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At present, the most important problems of medical ethics related to the issues of fair access to medicine and health care as the main human benefits are of particular importance. In this regard, the study of biological and social foundations seems to be especially relevant, allowing us to consider a person not only as a user of medical services, but also as a sense-making center, influenced by the value-driven norms and societal ideas. The aim of the study is to consider the following two aspects of conceptualizing a person in medical ethics: his/her biological and social status. Dialectical method, system analysis, cultural and phenomenological approaches constitute the article's methodological basis. Based on the discussion undertaken in modern scientific literature, these allow us to come to an understanding of a person in the system of medical ethics. It is noted that consideration of a person in the context of issues of medical ethics goes, first of all, in two main directions: first, the role of a person is revitalized in the process of choosing treatment methods and understanding the degree of risk associated with the treatment and prevention of his person as a biological being; the second is the immersion of a person, engaged in decision-making, into the system of values and traditions of society. It is shown that the second aspect is connected with the understanding of a citizen as a social being. Comprehension of a person should be undertaken through the study of his moral, spiritual, emotional, physical and biological foundations of being; at the same time, biological and social approaches should not act separately, but in unity, and lead to a holistic concept of man.

Key words: medical ethics, human, healthcare, medicine, health, society, humanitarian knowledge, natural sciences, consciousness

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БИОЛОГИЧЕСКОЕ И СОЦИАЛЬНОЕ — ДВА РАКУРСА ИДЕНТИЧНОСТИ ЧЕЛОВЕКА В КОНТЕКСТЕ МЕДИЦИНСКОЙ ЭТИКИ

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В настоящее время важнейшие проблемы медицинской этики, связанные с вопросами справедливого доступа к медицине и здравоохранению как основным благам человека, приобретают особое значение. В этом плане особенно актуальным представляется исследование биологических и социальных основ, позволяющих рассматривать человека не только как пользователя медицинских услуг, но и как смыслообразующего центра, испытывающего влияние ценностных норм и представлений, принятых в обществе. Цель исследования — рассмотреть два аспекта осмысления человека в медицинской этике: биологический и социальный статусы. Методологической основой статьи является диалектический метод, системный анализ, культурологический и феноменологический подходы, позволяющие на основе материалов дискуссии, предпринятой в современной научной литературе, прийти к осмыслению человека в системе медицинской этики. Отмечено, что рассмотрение человека в контексте проблем медицинской этики идет, прежде всего, по двум основным направлениям: первое — активизация роли человека в процессе выбора методов лечения и осмыслении степени риска, связанного с лечением и профилактикой его персоны как биологического существа; второе — погружение человека в процессе принятия решений в систему ценностей и традиций общества. Показано, что второй аспект связан с осмыслением гражданина как социального существа. Осмысление человека должно быть предпринято через изучение его нравственных, духовных, эмоциональных, физических и биологических основ бытия; при этом биологический и социальный подходы должны выступать не разрозненно, а в единстве и привести к целостному пониманию человека.

Ключевые слова: медицинская этика, человек, здравоохранение, медицина, здоровье, общество, гуманитарное знание, естественные науки, сознание

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Currently, the most important problems of medical ethics related to the issues of fair access to medicine and health care as the main human benefits assume special importance. In this regard, studying biological and social foundations allowing us to consider a person not only as a user of medical services, but also as a sense-making center, influenced by the value-driven norms and societal ideas, seems to be particularly relevant.

In today's environment, the citizen's decision-making within the bounds of medical care requires certain grounds. In this context, the principle of respect for human rights and human dignity is the key principle of medical ethics. Every citizen has the right to protection of health, however, as EV Bryzgalina rightly points out, "personal, professional and life experience, system of values, nonverification of multiple parameters and the impact of social norms make it possible to describe the healthcare resource allocation at the micro level as the bioethical choice, but not the act of deciding" [1, p. 43].

Considering a person in the context of the issues of medical ethics goes, first of all, in two main directions: first, the role of a person is revitalized in the process of choosing treatment methods and understanding the degree of risk associated with the treatment and prevention of his person as a biological being; the second is the immersion of a person engaged in decision-making into the system of values and traditions of society. It is obvious that the second aspect is connected with understanding the citizen as a social being.

From our point of view, comprehension of a person should be undertaken through the study of his moral, spiritual, emotional, physical and biological foundations of being. Both biological and social approaches not act in unity, and lead to a holistic concept of man.

In this regard, research is notable, conducted by Ralph Emerson, who was the figure in the transcendentalist movement. The filosopher substantiates the importance of the person's spiritual advancement. However, he writes about the necessity to consider the individual's biological needs as well. To his mind, mankind has done nothing to learn about the mystery of fate, and feeble efforts to conceptualize the human nature have put the human person on the edge of madness. That is why the researcher rejects all dogmatic measures applied to humans, neither biological, nor social. He aims to uplift the soul of every person to make him/her understand the moral beauty, and to hypnotize everyone into understanding the importance of human dignity. Emerson encourages every person to discover oneself and identify the person's better qualities. His book Moral Philosophy is the apotheosis of unity of the human spiritual and corporeal being mediated by Supreme Wisdom: "Human spirit should prefigure our philosophical plans exactly how the human body needs are taken into consideration when building the dwelling house" [2, p.7].

Biological substantiation of human evolution made in the 19th century evoked protests from many philosophers. In this regard, VS Soloviev has noted the following: in case we hide behind the idea of humanity as an abstract concept, we would begin to replace true values with imaginary ones. According to V. S. Soloviev, we would begin to see "in our nation the zoological side, its brutal instincts, strengthen its brutal character; whom and what do we love here, whom and what do we serve?" [3, v. 5, p. 393]. When criticizing the attitude toward a person from the perspective of the prevailing biological nature, Friedrich Nietzsche wrote the following about the renegades: "Those young hearts have already all become old — and not old even! Only weary, ordinary, comfortable… their first companions must be corpses and buffoons" [4, pp.154–155].

In the 20th century, evolutionary ideas were criticized by mane researchers. E. Durkheim opposed absolutizing the biological basis of humans in the context of sociology [5]. VF Malinovsky [6] completely excluded evolutionary concept from social anthropology. In this regard, it is important to emphasize that empirical methods of acquiring knowledge continued to have a strong influence on the human nature conceptualization in the early 20th century in the context of both naural science and the system of humanitarian knowledge. Conversely, medicine in general and the development of medical ethics in particular were greatly influenced by the functionalist concept, which interpreted human life through the prism of one's status in the family, social group, society. Thus, Leland Yeager wrote that history did not prove that people had invented ethical norms on purpose. Furthermore, he pointed out that "some rules of families and other groups, including statutes enforced by governments, have been deliberately adopted" [7, p. 97].

Clear delineation of the terms "biological" and "social" primarily on ethical grounds was first noted in the mid-20th century. According to T Dobzhansky, exaggerated importance of bilogical component in the conceptualization of man is the red herring for the mystery of man. Dobzhansky emphasized the danger of relapse into the racial theories, being equipped with the biological basis for determining human nature only. He stressed the implications of the one-sided version of human nature: "some biologists make fools of themselves over and over by enforcing the solution for social and political problems, which is based on the idea that man is just an animal" [8, p. 157].

Conditional division of the functions of natural sciences and humanities was achieved by the mid-20th century. Furthermore, studying the biological basis for the existence of nature and man was the main object of natural science, and humanities focused mainly on the spiritual, social, cultural and ethical aspects of the human being. Thus for example, Erwin Schrodinger, Austrian physicist, carries the biological patterns over to the emotional and psychological sphere of human life. He notes the fact that many elements of the individual's conscious activity (where the person feels happy when reaching a goal) are not subject to volitional control, and some physiological processes (for example, breathing in the room full of smoke) on the contrary may slow down. Schrodinger calls these phenomena "misconceptions of mnemonic hereditary nature" [9, p. 13]. That is why he describes the manifested human spirituality, such as the emerging faith and religion, as the "absurd support" fearfully grasped by the "weak, deceived human spirit" [9, p. 205]. In this regard, it is interesting to note that Descartes excluded sensations from the category of mental quite often: "when we see an animal heading towards us…, when this figure is extraordinary and very scary, i. e. when it vividly brings to mind something that hurt the body in the past, it sparkles the passion of fear in the mind, which could be followed by the passion of courage…" [10, p. 575].

Here we are talking about the Freud's idea that many mental acts are unconscious and therefore there could be some unconscious desires and beliefs. According to Freud, desire is covertly constructed as the condition, which produces certain behavior. Thus, Freud has come to believe that conscious access to certain conditions is insignificant in explaining behavior. Consequently, the person's awareness never constructs the being of something as the belief: "…there are present in all men destructive, and therefore anti-social and anti-cultural, trends and that in a great number of people these are strong enough to determine their behaviour in human society" [11, p. 20].

Representatives of the behaviorism movement developed a new psychological explanation of human activity, which left no room for the informed assessment. The belief that the internal states were not related to the explanation of human behaviour was the primary reason for this view. That is why interpretation of human activity is independent of phenomenal concepts. Currently, David Chalmers tries to rationalize the concepts of behaviorism. He points out that defining the role of mental in the production of human behavior requires focusing on psychological properties. When considering the experience of the human consciousness mental states, we should base on phenomenal concepts: "To assimilate the phenomenal to the psychological prior to some deep explanation would be to trivialize the problem of conscious experience; and to assimilate the psychological to the phenomenal would be to vastly limit the role of the mental in explaining behavior" [12, p. 35].

In this regard, fundamental research was performed by Konrad Lorenz, who tried to define the term "instinct" by monitoring animal behavior, and studied the inherited patterns of behavior in animals. Comparative analysis of behavior in wild and domestic animals led Lorenz to believe in the loss of vitality in domestic animals. The thinker also noted the adverse impact of urban infrastructure on the domesticated animal management. By extrapolating his observations into the development of modern civilization, Lorenz came to understanding the ambiguity of the moral and esthetic

foundations of humanity. He considered political activism in the society as the aberrant aggressive instinct. Lorenz came to a conclusion that human cognition emerged in the course of evolution to preserve the species: "this should be studied as a function of some real system that has emerged naturally and interacts with the equally real world" [13, p. 15].

Ideas of Konrad Lorenz did not go unnoticed by the academic world. These were further developed by Edward Wilson, Harvard University, in his book On Human Nature. Wilson, who was one of the founders of sociobiology, defined the goal of the new science, sociobiology, as a "systematic study of the biological basis of all forms of social behavior in all kinds of organisms, including man" [14, p. 5]. He tried to shift the humanities towards absolutization of the biological basis of the human being based on evolution theory, providing true interpretation of human behavior. Wilson promoted the social development strategies in the same way as the "human animal survival strategy" insisting that social relationship had the biological basis [14, p. 96]. The thinker believed that even science was not totally free of constraints imposed by the human evolutionary inheritance. Wilson aimed to define and specify certain levers allowing one to both explain and predict human behavior in the framework of the natural selection theory. For example, the researcher attributed the incest taboo to the fact that primitive society had a genetic intention to increase their capability of reproducing. Wilson paid close attention to four major (in his view) categories of behavior, such as altruism, sex, aggression and religion, and treated each category as a human evolutionary strategy.

