing block to a temperature below

Ac1 (for rebar) in the laying head zone. The second stage involves air cooling on a Stelmore-designed roller table (Fig. 4, b) after the coils are formed on the laying head. The coils move along the roller table, with adjustable speed and air flow from up to 20 fans, with the thermally insulated covers open or closed.

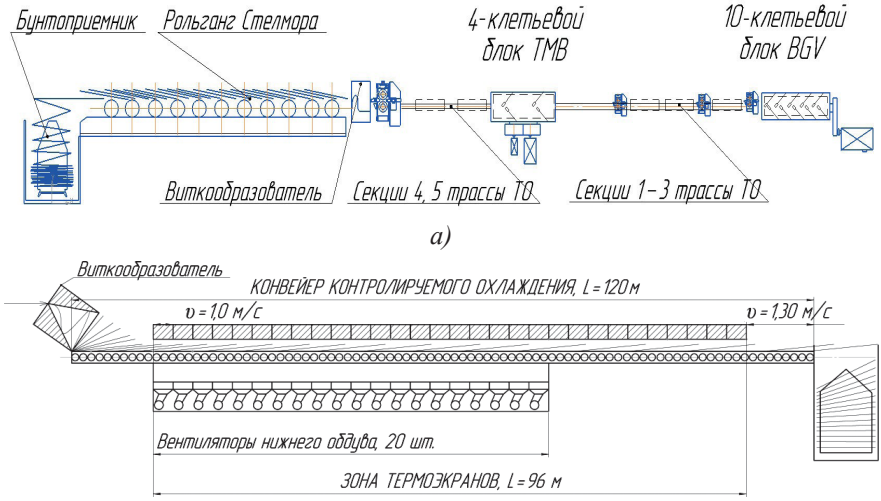


Figure 4. *Flow cooling diagram in the 370/150 mill wire rod line:*

a – layout of two-stage cooling elements;
b – Stelmore roller table diagram

During the development of rebar production, a cooling mode (Table 1) was proposed with gentle blowing on the first five fans (20% capacity) at a coil conveying speed of 0.45–0.55 m/s. The obtained yield strength values for the rolled products (Table 2) were at the lower limit of permissible values, meaning that the proposed modes will ensure guaranteed production within the requirements of GOST 34028–2016.

Table 2.

Cooling mode for the basic option

Profile number	Rolling speed, m/s	Temperature after descaling, ° C	Roll temperature, °C		Fans		Speed of roller conveyor sectors		Position of roller conveyor covers by numbers
			at the entrance to the block BGV	in the laying head zone	number of working fans	switching power, %	Stelmore speed, м/с	sector number / %	
6	46–55	1020–1060	900–940	580 ± 20	1–5	20	+0,45–0,55	2–14/+2; 15–18/0; 19/–3; 20/+2	1–32 open

Table 3.

Mechanical properties for the basic version

Prototype number	Yield strength Re, N/mm ²	Tensile strength Rm, Н/мм²	Plastic, Rm/Re
1	504	645	1,28
2	514	650	1,26
3	536	661	1,23
4	501	644	1,29
5	509	646	1,27
6	523	652	1,25
7	511	651	1,27
8	536	658	1,23
Average values	516,8	650,9	1,26
GOST requirements 34028–2016	at least 500	at least 600	not less than 1.05

To improve the mechanical properties of the rebar, a decision was made in the second stage of the research to increase the lower limit of the following elements: carbon from 0.18 to 0.19%; silicon from 0.25 to 0.35%; manganese from 1.00 to 1.17% (Table 4), and to increase the cooling intensity from 20 to 30% with an increase in the transport speed to 1.06 m/s in accordance with the methodology [12].

In the second campaign, 28 blanks were rolled using an improved chemical composition and a two-stage cooling mode. The test results are presented in Table 6.

Analysis of the mechanical properties of the rolled products shows that the improved version allows for the production of No. 6 rebar of strength class A500C, shape 2f, with guaranteed compliance with the requirements of GOST 34028–2016.