Edward Wilson concluded that knowledge of genetic strategies was the basis of human sciences. That is why the researcher substantiates the fact that "there is a threshold beyong which biological evolution would start reversing the cultural evolution" [14, p. 80]. His famous saying, "Genes hold culture on a leash" [14, p. 167], demonstrates the desire to justify the priority of the human being biological determinants over the social bases. It is also important to pay attention to the distruction of the basis of medical ethics attempted by thus author, since, according to Wilson, there is no way to prove that ethics is more important to define the behavioral determinants compared to genetic basis. That is why the person's fear of sickness or death impedes the individual's activity, whether he/she is a doctor or a patient. Therefore, the Wilson's conclusion is as follows: ethics and culture should only be considered in terms of necessity of these spheres of the human being for evolution.

In the current context, many ideas of Konrad Lorenz are further developed by Paul Nurse, the distinguished British scientist and and Nobel laureate. He substantiates the concept of natural selection and declares widespread use of this concept in the areas other than biology. The thinker demonstrates the importance of natural selection for economics and computer science. He emphasizes the fact that the algorithms used to operate technical devices simulate the natural selection. In his writings, he revives the idea of man gradually transforming into machine, proposed by philosopher La Mettrie: "Is it likely to ever meet any other life forms?… I am sure that they, like us, will be self-sustaining chemical and physical machines, built around information-encoding polymers that have been produced through evolution by natural selection" [15, p. 219–220].

Donna Haraway, American historian, takes the opposite view. After studying reports on the life of primates, the researcher concluded that males dominated in the groups. She disputed the finding that gender differences were natural. This provision provided the basis for criticizing the priority of biological foundation in understanding the human being. She demonstrated the difference between the terms "gender" and "sex". Haraway showed that the human life biological basis itself was produced by means of social relationships, could be only remotely related to the natural basis, and moreover, could not be explained by evolution theory [16, p. 23]. The researcher criticized the feminist call for determining the foundation of women's emancipation. She denied the possible biological and social rationale for the free choice of "sexual identity".

Victor Ten has adopted a conciliatory position between the advocates of biological approach and the supporters of sociological justification of human behavior. In his writings, he tries to provide a way out of the cul-de-sac, the science, unable to shift from the reflex theory, has been stuck in. He is offering to start a new science, psychophysiology, which would be capable of answering the following questions:

1. How did humans manage to free themselves of reflexes?
2. What tragedies did they experience in the transitional stage?

After studying the writings of physiologists, Victor Ten concludes that animal reactions are always preset by their biological nature and constantly unambiguous by the way of realization. The animal behavior variation may be only tolerable within the narrow confines of species by means of the well-formed conditioned reflexes. And humans are capable of responding to certain situations in the completely unpredictable manner: "he can shout (curse) like a dog, run away as a hare; he can climb the tree as a squirrel; he can get into a fight as a bear standing on two legs; he can act like Socrates and stay calm" [17, p. 259]. Thus, the researcher finds that the human nature is universal. His anthropological theory is based on accepting polymotivation of the human being. In this regard, were are unable to find exact motives of human behavior. The motives would always be mediated not only by instincts and volitional beginning, but would also show the lack of basis, the intuitive freedom of choice. V Ten notes that "in philosophical speech, human behavior is considered activity, i. e. represents the inverted subject–object relationship" [17, pp. 259–260]. However, according to the author, when engaged in activity, man objectifies his personality and "subjectifies" the object of his activity. Animal behavior does not consitute activity, it is just a reflex behavior. Animals have no resource for the situation conceptualization, that is why animal reactions are immediate and result from unconditioned and conditioned reflexes.

David Reich, American geneticist, studied the modern human populations and set the goal to discover the population diversity. The researcher compared DNA of modern humans with DNA of our earliest ancestors and concluded that the wide diversity of human traits cannot be fully explained by genetic factors. In this regard, the individual's behavioral characteristics, athletic performance, artistic talents, and intelligence are not affected by the parameters of the population. Therefore, David Reich concludes that social bases of the human being are a priority. However, he cautions against exaggerating the importance of biological origin in the human life, which is inherent in certain scientists, since the biological concept absolutization always gives birth to racist theories, which are based on group stereotypes. David Reich opposes any "stereotype labels" applied to people: "Phrases such as "you are black, then you are surely musically gifted" or " you are a jew, so you have to be smart" are definitely harmful" [18, p. 351]. With that in mind, the researcher concludes that in case of well-chosen social conditions everyone can develop their potential and achieve great success in any sphere of activity, even with low genetic predisposition to this sphere. David Reich encourages us to treat every person as an extraordinary

person, and the society should give everyone the chance to realize their potential. It is respect of the rights and capacities of every person that is the main leitmotif of his writings.

IL Andreyev, expert in cultural and historical anthropology, aims to consider the neurophysiological basis of consciousness and functional state of the brain with regard to explaining human social behavior. He identifies the main difference between humans and animals, and sees not only the premise of language and abstract thought, but also the basis for reflection in the left cerebral hemisphere. According to the researcher, the man's ability to adhere to the norms of morality, law, and cultural beliefs accepted in society results from the hemispheric asymmetry. The author consistently supports the priority of evolution theory in the context of the human formation conceptualization. He rationalizes the idea that "evolutionary and age-related metamorphosis of the brain in the course of the disease or during ageing has its basis in the trend of the brain's situational or permanent return to the status of endocrine organ in the spirit of the Hegelian principle of negation of the negation…" [19, p. 26]. In this regard, we cannot agree with IL Andreyev, who concludes that mass panic, conformist behavior, fashion and other kinds of "psychic contagion" are induced by hormonal impulse. Thus, in accordance with his concept, intellectual potential of mankind would become a powerful evolutionary impulse.

The book Operation Mensch by Ariel Noltze is important for conceptualization of biological and spiritual bases of the human being. The main goal of the book is to show the reader the path towards harmony in all spheres of life. The author demonstrates gravity of disregard for the spiritual aspects of understanding a person when providing medical care. His book is focused on the search for true foundations of medical ethics. According to Noltze, declarative medicine is unable to provide the bases, which are required to understand human life in its entirety: "Removal of something large may be excessive, and removal of something small may later appear to be insufficient — this is a balancing act that may be committed only with humility and respect for life" [20, p. 50].

Ariel Noltze poses a very important issue of medical ethics, the issue of the doctor's responsibility for the patient's life and health on the one hand, and the issue of the patient's trust in the doctor as a person raised to the level of God. The researcher reflects on the situations when a person being subjected to medical intervention completely loses control over his/her life, he/she transfers control over his/her physiological parameters to the doctor. There is a difficult issue of medical ethics, the issue of the medical staff responsibility for the individual's life and health. Noltze cautions against slipping into understanding of any treatment methods as the "silent barter". The author tends to absolutize paternalistic approach to the doctor–patient relationship, since the sacral nature of transferring the responsibility for life from patient to physician is a true foundation of medical ethics. The patient's hope to find advantages and accept certain benefits always have a metaphysical foundation. However, the issue of the treatment-related risks widely debated in modern medical ethics may destroy all metaphysical foundations, underlying the patient's trust in the doctor. Noltze points out that it is trust in potential benefits that makes it possible to implement the doctor–patient cooperation. It is trust, strong and boundless, that has to somehow surpass the risks, emerging during treatment. In this regard, the words said by Ariel Noltze may be considered the true apotheosis of medical ethics: "God wants and is able to put your life in order. Are you willing to trust Jesus as your Savior? He can become your personal advisor. Would you entrust Him the essential restorative surgery of your heath and mind? Surely, you would still ignore this costly chance or would respond to this invitation to new life with an open heart" [20, p. 59].

Thus, in concluding the review of studies focused on the issue of the relationship between the "bological" and "social" categories, it is important to note that the majority of researchers tend to absolutize the biological basis of the human being. Arguments in favour of understanding man as a "crown jewel" of the evolution of life, such as reliance on the numerous genetic studies or appeal to studying animal behavior, cannot be regarded as conclusive evidence in the current context. However, provisions, resulting in complete leveling of man's biological nature and transfer of social factors in order to explain the physiological basis of the individual's life do not stand up to criticism as well. Therefore, the researchers' keen interest in this issue cannot fail to affect the crucial principles of medical ethics. When treating the biological nature of man as a constant, it is important not to lose sight of man's uniqueness, singularity of every person and, of course, the spiritual component of the term "Man". After all, man is not a "two-legged animal" (this idea was ridiculed by Socrates), and not a Nietzsche's "superman", but an extremely delicate creature in need for care and patronage. Here the following basic principles of medical ethics are established: "nonmaleficence" and "patients treated as ends, not as means". Consequently, the ultimate humanistic goal of medicine, preserving human health and life, becomes the basis of the reverence for life ethics.

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THE PROBLEM OF "DANGEROUS KNOWLEDGE" IN THE INTELLECTUAL MANIFESTO BY VR POTTER

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The article deals with the problem of ethical ambiguity of VR Potter's approaches to the tasks of the civilization development associated with "dangerous knowledge", primarily to demographic issues. The purpose of the study is to identify the methodological basis for a number of discussion theses in the program book by VR Potter "Bioethics: Bridge to the Futur". Material of the work is presented by VR Potter's "Bioethics: Bridge to the Future". The research was performed using the comparative-historical and cause-and-effect analysis. The paper analyzes the significance of the "dangerous knowledge" considered by VR Potter as part of the humanistic content of bioethics. The author comes to the conclusion that the discussion theses of VR Potter's bioethical concept are based on the methodological 'realism' of an expert who considered the current problems of society in the context of the rationalism of civilization.

Key words: bioethics, Potter VR, intellectuals, humanism, rationalism.

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ПРОБЛЕМА «ОПАСНОГО ЗНАНИЯ» В ИНТЕЛЛЕКТУАЛЬНОМ МАНИФЕСТЕ В. Р. ПОТТЕРА

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В статье рассматривается проблема этической неоднозначности подходов В. Р. Поттера к задачам развития цивилизации, связанным с «опасным знанием», в первую очередь к демографическим вопросам. Целью исследования явилось выявление методологического основания ряда дискуссионных тезисов программной книги В. Р. Поттера «Биоэтика: мост в будущее». Материал работы — текст В. Р. Поттера «Биоэтика: мост в будущее». Исследование приводилось путем сравнительно-исторического и причинно-следственного анализа. В работе проанализировано значение рассматриваемого В. Р. Поттером «опасного знания» в контексте гуманистического содержания биоэтики. Автор приходит к заключению, что дискуссионные тезисы биоэтической концепции В. Р. Поттера имеют основанием методологическую «реалистичность» эксперта, рассматривавшего актуальные проблемы общества в контексте рационализма цивилизации.

Ключевые слова: биоэтика, В. Р. Поттер, интеллектуалы, гуманизм, рационализм

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Within half a century since publication of "Bioethics: Bridge to the Future" (1971) by VR Potter [1], bioethical requirements have become an essential part of research practice [2, 3]. Thematic development of bioethical discussion completely corresponds to the thesis by VR Potter stating that 'cultural evolution would be very slow if not a human being's constant strives for introducing something new to his/her life and resisting being in line with what is being taught'.

Considering the work by VR Potter as an intellectual manifest [2], one can't help mentioning some theses contained therein that are controversial as far as generally acknowledged humanistic content of a bioethical concept goes. First and foremost, they include a demographic aspect of the "dangerous knowledge" issue [1, p.79], as reviewed by VR Potter.

According to VR Potter, "dangerous knowledge' is accumulated in a more rapid way than wisdom, required to control it'. VR Potter cites an experience of using poisoning gases during the 1st World War, and anthropogenic factors that are pressing for ecology since the middle of the XX century as an example of "dangerous knowledge" implementation in the XX century [1, p. 35–36, 67, 84–93].

According to VR Potter, "science produced new problems instead of solving the existing ones". At the same time, "discoveries, that prevent the subsequent spread of malaria, resulted in a significant improvement in child mortality. The saved children grew up, created families of their own, and thus these discoveries promoted explosion in population. Every scientist studying the problem understands that it's not necessary for every family to comprehend the issue of improved child mortality. It used to control the population growth… the mankind crossed the Rubicon, and can't come back to humane methods of population increase… the unfortunate truth is that the efforts made are not equal to the task set" [1, p. 81].

Considering various aspects of medical science development and stating that "the growth of the world population has been out of control", VR Potter cites the words by G. Khardin: "demographic problems have no technical solution; they demand proper expansion of morality", effective birth control [1, p. 167].

According to VR Potter, "a human being as a biological entity must be considered in the context of specific survival". Population growth is one of prioritized problems of the mankind. "Dilemma of a human being as a biological entity is that real success in preservation and development of human health is based on the knowledge of regularities that control the entire populations… if the knowledge is used without the respective control of birth, the results will be catastrophic… the necessary birth control can't exist on the basis of individual medical service and only state bodies can accept large-scale decisions required for that. But if people are not treated properly… the organized

minorities will resist and struggle against the birth control set by the majority".

VR Potter stresses that it is preferrable to use the resource of physiological and cultural adaptation [1, p. 173].

Summarizing the data about the demographic problem, VR Potter concludes as follows: "it's immoral to allow uncontrolled growth of human population wheresoever" [1, p. 174].

VR Potter's attitude to euthanasia is ambiguous. 'Medical science has already reached a certain border of solving a question concerning termination of a human life. Every day any diligent doctor faces a dilemma as to whether terminate or continue supporting therapeutic activities which could extend one's life, but wouldn't make it more tolerable for a suffering person. The decision about continuing supporting therapy is substantiated easily, but what to do when an elderly cancer patient is condemned to long-term and painful death? In this situation, it's better not to use medical intervention, as an inevitable death can't be prevented any way… All we need is to lead a productive life in childhood and middle age, and to end our life in dignity in old age' [1, p.83].

Analyzing the type of "realistic human knowledge" [1, p.36] by VR Potter, it must be considered that in spite of the declared 'scientific and philosophical basis of a bioethical concept, VR Potter sees his task set in "Bioethics: Bridge to the Future' as an ability" to understand the nature of a person and his/her attitude to the world', as 'the humanity urgently needs new wisdom, that would be "the knowledge of how to use the knowledge 'for the person to survive and improve his/her life" [1, p. 9]. It means that VR Potter considers a bioethical approach as the universal methodology of progress ethical assessment [2].

In this sense, the "pragmatism" of 'actual decisions' declared by VR Potter is not consistent pragmatism in its conceptual and philosophical meaning as, for example, by John Dewey or R. Rorty. VR Potter's approach to 'ethical' (basically, medical and social) issues is not of an ethical and philosophical type. It rather has a sense of statistical reasonability supported by a competent opinion of an investigator with 30 years of experience, on the one hand, and the pathos of "common wealth achievement", on the other hand [1, p. 5–7, 3, 36].

Thus, VR Potter's position is restricted by the opinion of a realistic [1, p. 13] expert and scientist [4], who seeks the basis for "integrating" the knowledge of "natural and humanitarian sciences" to form a social development strategy, "recommendations in the area of public activity" [1, p. 10, 14, 35].

According to AV Azov, from the point of view of philosophical methodology, "it is impossible to come back to the former state" when solving the tasks of knowledge "integration". Something that was divided earlier doesn't form the primary unity when collected (integrated violently). And this means losses. That's why we need to search for a philosophical and methodological basis of new integrative knowledge that is inaccessible when separate fragments are collected to form a single system. The principle of consistency is opposed to the principle of integrity" [5].

Developing the idea of three forms of "adaptation" (physiological, evolutional and cultural) and analyzing "psychological and behavioral changes based on physiological and cellular biological mechanisms, VR Potter doesn't consider the issue in a broader sense as the problem of philosophical (socio-cultural) anthropology with a focus on the axiological aspect of practical use of knowledge for their subsequent enhancement in favor of human population [1, p. 32–34].

According to VR Potter, "human ethics can't be examined without a realistic comprehension of ecology in the broadest sense. We shouldn't consider ethical values beyond the biological factors. We have a need in agricultural ethics, ethics of wild life, population ethics, ethics of consumption, international ethics, geriatric ethics, etc. They all include bioethics because survival of the entire ecosystem is a peculiar check of our value system" [1, p.5].

It should be noted that not just the underlined dominant of something "biological" in VR Potter's views introduces significant corrections in the assessment of its concept from the "interdisciplinarity" point of view, but also its bent for the wide periphery of a comparative analysis. A really integrating basis for bioethics as "new knowledge" was its humanistic value as a typical "intellectual manifest' of its epoch [2]. Meanwhile, being a typical event of that time, VR Potter" concept has peculiarities associated with sociocultural context.

In European (or, in a broader sense, western) history, intellectuals were literally 'connected' with the authority. This organic social and cultural symbiosis was a consequence of the historical correlation of "power" and "will" factors in the development of social regulations [2].

Unlike the people of the "Old World", the post-war American society, that was unaware of the 2nd World War's dramatic depth, didn't require a "neorealistic" selection of the new generation of intellectuals not organically associated with the "New Deal" political strategy of F. Roosevelt's epoch. The "academic" American intellectual didn't only retain his state-run speaker positions, but could also literally "identify" himself as the authority (what happened to D. Kennedy can serve as an example). However, at the cusp of the 1960s-1970s and under the conditions of crisis of the Great Society by L. Johnson, a typical alliance "authority and intellectual" was perceived as "a misalliance" by the massive American consciousness. The most socially active part of the American society, that underwent active separation in the early McCarty years and never consolidated at the times of D. Kennedy, was ready to perceive with a more sympathy not the politically respectable position of "servile intellectuals" of the establishment, but out-of-class charismaticness of "independent" and unobviously biased progressive pillars of culture (from Martin Luther King to Bob Dylan).

Under these conditions, conceptual manifestation of the "academician" intellectual, who still preserved its independent status in collective consciousness, could not help being heard. Even the evidently seeming "democratic character" of bioethics, essentially addressed to a narrow circle of like-minded intellectuals, was not an obstacle for that [1, p. 10].

VR Potter's deliberate "mechanistic pragmatism" as a "specialist's competent opinion", which is of little interest for the mass audience, ultimately gave way to the humanistic value of its intellectual manifestation by the value for interpreters. His message is in ways idealistic and partially artistic. The world of the future in VR Potter's concept is like an 'immersive installation' similar to the works by Sam Gilliam. He was popular in Madison (where VR Potter lived and worked) in the 1960s-1970s. In accordance with the theses that summarize VR Potter's conceptual program "Bioethical Credo" of the personality, a person of the future is included into the reality of the progress tasks marked with wide artistic strokes as an active transformer equipped with the "integrative knowledge" about not only life, but death as well [1, p. 209].

Intellectuals' approach to the issues of "integrative knowledge" means a lack of interest to usual values. It is important to find the axiological basis of simplicity, relevance and humanistic rationality of motivation of a human being and entire humanity [6]. This is the task solved by VR Potter from the position of actual social experience of these days.

Social history of the XX century repeatedly showed the possibility of humanity transition into the state close to the primitive rules of survival of the strongest, and superiority based on the "laws of the forest". In the metaphysical and literal sense, the borderline of the "forest" is the most vivid symbol of the rational humanism demarcation. In this sense, VR Potter's 'bioethics' reflected the most important requirement of the society in rational explanation of social reality inconsistency, i. e. hope for a human being of the future who can overcome the imperfectness of the present.

Relevance of humanistic prognoses concerning a human destiny, that appeal to scientific substantiations, especially on the "borders" of epochs and when new civilization threats are incrementing, comes as no surprise. Design of the optimistic future is a task of intellectuals. VR Potter's position, which is pragmatic by shape, but evidently humanistic by essence, is not an exception. Disputing theses of his book ('Bioethics: Bridge to the Future') are based on the methodological "reality", typical of the approach of an expert, who considers the actual problems of the society against the background of civilization rationalism.

Admitted competency of VR Potter as a practical specialist allowed the bioethical concept to integrate into the context of professional discussion of not just medical and biological, but also of a scientific society in a broader sense. The bioethical theses continue to serve as a basis of theoretical reinterpretation of global tasks and axiological substantiations of a practical activity and various forms of social practice [3].

Meanwhile, a modern reader, commenter and interpreter of VR Potter's bioethical concept should be aware, that the development strategy simulated by him, can be implemented using not only the objective attitude to bioethical principles, but also the real estimation of resources, and necessary potential of practical efforts concerning their usage by every specialist and every human being [1, p. 84].

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THE VACCINE DIPLOMACY IN INTERNATIONAL RELATIONS*

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The author considers the phenomenon of vaccine diplomacy throughout history. The purpose of the study is to trace the history and modernity of medical cooperation in the field of combating infectious diseases, the role and place of "vaccine diplomacy" in international relations, and its development in the context of global health diplomacy. Historical-chronological and comparative methods were used in the work. It is stated in the article that a vaccine is the most powerful and effective medical intervention in the human body that enables to preserve its life and health. It is asserted that Russian vaccine diplomacy, continuing the traditions of the Russian civilizational code based on humanism and compassion, acts as an effective "soft power" that influences the minds and wins supporters with its attractiveness. It is concluded that for Russia, vaccine diplomacy, based on the remarkable success of domestic science, which has managed to develop and offer the world a highly effective vaccine against COVID-19, opens up new opportunities for many partnerships along the path of broader pharmaceutical diplomacy.

Keywords: vaccine, vaccination, vaccine diplomacy, global health diplomacy

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ВАКЦИННАЯ ДИПЛОМАТИЯ В МЕЖДУНАРОДНЫХ ОТНОШЕНИЯХ*

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Автор рассматривает феномен вакцинной дипломатии на протяжении истории. Цель работы — проследить историю и современность медицинского сотрудничества в области борьбы с инфекционными заболеваниями, роль и место «вакцинной дипломатии» в международных отношениях, ее развитие в контексте глобальной дипломатии здоровья. В работе был использован историко-хронологический и сравнительный методы. В статье отмечается, что вакцины являются наиболее мощным и результативным медицинским вмешательством в организм человека в целях сохранения его жизни и здоровья. Утверждается, что вакцинная дипломатия России, основанная в своей сути на гуманизме и сострадании, выступает как эффективная «мягкая сила», которая влияет на умы и завоевывает сторонников во всем мире. В заключении делается вывод, что для России вакцинная дипломатия, опирающаяся на замечательный успех отечественной науки, сумевшей разработать и предложить миру высокоэффективную вакцину против COVID-19, открывает новые возможности для многих партнерств на пути более широкой фармацевтической дипломатии.

Ключевые слова: вакцина, вакцинирование, вакцинная дипломатия, глобальная дипломатия здоровья

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With COVID-19 pandemics, the term 'vaccine diplomacy' has been increasingly used in a political, medical and social discourse as a specific component of international relations of key importance, where international cooperation in the area of controlling infectious diseases has rather a long history.