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地理信息技术在农业土地利用分析和规划中的作用
THE ROLE OF GEOINFORMATION TECHNOLOGIES IN THE ANALYSIS AND PLANNING OF AGRICULTURAL LAND USE

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摘要：本文探讨了地理信息技术在农业数字化背景下在农业用地分析和规划中的作用。特别关注地理信息系统 (GIS) 和遥感数据在土壤条件评估、土地利用监测、产量预测和管理决策优化中的应用。结果表明，将 GIS 融入农业管理系统能够全面分析空间数据，识别土壤退化和资源低效利用的趋势，并开发更可持续的土地利用模式。本文还分析了俄罗斯、哈萨克斯坦以及国际上应用 GIS 技术的现代案例，展示了该方法的多功能性。强调指出，地理信息方法的使用不仅有助于提高农业生产的经济效率，还能解决与土地资源合理分配和保护地域自然潜力相关的环境问题。文章最后指出，农业用地的未来发展与数字技术的进一步发展密切相关，而 GIS 是这一过程中战略规划的关键工具。

关键词：地理信息技术、农业土地利用、GIS、遥感。

Abstract. *This article examines the role of geographic information technologies in the analysis and planning of agricultural land use in the context of digitalization of the agricultural sector. Particular attention is paid to the use of geographic information systems (GIS) and remote sensing data for assessing soil conditions, monitoring land use, forecasting yields, and optimizing management decisions. It is shown that integrating GIS into agricultural management systems enables comprehensive analysis of spatial data, identifying trends in soil degradation and inefficient resource use, and developing more sustainable land use models. Modern examples of technology implementation in Russia and Kazakhstan, as well as international practice, are considered, demonstrating the versatility of this approach. It is emphasized that the use of geographic information methods not only contributes to increased economic efficiency in agricultural production but also addresses environmental issues related to the rational distribution of land resources and the preservation of the natural potential of territories. The article*

concludes by noting that the future of agricultural land use is directly linked to the further development of digital technologies, and GIS is a key tool for strategic planning in this process.

Keywords: *geoinformation technologies, agricultural land use, GIS, remote sensing.*

Introduction

Amid global challenges related to population growth, climate change, and limited natural resources, agriculture faces challenges that require fundamentally new approaches to land management. Land has always been considered the primary factor of production in agriculture, but today, its rational and efficient use is becoming a strategic prerequisite for food security and sustainable development. Traditional management methods based on visual observations and intuitive decisions are no longer capable of fully ensuring the necessary accuracy and depth of analysis. They are being replaced by modern digital tools, among which geoinformation technologies occupy a key place.

Geoinformation systems (GIS) and remote sensing technologies offer new opportunities for comprehensive land analysis, land use monitoring, and change forecasting. Thanks to the development of satellite and unmanned aerial technologies, it has become possible to obtain reliable real-time data on soil and climate conditions, vegetation dynamics, and the degree of anthropogenic pressure on an area. This allows farmers and researchers not only to record the current situation but also to develop more accurate planning models, minimizing risks and increasing agricultural efficiency.

GIS technologies are particularly important in a changing climate. Agriculture, as one of the most vulnerable sectors, is acutely sensitive to fluctuations in temperature, precipitation, and the frequency of extreme weather events. Using GIS allows us to identify potential risk zones, assess the resilience of agricultural landscapes, and develop adaptive land use strategies. This creates the possibility of rationally distributing crops depending on specific environmental conditions, which ultimately leads to increased yields and reduced costs.

A significant task for the modern agricultural sector is maintaining soil fertility and preventing degradation processes. Overexploitation of land, improper crop rotation, or intensive use of chemical fertilizers often lead to the depletion of soil resources. GIS technologies make it possible to monitor changes in land structure, identify degraded areas, and take measures to restore them. Thus, digital analysis methods are becoming a tool not only for economic efficiency but also for the environmental sustainability of agricultural production [1].

The socioeconomic aspect should not be forgotten either. In a market economy, land use cannot be considered solely in terms of its natural characteristics.

Analysis of the infrastructure availability of territories, accessibility of transportation routes, and proximity to markets is becoming an important element. Geographic information systems make it possible to combine diverse data—from soil and water resource maps to demographic indicators and farm structure—thus forming a holistic understanding of the spatial organization of rural areas. This is especially relevant for the development of regional and national agricultural development programs.