It dates back at least to the XIV century, when a quarantine system was used in the city of Dubrovnik on the Adriatic coast of the Mediterranean Sea during the Middle Ages [1], and turns into multilateral cooperation in 1851, when the International Sanitary Conference on Cholera Prevention took place with subsequent control of plague and yellow fever threats [2].

This resulted in formation first of the Pan American Health Organization [3] and then of the World Health Organization (WHO), which is currently a specialized institution and part of the United Nations [4].

According to the western sources, vaccination is commonly associated with a name of Edward Jenner, an English doctor, who created a safe smallpox vaccine. But this event occurred in 1796 only, whereas Catherine the Great was vaccinated against smallpox 30 years before it, on October 23, 1768. Variolation was not a totally safe technique, and caused mortality of up to 2%. It, however, could save from death, that affected up to 40% of population. The technique consisted in taking infected material from a person affected with smallpox and putting it beneath an unaffected person's skin. The inoculated individual had a mild case of smallpox, and a more serious case was prevented. Catherine the Great ordered to publish and widely distribute data about her vaccination both in Russia, and abroad, 'so that others could also use the same techniques and save themselves from danger easily' [5]. This is as an example of Russian and international vaccine diplomacy, as the Empress made the vaccine fashionable, Russia's image was perceived as positive and Catherine II was treated as an educated and progressive ruler. Noblemen and sovereigns took up the initiative and vaccination started a parade over the globe. However, the word 'vaccine' was not used yet; it came into official use

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when Jenner created a cowpox vaccine, derived from the Latin word 'vacca' for 'cow'. A Catherine II medal inscribed 'She has set an example' was established to commemorate the first vaccine.

The subject of the Empress's vaccination was even touched by the Italian ballet master Gasparo Angiolini in 'Defeated Prejudice', where science had an allegorical struggle against superstition. As Russia occupied leading positions in the fight with smallpox using vaccination, France's Louis XV died of the disease. Having found the news, Catherine II reportedly called the death a "barbarism", as 'science can heal the disease already' [5].

Jenner, who created the vaccine, used his influence during the war between England and France in 1803–1815 for humanitarian purposes to reduce the stress of war and help prisoners and other people who got into trouble. Napoleon once said. 'Jenner — we can't refuse that man anything' [6].

Development of Russian vaccination, creation of vaccines and international advances in that area, initiated since the reign of Catherine II, were marked with outstanding achievements and gave many benefits to the world. The Russian vaccine diplomacy supported the vaccine for rabies created by a French microbiologist Louis Pasteur in 1885, and was marked by a contribution of 100,000 francs by Tsar Alexander III for the Pasteur Institute and foundation of the second and third biological stations in Odessa and Moscow in 1886.

Nikolay Sklifosofsky was an initiator of the Pasteur station in Moscow. When the station opened, Louis Pasteur sent his signed portrait, which is preserved till now. Our country confirmed its leading role in vaccination, when a network of 80 Pasteur vaccination stations and a hundred of its branches were created throughout the country by 1938, and when our vaccine could win the victory over poliomyelitis in the 1960-s, attaining international acknowledgement and admiration. The vaccine produced by the Institute of Poliomyelitis and Viral Encephalitis of the USSR Academy of Medical Sciences was imported to over than 60 countries [5].

In Japan, mothers of children with poliomyelitis came out in the streets and demanded to allow import and use of the Soviet vaccine. The authority has to offer concessions, which saved over 20 million children.

A Soviet-Japanese movie Step was released inspired by the story of overcoming political hurdles for the sake of life. It introduced the topic of vaccine diplomacy to the screen.

Vaccination against poliomyelitis in the form of pills offered by Professor Mikhail Chumakov was an element of Russian vaccine diplomacy. The candy pills were given to schoolchildren during lessons and enjoyed high popularity among children and adults, not requiring participation of medical personnel. The simple idea seemed to have a wide response and was considered as a discovery.

At the international level, professor Chumakov called upon special care when working with dangerous viruses and careful tracing of their genesis. When the WHO decided to destroy all black smallpox strains in 1990, the professor strongly disagreed with this point of view. He explained that in case of a new outbreak the mankind would turn out to be helpless due to the lack of source material.

The term 'global health diplomacy', offered by Dr. Peter Bourne, Special Assistant to President Jimmy Carter for Health Issues, has already been used by that time [7]. Global health was confirmed within the Millennium Development Goals (2000) and global health diplomacy was placed firmly in the area of international diplomacy [8].

Vaccine diplomacy is taken as part of global health diplomacy, though the international efforts to control dangerous infectious diseases and development of events against the background of COVID-19 pandemics determined an independent role and special value of the diplomacy. In a crisis environment, when a threat to health and lives of people emerged at the national, regional and global scale, it was comprehended that such dangerous diseases as HIV/AIDS, Ebola, bird flu, etc. pose a threat to economic development, safety and interests of countries and their population [9]. Potential threats of bioterrorism and use of biological weapon, leakage of biodestructive materials and viruses from biolaboratories and research centers were added to challenges in the form of epidemics. Concentrated efforts of the world community, associated with prevention of dangerous diseases, were urgently required. However, some countries were guided by their narrow national interests or traditions and avoided cooperation; for instance, Indonesia, that refused to share its data about bird flu, or Nigeria and Pakistan, which were against vaccination for religious reasons [10, 11].

According to the declaration of Ministers of Foreign Affairs adopted by seven countries such as Brazil, France, Indonesia, Norway, Senegal, South Africa and Thailand in Oslo in 2007, global health was taken as part of external policy [12].

Global health diplomacy was considered as a process, in which health is positioned in foreign policy negotiations and new types of global healthcare management are created [13, 14]. Quite recently it was defined as 'a system of organization, communications and negotiations, shaping the global political environment in the area of healthcare and its determinants' [15].

In this case, not only diplomats, but also experts with certain knowledge in respective areas of healthcare are responsible for development of certain problems and negotiations, and this is a specific feature of global health diplomacy [16].

Global health diplomacy is implemented both in the classical forms of bilateral and multilateral diplomacy in accordance with the Westfalen principles and provisions of the Charter of the United Nations with conclusion of agreements and conventions, and by way of interactions of non-governmental organizations, professional community and participation of interested business communities, manufacturers and consumers of pharmaceuticals and medical services [17, 18].

Science diplomacy is an important element of global health diplomacy. It is used to ensure interaction of scientists and implement their professional solidarity regarding healthcare; it commonly opposes the struggle against health priority and safety of a human being to political and commercial interests of the strong and those companies that focus on pure profit making.

Vaccine diplomacy affects almost all principal aspects of health diplomacy. It is motivated by requirements for prevention, decrease of distribution and elimination of dangerous diseases with vaccination, dealing with the entire complex of issues associated with development, delivery to customers and ultimate use of the vaccines. Development and production of vaccines as an effective and safe biological product demand high level of science and technology, special knowledge, qualified personnel and respective production conditions and capabilities typical of not that many countries.

As it was dramatically illustrated by COVID-19 pandemic, Russia, USA, Great Britain, China and India were able to provide a fast response to the challenge and create an

adequate vaccine to save millions of people. Moreover, Russia was the first to register Sputnik V vaccine and offer two more other vaccines subsequently. The result was not accidental. The achieved success was based on highly efficient Russian scientific school and over 250 years of vaccination experience in our country, leading by example.

However, instead of combining efforts of the key countries in the West and East, that are the principal actors of vaccine diplomacy, and fostering the efforts to suppress the pandemic, western politicians did something quite the opposite. Pharmacological companies, running into money when producing and marketing pharmaceuticals, weren't going to solve the humanitarian problems of survival during the pandemic and miss profit. Doctors and experts engaged in trials, use and promotion of vaccines, weren't ready for that as well. They got used to sell their services at a high price and didn't want to be deprived of their habitual profit. Geopolitical competitors of the Russian Sputnik V such as Pfizer and Moderna represent business projects not designed for charity. The USA didn't intent to buy millions of doses to render assistance to needy countries, laying emphasis on priority support of its own people.

At the same time, the USA didn't want to lose a good opportunity for their global promotion due to vaccine diplomacy, being aware that they are outpaced by their geopolitical competitors Russia, China and India, as the latter submitted vaccines to other countries on special terms or free of charge. Preferential terms can include transfer of technologies and aid in establishing own production of vaccines.

The traditional instruments of a country's expanded influence in other countries (profitable loan, customs credit and tax benefit, indirect financing through delivery of raw materials and goods at an understated price, scientific and cultural exchange, admission at institutions, etc.) were added to the instruments of vaccine diplomacy. Their active use began when a vaccine against coronavirus was required.

Unexpectedly for the western competitors, Russia gained the lead in the evolving vaccine race. It was found out that Sputnik V was more effective, with its clinical and diplomatic effect being more powerful than the vaccine diplomacy of competitors.

Using the example of San Marino, it was obvious that Russia, which provided its vaccine, was now perceived by inhabitants of this small country not as a large and faraway state, but as a close friend in distress. By continuing the traditions of the Russian civilization code based on humanism and compassion, vaccine diplomacy of Russia acts as an effective soft force, influencing the minds and gaining followers owing to its attractiveness, whereas the West relies on force and violence.

However, western politicians never continue their attempts to dishonor competitors, implant doubt in their vaccine quality and accuse them of maintaining venal vaccine diplomacy for political profit. When visiting the plant of the US pharmaceutical giant Pfizer in Michigan, H. Maas, a German politician, who served as the Minister of Foreign Affairs, stated that 'the Russian and Chinese can't maintain their complex vaccination diplomacy aimed at increase of their prominence in the world only' [19]. He then concluded that it was necessary to advance a vaccine by Pfizer, with its production based in Germany.

By responding to the announcement, the Press Secretary for the President of Russia Dmitry Peskov condemned politization of vaccination, whereas the Press Secretary for the Ministry of Foreign Affairs of the Russian Federation Maria Zakharova said that the statements by the Minister of Foreign Affairs Clément Beaune about non-admission to France of those tourists vaccinated with a Russian vaccine were unacceptable [19].

Speaking at the summit of the EU concerning vaccination in the end of February 2021, President of France E. Macron declared that China and Russia had triggered a vaccine war. It was probably associated with the fact that citizens of different European countries accused the EU in delaying recognition of the Russian vaccine and demanded its approval. It was obvious that 'COVID-19 subjected the solidarity of the EU countries to testing, as they didn't always hasten to help one another' [20].

The pandemic challenge implied that 'in accordance with the research of sociologists, in March 2021, almost every second person in the world (45%) considered COVID-19 as the most troublesome problem' [21].

Along with severe pandemic consequences for the entire world, geopolitical competition, mistrust, protectionism and unequal access to vaccination, concern of a person with protection against coronavirus is a powerful driver of vaccine diplomacy.

Pandemic-born human dramas and tragedies are currently occurring in different parts and countries of the world that suffer from a shortage or lack of vaccines. The countries that need vaccines are helped not only by Russia, but also by China and India, though certain competitive obligations are present in the relations and vaccine diplomacy of the two global players. For instance, India deprived leadership from China by selling the vaccine in Nepal and on the Maldives, but refused to provide the vaccine to Pakistan, allowing China immediately to capture the market, where the Russian Sputnik V had already been presented [22].