In recent decades, the concept of "precision farming" has been actively implemented, based on a differentiated approach to crop and resource management. Geoinformation technologies play a crucial role here: they enable the creation of yield maps and the management of fertilizer and crop protection applications based on the characteristics of individual field sections. This approach not only promotes increased productivity but also promotes a more careful use of natural resources, reducing the burden on the ecosystem [2].

At the same time, the use of geoinformation technologies requires certain conditions: the availability of specialists skilled in working with digital maps and satellite data, the availability of software and equipment, and the willingness of agricultural producers to implement innovations. Despite this, recent experience shows that the integration of GIS into land use analysis and planning processes is becoming increasingly popular. It enables the connection of scientific research with real-world production tasks, enabling the agricultural sector to reach a new level of efficiency and sustainability.

Thus, the role of geoinformation technologies in agriculture extends far beyond that of an auxiliary tool. They are becoming an integral element of strategic land management, creating the basis for scientifically based planning, risk mitigation, and long-term food security. Modern agricultural production is unimaginable without systematic data analysis, meaning that GIS and remote sensing are currently shaping a new paradigm for land use.

Main Part

Agricultural development directly depends on the ability to manage spatial data, as each plot of land has unique characteristics: soil type, moisture, topography, erosion level, proximity to water bodies and infrastructure. Traditionally, such data was collected manually and often became outdated, but with the advent of geographic information technologies, this situation has changed.

Geographical information systems (GIS) enable the integration and analysis of large amounts of information from various sources—satellite imagery, drones, remote sensing data, and ground observations. This makes it possible to create dynamic maps that reflect the condition of agricultural land in real time.

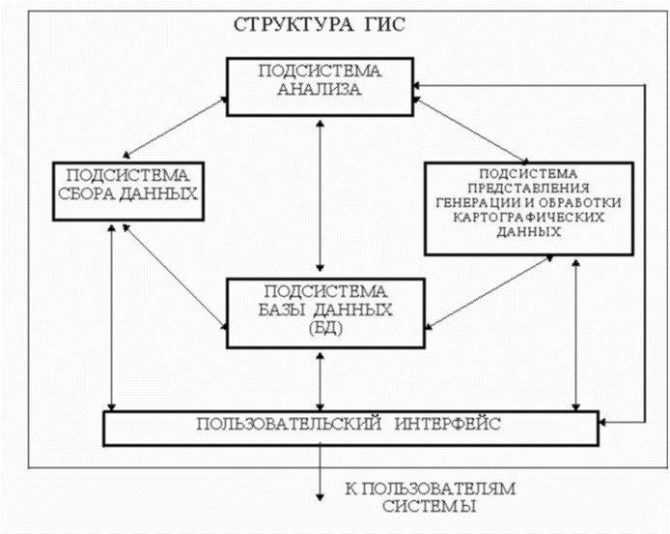

Figure 1. *GIS structure*

Soil is the primary resource for agriculture. Maintaining its fertility is a matter of national importance, as land degradation leads to reduced crop yields and food security.

Using GIS and remote sensing technologies, it is possible to:

• identify changes in soil structure (compaction, salinization, erosion);

• monitor moisture content dynamics;

• monitor degradation processes and restore damaged areas.

For example, soil erosion maps allow agricultural enterprises to take measures to minimize land destruction by changing tillage systems, introducing anti-erosion crop rotations, or stabilizing slopes [3].

Table 1

Soil monitoring indicators using GIS

Indicator	Data source	Analysis capabilities
Soil moisture	Satellites, drones	Determining irrigation rates
Salinity	Remote sensing, laboratory analysis	Identifying degraded areas
Organic matter	Remote sensing + soil samples	Fertilizer planning
Erosion processes	Topographic maps	Protective measures

Geoinformation technologies enable modeling the optimal placement of agricultural crops based on an analysis of natural conditions. For example, using soil

maps and climate parameters, it is possible to determine which crops will yield the highest yields in a specific region.

The advantage of geoinformation technologies in agriculture creates the basis for making more rational decisions based on accurate spatial data [4].