Vaccine diplomacy is being developed at the diverse level, both within the activity of the UN and its special institutions with the primary responsibility of the World Health Organization, and in global and regional formats of G7, G20, BRICS, SCO, many international organizations, intergovernmental and non-governmental associations. Vaccine diplomacy has a considerable peace-making and humanitarian potential, an ability to carry mediation between the conflicting parties and discontinue military activities with the vaccination campaign [23].

The term 'scientific vaccine diplomacy' has been created as part of the vaccine diplomacy concept within the ideas of global health diplomacy. The term denotes interaction and collaboration of scientists regarding the issues of scientific development and usage of vaccines and conducting associated studies and experiments [24].

CONCLUSION

Thus, the unique character of vaccine diplomacy is owing to originality of vaccines themselves. They are considered as the most powerful and effective medical intervention into a human organism to preserve life and health. According to some estimates, modern vaccines saved more lives than it was lost during the world wars of the XX century [25].

It, however, should be noticed that the Russian vaccine diplomacy, that rests upon the significant success of Russian science and was the first to develop and offer a coronavirus vaccine to the world, opens up new opportunities for many partnerships along the path of broader pharmaceutical diplomacy.

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DRUG REPOSITIONING: LESSONS FROM THE COVID-19 PANDEMIC

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We overview the possibilities and limitations of drug repositioning in the context of the COVID-19 pandemic and ways to reduce the new biogenic threats in the future. Drug repositioning — identifying new indications for approved drugs — is a natural prompt response to SARS-CoV-2 / COVID-19 viral infection. The current state of the research and development of drugs for the therapy of COVID-19 using *in silico* and *in vitro* methods is considered. In conclusion, it is noted that nowadays, the creation of innovative medicines, despite the success of translational science, takes a lot of time. Therefore, in order to select the most promising pharmaceutical agents, it is essential to integrate and analyze entire available information obtained using *in silico*, *in vitro* and *in vivo* methods.

Key words: SARS-CoV-2, COVID-19, pharmacological targets, drug repositioning, virtual screening, molecular modeling, machine learning, *in vitro* studies

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РЕПОЗИЦИОНИРОВАНИЕ ЛЕКАРСТВ: УРОКИ ПАНДЕМИИ COVID-19

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В статье обсуждаются возможности и ограничения репозиционирования лекарств в условиях пандемии COVID-19 и пути для снижения опасности новых биогенных угроз в будущем. Репозиционирование лекарств — выявление новых показаний у разрешенных к медицинскому применению лекарственных препаратов — является естественным оперативным ответом на вирусную инфекцию SARS-CoV-2/COVID-19. Рассмотрено современное состояние поиска и разработки лекарственных препаратов для терапии COVID-19 с применением *in silico* и *in vitro* методов. В заключение отмечается, что в современных условиях создание инновационных лекарственных средств, несмотря на успехи трансляционной медицины, занимает достаточно много времени. В силу этого для отбора наиболее перспективных препаратов крайне необходима интеграция и анализ всей доступной информации, полученной с применением всех выше обозначенных методов.

Ключевые слова: SARS-CoV-2, COVID-19, фармакологические мишени, репозиционирование лекарств, виртуальный скрининг, молекулярное моделирование, машинное обучение, исследования *in vitro*

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Drug repositioning is the identification of the new indications for drugs approved for medical use. The availability of information on the pharmacological and toxicological characteristics of a known drug enables its swift adoption in a new nosology [1]. The need for a rapid response to the COVID-19 pandemic has given the impetus to a large-scale research into the associated opportunities. A Google search for “COVID-19 AND drug repurposing” returns over six million results. Remdesivir, Favipiravir and Umifenovir (Arbidol) were originally designed for other indications and later repositioned to treat the SARS-CoV-2 infection. Same is true about Triazavirin, Nobasit, Nafamostat and a few other drugs that currently are subjects of clinical trials involving COVID-19 patients.

The search for the new pharmacological effects that known drugs may have involves *in silico* and *in vitro* studies. Computer-aided investigations rely on models of interaction of the analyzed compounds with molecular targets, identification of analogs based on the structural similarity, analysis of the “structure-activity” relationships using machine learning, and establishing associations by the network pharmacology [2]. The *in silico* approach can be applied to virtual (not yet synthesized) molecules providing the initial set of “hits”. Next, the predictions delivered by such computer-aided investigations are validated in the *in vitro* experiments. The *in vitro* determination of anticoronavirus potency relies on biochemical and cellular assays [3, 4]. Preliminary selection (virtual screening) of the potentially active compounds that is based on the data obtained through *in silico* investigations significantly increases the chances of success [5].

A number of large-scale experimental studies aimed to screen *in vitro* 1,400 to 12,000 drugs against one or several targets; the efforts yielded shortlists of candidates for repositioning. In many cases, different test systems gave different results for the same drug [3,4,6]. The reasons behind this inconsistence are lack of generally accepted reference drugs and absence of unifying standards for assays, which are developed independently by different researchers.

As noted by the authors of a recent analytical review published in the Chemical Society Reviews that looked into the computational approaches employed for COVID-19 drug

discovery: «… truly impactful computational tools must deliver actionable, experimentally testable hypotheses enabling the discovery of novel drugs and drug combinations, and that open science and rapid sharing of research results are critical to accelerate the development of novel, much needed therapeutics for COVID-19» [2].

In conclusion, it should be noted that current conditions make drug repositioning especially relevant. The reason behind this relevancy is the significant time required to develop innovative drugs in a pandemic, regardless of the advancements of translational medicine. At the same time, to select the most promising drugs for further experimental validation of their effects in the context of repositioning for SARS-CoV-2/COVID-19 (based on the analysis of the available data), it is necessary to integrate and analyze all the available information obtained *in silico*, *in vitro* and *in vivo* studies.

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ETHICAL ASPECTS OF CLINICAL TRIALS OF BLOOD CLOTTING FACTORS IN CHILDREN WITH HEMOPHILIA

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The proportion of drugs for use in juvenile patients is much less than for the adult population. This is due both to the lack of specific drugs for a number of childhood diseases, and the need to conduct special clinical studies in different age groups to assess safety and efficacy parameters. When developing a program for clinical trials of an orphan drug, ethical aspects of the participation of underage patients are considered, taking into account the current international and Russian legislation. Obtaining the informed consent of a minor patient from one of the parents requires detailed prior information and the establishment of a trusting relationship before the participation of a minor patient in a clinical trial. The results of clinical and observational studies of orphan drugs on the example of moroctocog alfa in previously treated pediatric patients with hemophilia A in different age groups contribute to an increase in the arsenal of drugs for the treatment of orphan diseases in the pediatric population and determine the optimal conditions for the use of moroctocog alfa in different age groups.

Key words: clinical trials, observational trials, underage patients, informed consent, hemophilia A, moroctocog alfa

Authors contribution: Kudlay DA — article design development, analysis of scientific material, review of publications on the topic of the article, article editing; Vdovin VV — literary editing of the article, scientific editing of the article; Schiller EE — analysis of scientific material, review of publications on the topic of the article, editing of the article; Khokhlov AL — literary editing; scientific editing of the article; Davydkin IL — literary editing, scientific editing of the article, summary writing; Borozinets AYu — development of article design, analysis of scientific material, review of publications on the topic of the article, compilation of a summary, writing the text of the article, preparation of a list of references.

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ЭТИЧЕСКИЕ АСПЕКТЫ КЛИНИЧЕСКИХ ИССЛЕДОВАНИЙ ФАКТОРОВ СВЕРТЫВАНИЯ КРОВИ У ДЕТЕЙ С ГЕМОФИЛИЕЙ

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Доля лекарственных препаратов для применения у несовершеннолетних пациентов значительно меньше, чем для взрослой популяции. Это связано как с отсутствием специфических лекарственных препаратов при целом ряде детских заболеваний, так и с необходимостью проведения специальных клинических исследований в различных возрастных группах для оценки параметров безопасности и эффективности. При разработке программы клинических исследований орфанного препарата принимаются во внимание этические аспекты участия несовершеннолетних пациентов с учетом действующего международного и российского законодательства. Получение информированного согласия несовершеннолетнего пациента от одного из родителей требует подробного предварительного информирования и установления доверительных отношений до начала участия несовершеннолетнего пациента в клиническом исследовании. Результаты клинических и наблюдательных исследований орфанных препаратов на примере мороктокога альфа у ранее леченных пациентов детского возраста с гемофилией А в различных возрастных группах способствуют увеличению арсенала лекарственных средств для лечения орфанных заболеваний в детской популяции и определяют оптимальные условия применения мороктокога альфа в разных возрастных группах.

Ключевые слова: клинические исследования, наблюдательные исследования, несовершеннолетние пациенты, информированное согласие, гемофилия А, мороктоког альфа

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The proportion of drugs approved for use in juvenile patients is much less than for the adult population. On the one hand, this is due to the lack of specific drugs for a number of childhood diseases, and the need to conduct special clinical studies in a number of pediatric diseases [1]. On the other hand, development of new drugs for children with an inherited or acquired pathology requires a clinical study in different age groups with a detailed and complex assessment of safety and effectiveness parameters [2]. Planning, organization and conduction of clinical trials of new molecules in underage patients constitute a complex and time-consuming task. In the lack of indications to using the drug in children and results of clinical trials for the corresponding age group, underage patients with certain diseases are given medicinal preparations not registered for use in children of this age [3]. Shortage of medicinal agents approved for use in certain age groups of underage patients can urge pediatric specialists to run the risk by administering medicinal preparations according to vital indications not indicated for use in children of certain age. This risk is especially increased in children with pathology of an early age, and also in severe disorders, including orphan and rare diseases.

An approximate proportion of using non-registered drugs for underage patients varies from 45% on the inpatient basis to 10–20% on the outpatient basis [2]. The complexity of clinical trials in underage patients, especially the ones with an orphan pathology, is mainly associated with their difficult inclusion into a trial, limited number of patients with a certain pathology, and in some cases with necessary regular intravenous injections of the examined drug and frequent collection of blood biosamples to conduct a coagulologic trial [4].

Underage patients can participate in clinical trials only following proper expertise and approval of the protocol and clinical trial documentation by the central and local ethics committees. The committees protect interests of every underage participant of the clinical trial and guarantee observance of the required ethical and legal standards [5].

In accordance with the Russian legislation, children can be considered as potential patients of a clinical trial only if it is necessary to promote their health or prevent infectious diseases in childhood or if the purpose of the trial is to obtain data about the best dosage of a medicinal agent for pediatric treatment. Planning of the trial should be preceded by a clinical trial of a medicinal agent in underage patients. Cases when the examined medicinal agent is indicated for underage patients only are excluded [6].

The principal difficulties seen during clinical trials in underage patients can include the need in establishment of trust relationships with the parents of the underage patient and obtaining an informed consent from them, difficulties with inclusion of children in trials, low compliance of children and their parents, significant heterogeneity of pediatric population, particularly, of those with an orphan pathology, possible development of specific adverse reactions, difficulties in choosing the criteria assessing effectiveness and safety of the drug considering different types of clinical trial design in pediatrics and hematology [7].

PECULIARITIES OF OBTAINING AN INFORMED CONSENT

Participation of children in a clinical trial of a medicinal agent is allowed only when a written consent of their biological and adoptive parents is provided. Thus, it is prohibited to conduct a clinical trial of a medicinal agent involving orphaned children and children deprived of parental care [6].