Furthermore, GIS helps develop effective crop rotation systems. Crop rotation is essential for restoring soil fertility and reducing phytosanitary risks. Spatial analysis allows for calculating the optimal crop sequence and minimizing soil resource depletion.

Over four years of active use of space monitoring in the Republic of Kazakhstan, practice has demonstrated its effectiveness in addressing issues such as misuse, identifying unused land, recording species yields, and determining acreage [5].

In recent years, the concept of precision farming, which is based on a differentiated approach to agricultural production management, has become increasingly widespread. Using GIS and satellite data, it is possible to create yield maps that identify areas of high and low productivity.

Water supply plays a crucial role in agriculture. GIS are used to assess water availability, model irrigation systems, and monitor their efficiency.

Remote sensing can be used to determine soil moisture levels and predict irrigation needs. This is especially important in regions with arid climates, where improper water distribution can lead to significant crop losses [6].

In addition to accounting for species diversity and monitoring water supply, GIS technologies, along with the resulting algorithms and software, incorporate such mechanics as mathematical pattern recognition theory and the maximum likelihood algorithm. The availability of such algorithms can highlight the potential for implementing artificial intelligence, as a training sample is created [7].

Modern agriculture must consider not only economic but also environmental factors. Improper land management leads to erosion, soil degradation, and water pollution. Geoinformation technologies make it possible to monitor the state of ecosystems, identify areas with critical loads, and develop measures for their restoration.

Despite the obvious advantages, the widespread implementation of geoinformation technologies in agriculture faces a number of barriers. These include the high cost of equipment, a shortage of qualified specialists, and limited digital literacy among farmers [8,9].

Professor Zhildikbaeva, A.N., emphasizes the importance of rotation and transformation of agricultural production. This requires the development of not only traditional crops, but also the introduction of new varieties, organic farming, and the processing of secondary derivatives. Her position is that high-quality land management requires harnessing the natural potential of regions and districts and

integrating technological solutions with current local conditions [10]. Among a number of proposed measures to address soil degradation, Usipbaev, G.B., Omarbekova, A., Sagandykova, D., & Begazimov, D., note that agricultural sector policy should focus on access to financial resources and technology [11].

However, the global trend is that further development of the agricultural sector is impossible without the use of GIS. In the future, we can expect the integration of GIS with artificial intelligence, the Internet of Things, and big data. This will automate decision-making processes, create more accurate forecasts, and minimize human error.

Conclusion

Modern agriculture is undergoing a digital transformation, and geographic information technologies (GIS) play a key role in this process. They enable the integration of spatial data, its analysis, and its use as a basis for management decisions. In the face of climate change and growing food demands, GIS is becoming a tool capable of balancing production efficiency and the conservation of natural resources.

The use of GIS has proven its value in various areas: monitoring soil and land conditions, preventing degradation, optimizing crop rotations, and precisely allocating crops. Thanks to satellite data and remote sensing technologies, it has become possible to monitor processes in real time and adapt production to changing conditions. Crucially, the use of GIS not only increases yields but also reduces costs, making farming more rational and sustainable.

Precision farming is becoming an integral part of modern agricultural practice. It enables farms to manage resources in a differentiated manner: adjusting irrigation rates, adjusting fertilizer application, and taking into account soil heterogeneity. This approach increases productivity while reducing the burden on the ecosystem, making it a promising tool for long-term planning.

GIS technologies also play a vital role in the socioeconomic development of rural areas. They enable the assessment of infrastructure accessibility, transportation routes, and market proximity, and the development of comprehensive regional development strategies. This makes GIS not only a tool for agricultural production but also an element of government policy on food security.

Despite existing barriers—the high cost of equipment and the shortage of qualified specialists—the implementation of GIS is becoming inevitable. In the near future, their integration with artificial intelligence, the Internet of Things, and big data analysis is expected, taking agricultural management to a new level.

Thus, GIS technologies are no longer an auxiliary tool but are becoming the foundation of a new land management paradigm. They enable the combination of economic benefit and environmental sustainability, ensuring the competitiveness of the agricultural sector and food security for society. The future of agriculture

is inextricably linked to the development and application of GIS, which fosters a culture of precise and responsible stewardship of the land.

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