An information leaflet for parents of the underage, information leaflet for the underage patient (15 to 18 years of age) with the informed consent form must be approved in writing by the Ethics Council of the Ministry of Health of the Russian Federation and local ethics committees of research centers prior to the clinical trial [8].

A biological or adoptive parent of an underage child needs to examine the information leaflet for the parents of the underage patient prior to the clinical trial and provide a consent to participation in the trial by signing and dating the informed consent form of the leaflet. The written version of the informed consent form can be signed by one parent only. If those participating in the clinical trial (a parent or a child) disagree with each other, their inclusion into the trial is not possible.

In accordance with the Russian legislation, the minors, drug addicts elder than 16 years old and other underage elder than 15 years old can provide or withdraw an informed voluntary consent to a medical intervention, except for the cases of provision of medical aid according to urgent indications, in the presence of severe mental diseases, when committing socially dangerous acts and due to other reasons in accordance with parts 2 and 9 of article 20 of Federal Law No. 323-FZ [9].

Due to that, an underage patient aged 15 to 18 years along with one of his biological or adoptive parent must provide a consent to participation in the trial by signing and dating the respective informed consent form in the information leaflet for an underage patient aged 15 to 18 years. In this case a biological or adoptive parent of an underage patient aged 15 to 18 years must also read the information leaflet for the underage patient's parents and consent to participation in the trial by signing and dating the informed consent form.

Neither a researcher, nor other persons engaged in the trial must force or use other improper methods of exposure making an underage person and his biological or adoptive parents to participate or continue to participate in the trial. The researcher must inform the subject and his biological or adoptive parents of all significant aspects of the trial and provide them with the written information about the trial and positive conclusions of the Ethics Council and local ethics committees in the research center. Prior to signing an information leaflet, a researcher must provide underage patients and their biological or adoptive parents with enough time and possibility of obtaining more detailed information about the trial and taking a decision about a child's participation or refusal to participate. The patient and his biological or adoptive parents must obtain clear answers to all possible questions concerning the trial. Prior to the trial, the investigator who conducts an explanatory talk must sign and date the informed consent form in the information leaflet for the underage patient's parent and information leaflet for the underage patient along with the patient and one of his biological or adoptive parents, and provide the contact number.

During the explanatory talk, it must be explained as follows: purpose and procedures of the trial, patient's obligations, expected benefit, risk or inconvenience for a patient, other procedures or methods of treatment that can be available to the patients, apart from those allowed in the trial, and their potential benefit and risk, treatment that can be given to a patient if his or her health was inflicted during the trial. Important aspects include voluntary participation, and a possibility for an underage patient or biological or adoptive parents to refuse from participation or leave the trial at any moment without any sanctions or loss of agreed benefits. The underage patient and his biological or adoptive parents must timely read new information that can influence the wish of the patient and his/her biological or adoptive parent to continue participating in the

trial; have contact data of those persons who can be referred to for additional information about the trial and rights of patients in the trial; understand possible circumstances or reasons due to which participation in the trial can be terminated. During the explanatory talk, an underage patient and his or her biological or adoptive parents obtain data about the suggested duration of a patient's participation in the trial and approximate number of patients to be included into the trial [10].

CONDUCTING CLINICAL TRIALS IN UNDERAGE PATIENTS WITH HEMOPHILIA

Clinical trials of effectiveness and safety of new medicinal preparations to treat hemophilia in children are characterized by significant peculiarities and regulated by certain requirements. Hemophilia is a hereditary hemorrhagic disorder occurring due to the lack of clotting factor VIII or IX in the blood [11, 12]. The majority of patients with hemophilia are represented by men. In many countries, the prevalence rate of hemophilia is 10–14 patients per 100,000 men. Meanwhile, the ratio of hemophilia A and hemophilia B is 4:1 or 1 case per 10,000–15,000 of newborn boys for hemophilia A and 1 case per 50,000 of those for hemophilia B [13, 14].

It must be noted that a number of patients with hemophilia in Russia has a tendency to increase during the last years. This is probably due to better detectability of a disease, increased longevity and quality of life in patients, migration to the regions where the specialized medical service is available. According to the World Federation of Hemophilia (WFH), 7,706 patients with hemophilia were registered in Russia with hemophilia A being diagnosed in 6,525 patients and hemophilia B in 1,181 patients [15].

In accordance with the international recommendations, clinical trials of recombinant and human plasma-derived coagulation factors VIII (FVIII) and IX (FIX) are conducted in different age groups. Thus, unlike the Russian legislation, the European Medical Agency (EMA) recommends to start a clinical trial of a new recombinant or human plasma-derived FVIII and FIX product in previously treated patients (PTP) with hemophilia of adults and children greater than 12 years of age due to alike pharmacokinetics [16, 17]. Obtaining results confirming effectiveness (E), safety (S) and comparable pharmacokinetic (PK) properties in 12 PTP with hemophilia A or B greater than 12 years of age during 50 days of administration (DA) is the basis for initiation of a similar trials in children who are 6 to 12 years of age. Obtaining the results of PK assessment, effectiveness in 12 PTP of 6 to 12 years of age, and 12 PTP of 0 to 6 years of age during 50 DA is sufficient to decide in favor of transition to clinical trials of effectiveness and safety of a new medicinal agent in previously not treated patients (PNTP) aged 0 and elder. Meanwhile, results of a clinical trial are required to include an indication into prescribing information for a new age, for instance, new factor FVIII products in 50 PTP with a severe form of hemophilia A in children both less and greater than 12 years of age, and at least 50 PTP who obtained a new factor FVIII product for up to 50 DA (fig.).

Registration of factor FVIII is followed by a post-registration trial in 200 PTP. 60 of them must be less than 12 years of age. In the post-registration period, treatment duration is up to 100 DA.

STEP-WISE CLINICAL TRIALS OF RUSSIAN RECOMBINANT COAGULATION FACTORS IN UNDERAGE PATIENTS

The 'Development of pharmaceutical and medical industry' program for 2013–2020 has been implemented in the Russian Federation during the last 10 years. Its aim was to increase production and ensure availability of vital and most important Russian medicinal agents including drugs to treat hemophilia B [18, 19]. Implementation of the program in Russia resulted in proper development, industrial production and examination of a group of medicinal agents based on recombinant coagulation factors VII, VIII and IX to treat hemophilia A, hemophilia B and inhibitory hemophilia [20].

The hybrid program of clinical trials of Russian recombinant factor FVIII (moroctocog alfa, Octofactor) products combines the requirements of international and Russian regulatory documents concerning clinical trials in children with hemophilia A. The program was developed and implemented in accordance with EMA guidelines on clinical trials of factor FVIII, national requirements to clinical trials of medicinal agents, biological agents, principles of the World Medical Association's Declaration of Helsinki and principles of Good Clinical Practice of the Eurasian Economic Union [21, 22, 23].

The program of clinical trials of Russian recombinant factor FVIII products was implemented stage by stage in preregistration and post-registration periods for various age groups. Phase I clinical trial was carried out to examine pharmacokinetic properties, safety and tolerability of moroctocog alfa after its single use in 12 PTP who were 18 years of age and elder with severe and moderate hemophilia B [24, 25]. Phase II–III clinical trials were conducted to assess safety and effectiveness of moroctocog alfa in a multi-center, controlled, randomized, open-label, parallel-group clinical trial as compared with Octanate in 36 PTP with severe and moderate hemophilia A who were elder than 18 years of age [26, 27]. Based on the results of the clinical trials conducted in 2013, Octofactor (moroctocog alfa) was approved for human use in the Russian Federation [28]. A prospective, multi-center clinical trial of effectiveness and safety in 12 children who were 12 to 18 years of age with severe hemophilia A (phase IV) was conducted after registration of the drug to treat adult patients elder than 18 years of age.

Effectiveness of moroctocog alfa for prevention and on-demand therapy, and high safety in children with hemophilia A of 12 to 18 years of age was confirmed during the trial [29, 30].

A prospective, multi-center clinical trial of effectiveness and safety of moroctocog alfa in patients with severe hemophilia A elder than 18 years of age (phase IV) was also conducted after registration of the drug. It demonstrated preventive effectiveness and safety of factor FVIII products in 30 adult patients with severe hemophilia A [31].

Summed up data containing the results of clinical trials of moroctocog alfa in 50 PTP with hemophilia A elder than 18 years of age and children aged 12–18 years were the basis for initiating an open-label, prospective, non-comparative, multi-center, clinical trial of effectiveness, safety and pharmacokinetics of moroctocog alfa in 50 children with severe hemophilia A (phase III). Data of cohort I, which included 27 children 6 to 12 years of age, and cohort II with 6 children 2 to 6 years of age were analyzed separately. Patients were included into cohort II only when the clinical part of the trial was completed by all patients from cohort I and after intermediate analysis of effectiveness and safety. The obtained results show that moroctocog alfa was effective in both cohorts [32, 33].

In the post-registration period, two observational trials were conducted to collect additional information about safety and effectiveness of moroctocog alfa for patients with hemophilia A in real clinical practice. In a prospective, multi-center, open-label, observational trial of effectiveness and safety of moroctocog alfa in 237 patients with moderate and severe hemophilia A, data about preventive therapy results were collected during a year. Spontaneous bleedings occurring at

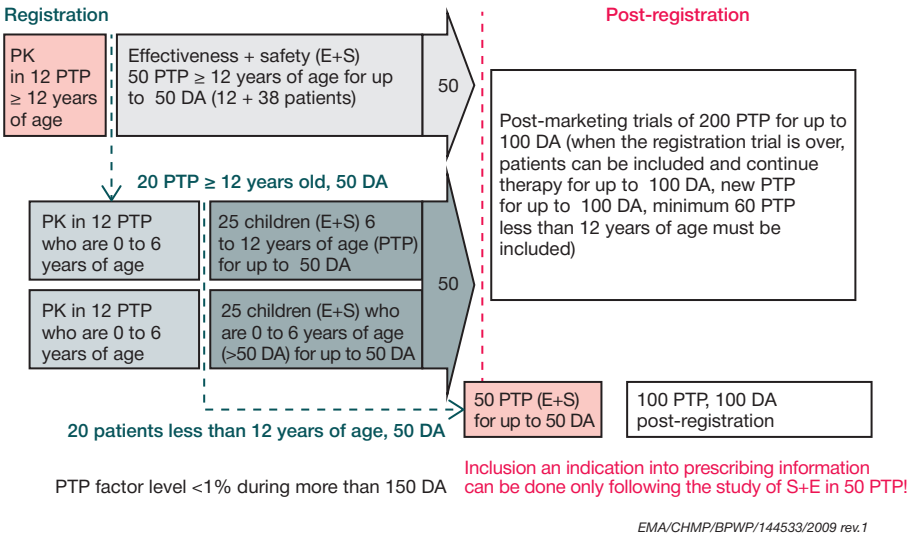

Fig. Sequence of clinical trials of new medicinal preparations of blood coagulation factor FVIII in different age groups [16]

2–3 days after administration of factor FVIII products were lacking in the majority of patients (61.7%). The average number of spontaneous hemorrhages occurring within 2–3 days after administration of the drug for a year for preventive purposes was 1.4±2.9 episodes per patient. During the trial, the drug demonstrated a high safety profile [34].

A prospective, multi-center, open-label, observational trial of effectiveness and safety of moroctocog alfa was additionally conducted in children with hemophilia A of 12 to 18 years of age in real-life clinical practice setting. During the trial the results of an examination and treatment of 24 PTP with hemophilia A were collected. They confirmed effectiveness of the agent in preventive treatment and its safety in the examined group of underage patients [35].

CONCLUSION

Active use of modern technologies in the development of new medicinal agents for pediatric patients promotes expansion of therapeutic possibilities of various diseases by pediatric specialists and requires planning and conduction of necessary clinical trials.

Conduction of clinical trials of new medicinal agents in children with orphan diseases including hemophilia is still a complicated task due to difficulties of their inclusion, limited number of orphan patients, complex design of a trial with step-by-step inclusion in different age groups, need in a pharmacokinetic trial with a good venous access for frequent blood sampling and intravenous injections.

When developing the program of clinical trials of an orphan medicinal agent, ethical aspects of participation of the underage must be considered taking into account the current international and Russian legislation. The role of an underage patient's parents in the provision of an informed consent needs to be estimated properly as well. Thus, prior to participation of an underage in a clinical trial, they need to be well informed, all the issues have to be resolved, and trust relationships need to be established.

The accumulated results of clinical and observational trials in pediatric PTP with hemophilia A in different age groups enable to expand a number of drugs to treat orphan diseases in childhood, make treatment of hemophilia A more available for the underage patients and set optimal conditions of using moroctocog alfa in different age groups.

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SECONDARY PROGRESSIVE MULTIPLE SCLEROSIS IN RUSSIA: PROBLEMS AND NEEDS OF PATIENTS, ASSESSMENT OF THE QUALITY OF MEDICAL CARE THROUGH THE EYES OF PATIENTS AND SPECIALISTS

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The article discusses the most unfavorable course of multiple sclerosis — the secondary progressive form. In the course of the study, conducted by a questionnaire survey of patients with secondary progressive multiple sclerosis and specialists from multiple sclerosis centers from 15 regions of Russia, medical, labor and other characteristics of patients, their problems and needs, subjective attitude to the effectiveness of therapy and rehabilitation were clarified. The main, according to doctors, defects in the organization of medical care for patients with secondary progressive multiple sclerosis have been identified. In conclusion, it was concluded that there is a significant variability in the social status and living conditions of patients with secondary progressive multiple sclerosis. The authors consider the registration in the Russian Federation of highly effective drugs for the treatment of patients with secondary progressive multiple sclerosis to be one of the most important measures.

Key words: multiple sclerosis, secondary progressive, social activity, treatment of secondary progressive multiple sclerosis, disease-modifying therapy

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Compliance with the ethical standards: this study was approved by the Ethics Committee of the Yaroslavl State Medical University of the Ministry of Health of Russia (minutes #21 of February 8, 2018). Each participant signed and submitted the voluntary informed consent form. Adult participants filled out questionnaires voluntarily. The conducted study does not endanger the participants and complies with the biomedical ethics requirements.

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ВТОРИЧНО-ПРОГРЕССИРУЮЩИЙ РАССЕЯННЫЙ СКЛЕРОЗ В РОССИИ: ПРОБЛЕМЫ И ПОТРЕБНОСТИ ПАЦИЕНТОВ, ОЦЕНКА КАЧЕСТВА ОКАЗАНИЯ МЕДИЦИНСКОЙ ПОМОЩИ ГЛАЗАМИ ПАЦИЕНТОВ И СПЕЦИАЛИСТОВ

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В статье обсуждается наиболее неблагоприятный тип течения рассеянного склероза — вторично-прогрессирующая форма. В ходе исследования, проведенного методом анкетного опроса пациентов с вторично-прогрессирующим рассеянным склерозом и специалистов центров рассеянного склероза из 15 регионов России, выяснены медицинские, трудовые и другие характеристики пациентов, их проблемы и потребности, субъективное отношение к эффективности терапии и реабилитации. Выявлены основные, по мнению врачей, дефекты организации оказания медицинской помощи пациентам с вторично-прогрессирующим рассеянным склерозом. В заключение сделан вывод о наличии значительной вариабельности социального статуса и условий жизни пациентов с вторично-прогрессирующим рассеянным склерозом. Одним из наиболее важных мероприятий авторы считают регистрацию в РФ высокоэффективных средств для терапии пациентов с вторично-прогрессирующим рассеянным склерозом.

Ключевые слова: рассеянный склероз, вторично прогрессирующий, социальная активность, лечение ВПРС, ПИТРС

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INTRODUCTION

Multiple sclerosis (MS) is a chronic inflammatory demyelinating disease the etiology of which is multifactorial. MS triggers a set of autoimmune and neurodegenerative processes that damage central nervous system and lead to significant neurological deficit and disability already at the early stages of the development of the disease [1]. It is the most widely

Table 1. Interviewed patients by region

Region	Number of people	Share,%
Moscow	36	7,2
Moscow region	28	5,6
Saint Petersburg	29	5,8
Leningrad region	25	5,0
Volgograd region	33	6,6
Republic of Tatarstan	35	7,0
Novosibirsk region	33	6,6
Perm region	33	6,6
Rostov Region	30	6,0
Samara Region	45	9,0
Tomsk region	33	6,6
Tyumen region	34	6,8
Ulyanovsk region	41	8,2
Republic of Bashkortostan	32	6,4
Chelyabinsk region	33	6,6
Total	500	100,0

spread demyelinating disease: worldwide, there are about 2.5 million people diagnosed with MS, and in Russia the number is approximately 200 thousand [2, 3]. A significant proportion of MS patients are young people of working age; 15 years from the onset, 50% of them have confirmed disability of the 2nd degree, and over 20 years with MS typically translate into a disability of the 1st degree [4]. At the later stages of the disease, patients lose the ability to support themselves independently in routine daily activities and thus need constant support from relatives and social workers, which adds to the high socioeconomic significance of MS.

Conventionally, there are three types of MS distinguished: primary progressive MS (PPMS), which is diagnosed in 10–15% of cases; relapsing-remitting MS (RRMS); and secondary progressive MS (SPMS) [5]. Same as the general prevalence of the disease, its prevalent type is region-dependent. As of May 82018, the Russian Register of CNS Demyelinating Diseases included 1188 patients, 85.8% of whom had RRMS, 1.9% had PPMS and 12.3% had SPMS. The ratio of MS types can vary significantly region to region. For example, in the city of Ufa, of the total number of MS patients 15% have RRMS, 3.5% are affected by PPMS and 81.5% have SPMS, while in the rest of Russia, in USA and the EU countries the share of patients diagnosed with SPMS ranges from 12 to 39% [6]. In three-quarters of RRMS patients the disease progresses into SPMS, but both patients and medical professionals try to avoid formal registration of the SPMS case as long as possible, since most MS disease modifying drugs (MS DMDs) prove ineffective against SPMS [7, 8, 9]. Poor therapeutic options available for SPMS lead to a more serious prognosis for RRMS course [10, 11].

Thus, out of 200 thousand MS patients currently registered in Russia, approximately 25 thousand have SPMS, with 127.5 thousand expected to join them after their RRMS progresses into SPMS. The ethical importance of studies investigating SPMS is high: the patients are of the working age, their social well-being declines sharply because of the disease, most of them acquire confirmed disabilities, the prognosis is typically unfavorable and there are no effective therapies against the disease available at the moment. The high social and economic significance of the SPMS problem supports the relevance of research efforts aimed at finding solutions thereto.

MATERIALS AND METHODS

The purpose of this work was to study the status of health and the living conditions of SPMS patients and to evaluate the efficacy of SPMS therapies and the goals currently seen as primary for them. The study was conducted by the All-Russian Public Organization of Disabled People with Multiple Sclerosis and supported by the Social Mechanics Center for Humanitarian Technologies and Research. The research method selected for the study involved questionnaires SPMS patients (formally established diagnosis) and neurologists specializing in MS were asked to fill out. The data collection period spanned from May 1 to October 1, 2020. All in all, 500 SPMS patients and 51 neurologist from 15 regions of Russia took part in the study. The minimum number of interviewed patients in a region was 25 (Leningrad region), the maximum — 45 (Samara region). The sample included patients that were available for filling out the questionnaires. The data from the filled out questionnaires were processed with IBM SPSS Statistics 26 statistical software. (Table 1)

RESULTS

General data. Two-thirds of the SPMS patients who participated in the study were female, and 73% of the participants were 40 years old or older (middle age and advanced age group). Most of the patients live in a family, 67.2% — with a partner; only 9% of the participants live alone. Over two-thirds of the participating patients (76.2%) have children: 43.2% have one child, 25% have two, 5.7% of patients have more than two children; the children of 30.6% of the respondents are minors. The level of education of SPMS patients is high: 52.7% of them graduated from a higher education establishment or studied there, 35.6% finished vocational schools. The participants had a long work history and high professional status before the disease, but currently most of them (71.6%) are unemployed because of the disability. (Diagram 1)

Duration of the disease and level of disability. Most of the SPMS patients participating in the study (79%) have had MS for over 8 years. Almost a quarter of them (23.4%) were diagnosed with SPMS 2–3 years ago, 24.4% first heard the diagnosis 4–6 years ago and 26% of the patients surveyed have been living with SPMS for over 7 years, while 17.6% received the updated diagnosis in the last year.

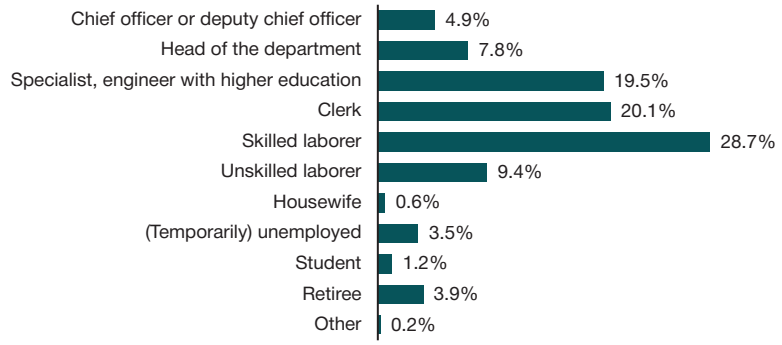

Diagram 1. Professional status of patients before the disease

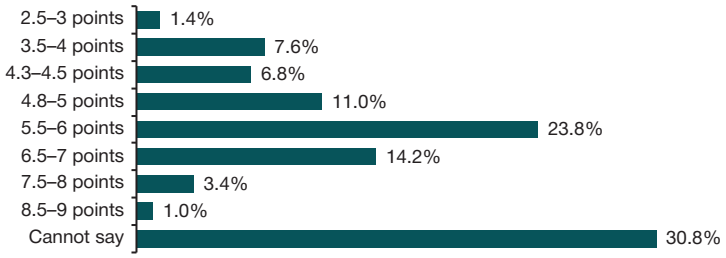

Diagram 2. SPMS patients about their EDSS scores

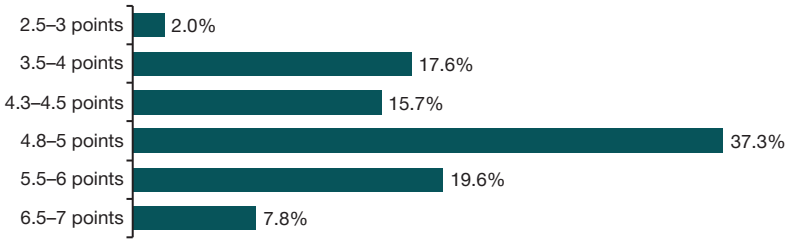

Diagram 3. Score estimated by neurologists for patients when establishing the SPMS diagnosis

The rate of manifestation of the symptoms of secondary progressive multiple sclerosis differs from patient to patient. For 32% of the participating patients, these symptoms became obvious within the first 3 years from the onset. In 20% of the respondents MS did not progress for the first 4–6 years of life with the disease. Multiple sclerosis did not develop further for 7–10 years in 28.4% of the participants, and about 20% have been living without SPMS making itself evident for over 10 years, which is a considerable period of time.

Official confirmation of disability has been given to 92.2% of the surveyed SPMS patients: 19% of them have disability of the 1st degree, 48.3% — 2nd degree disability and 25% belong to the group with disability of the 3rd degree. Typically, SPMS patients score 4.8–7 points on the EDSS scale (49% of the respondents), with 5.5–6 points being the most common result (23.8%). Patients with SPMS do not always monitor the formal parameters in assessing their condition: almost a third of the respondents (30.8%) found it difficult to answer the question about their EDSS score. Over half of participating patients (54.6%) have had the disability status for more than 7 years, 23.6% of the respondents have been officially disabled for less than 3 years and 21.8% received the formal confirmation of their disability from 4 to 6 years ago. (Diagram 2, Diagram 3.)

Self-perceived health and complaints. The majority of SPMS patients believe their health has deteriorated over the past year. The overall share of negative opinions was more than twice as great as the joint share of neutral and positive opinions (68.8% against 28.4%) However, with this many participating SPMS patients evaluating their health negatively, the share of those that stated lack of exacerbations over the past two years is relatively high: 37.4%. Among the participants that reported such incident 27.8% had one exacerbation, 16.5% had two exacerbations and 18.2% had three or more.

The symptoms that are the source of discomfort for the vast majority of SPMS patients are hindered movement and communication abilities (specific to activities outside the home), balance and gait disturbances, difficulties in moving around the house and doing household chores, fatigue and lack of energy. Over 55% of the respondents claimed to suffer manifestations of these symptoms constantly or frequently.

The symptoms that cause inconvenience to a significant number of SPMS patients have to do with individual manifestations: they find it difficult to concentrate, their urination and bowel functions are impaired, they feel dizzy; 35–50% of patients experience such symptoms constantly or often.

The list of occasional SPMS symptoms includes memory impairment, blurred vision, discomfort felt in the body, conditions like anxiety, depression and melancholy, irritability. Thirty percent of the respondents stated that they suffer manifestations of these symptoms often, 20–30% marked them as symptoms manifesting from time to time. The less common symptoms are annoyance, tearfulness, awkwardness in the presence of others and onset of depression when looked at by other people, as well as a sense of injustice. Over 50% of the participating patients have noted that these conditions are rare or unfamiliar to them. Table 2 contains answers to the question about the most disturbing manifestations of MS. (Table 2, Diagram 4.)

Table 2. Most discomforting symptoms

Complaint	Mentioned by	Complaint	Mentioned by
Ataxia	29	Nausea	1
Restricted mobility	52	Weakness, malaise	18
Balance disorder	61	Fatigue	13
Gait disturbance	65	Burning in the body	1
Weakness in the legs, dragging	53	Dizziness	29
Muscle spasticity	15	Headaches	8
Stiffness, heavy legs	13	Head numbness	1
Leg pain	10	Blocked ears	1
Leg parasthesia	9	Visual impairment	21
Leg cramps	4	Diplopia	3
Lameness	2	Rippled sight	1
Weak arms	19	Attention, memory disorders	19
Tremor	13	Irritability	4
Sensory disturbances in the hands	11	Reduced emotional background	3
Hand movement disorders	6	Anxiety	2
Difficulties with routine daily activities	4	Apathy	1
Urination disorder	64	Difficulties in communication	1
Pelvic disorders	24	Tearfulness	1
Bowel dysfunction	12	Speech disorders	6
Swallowing disorders	2	Pain in different parts of the back	4

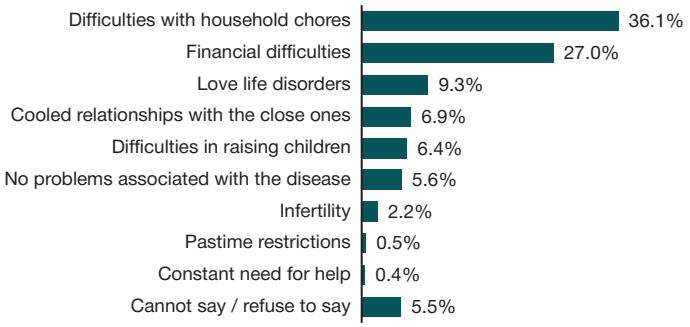

Diagram 4. Difficulties in family life caused by the disease

Living conditions of SPMS patients. As established by this study, 55% of patients with SPMS need help at home with housework and routine daily activities. Of the respondents that stated need for assistance at home, 81.5% receive help from their circle and 18.5% do not have a helper. Immediate family remains the main source of assistance in everyday life for SPMS patients: 74.8% of those who need such support receive it from their relatives. Often, the associated burden carried by the family members has no negative effect on their work. The majority of respondents (76.5%) mentioned that their relatives did not have to take a vacation, change their schedule or employment.

Most SPMS patients also receive psychological support from the family, with 67.3% of respondents mentioning family members trying to alleviate their condition, help, and another 21% noting a sympathetic attitude towards themselves. The proportion of those who say that the diagnosis has made their relations with the loved ones cooler is 7%. According to the patients, problems in the family are more often associated with mundane and material reasons and not with the psychological peculiarities of perception of the disease by the relatives.

The needs of patients with SPMS. The survey revealed some of the most pressing needs of patients. Innovative (effective) therapies, improved medical care, free drugs and monetary support were mentioned by 38–48% of the respondents. The second set of needs includes social aspects associated with belonging and reintegration: patients want to feel like full members of society, enjoy barrier-free environment and attention from others (28% of answers for each item). The third place in the rating of needs of SPMS patients was given to support and assistance, specifically, technical aids facilitating routine daily activities, movement and independent obtaining of information, as well as needs associated with timely consultations with legal/medical professionals and help with household chores (19–24% of answers). The availability of rehabilitation equipment to SPMS patients cannot be considered sufficient. Only 26–30% of the respondents have walking frames and wheelchairs, 23.6% have canes and 22% have diapers. There are handrails in the apartments of 13.8% of the participants and only 2.6% have special arms that allow unassisted activities in the kitchen. Handrails for the apartment were mentioned by 19.8% of the respondents as the equipment they need to buy; 19% did not have exercise therapy equipment but needed it; 13% stated the need for supporting arms in the kitchen to function there without assistance; 7.6% of the participants needed special shoes and 7.6% — diapers.

Eighteen percent of the respondents need professional retraining and employment. These are the patients who want to work and earn money but need help at the initial stage of retraining.

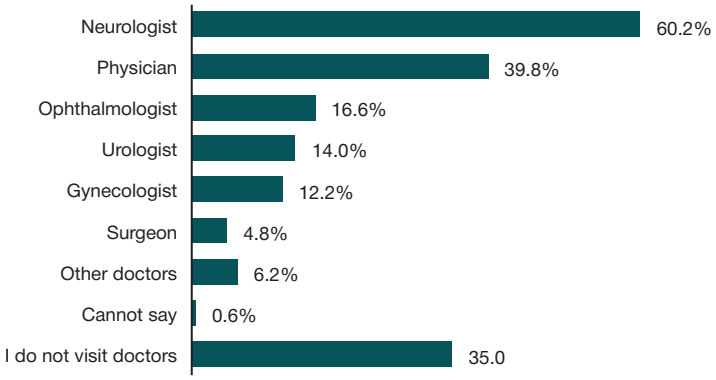

Diagram 5. Clinic doctors visited by SPMS patients

SPMS diagnosis criteria — a survey of specialists. The promptness of clarification of the diagnosis and change of therapy largely determine the success of all subsequent actions and suppression of progression of the disease. Manifestation of symptoms signaling of its development call for dynamic monitoring and timely assessment of the condition of patients. The change of the type of MS and its transition from RRMS to the progressive form is a gradual process. Clarifying the diagnosis, the neurologist takes into account patient's sensations and complaints, as well as the objective rise of severity/frequency of clinical manifestations of the disease.

Diagnosing SPMS or escalating the previous diagnosis to this type of MS, neurologists look at the increasing EDSS score registered outside of exacerbations: this criterion was mentioned by absolutely all the doctors who participated in the survey. Another phenomenon looked for when diagnosing SPMS is the disappearance of obvious exacerbations against the background of deteriorating motor activity (74% of doctors surveyed factor this criterion in when establishing the diagnosis). Repeated poor recovery after pulse therapy is the indicator taken into account somewhat less frequently: 38% of the doctors who participated in the survey pointed to this criterion. Patient complaints about cognitive or motor impairments and increased fatigue, as well as lack of therapy-induced alleviation, are not considered crucial in diagnosis clarification: only 26% and 20% of doctors surveyed, respectively, mentioned them.

The time it takes to diagnose a person with SPMS is perceived more or less similarly by medical professionals and patients. In most cases (75%), this period does not exceed 12 months. Basically, the time between manifestation of the symptoms of progression to the diagnosis can be 6 to 12 months, as stated by 38% of the interviewed patients and 42.9% of doctors, or 4 to 6 months, according to 27.3% of patients and 26.5% of neurologists. In almost a quarter of cases it may take over a year to clarify the MS diagnosis (pointed out by 24.7% of the participating patients and 24.5% of doctors). Late diagnosing of SPMS is a rare or relatively rare situation, as stated by 29.4% and 49% of the interviewed medical professionals, respectively. However, 21.6% of neurologists called this situation common. These opinions prove that improvement of the SPMS diagnosis clarification method is still an urgent matter.

The problem of late diagnosing of SPMS, according to the medical professionals surveyed, is primarily associated with the lack of clear criteria describing this disease and differentiating it from the current chronic condition of the patient (according to 65% of the respondents), as well as with the lack of SPMS therapy options (according to 56.9% of the interviewed doctors). Neurologists in polyclinics fail to focus on the problem of secondary progression of MS (according to 41.2% of the respondents), which complicates SPMS diagnosing, as does illiteracy of the patients themselves, who visit their doctors with symptoms of regression later than they should have (33% of respondents). Unavailability of equipment and lack of SPMS diagnosing methods are the reasons for late identification of the diseases that were mentioned by 19.6% of the doctors surveyed.

According to the medical professionals, MS patients should have certain skills in assessing their own condition and monitoring symptoms in order to contact a doctor in a timely manner to adjust therapy. Ignorance of patients makes the time to diagnosis even longer, which adds to the already high urgency of educational work among patients and their involvement in "patient schools" and other projects of this kind.

Outpatient care. Less than half of the patients undergo regular examinations at the place of residence (44.2% of the respondents). For 17.5%, the only reason to go to the clinic is exacerbation. Every third person diagnosed with SPMS does not visit the clinic (35.3% of the respondents), and only 7.7% of such patients skip on that activity for health reasons. The doctors SPMS primarily seek assistance of in the clinics are neurologists (60.2% of respondents) and, less often, therapists (39.8%). Up to 16% of respondents consult other medical professionals. (Diagram 5.)

The frequency of visits of SPMS patients to medical professionals depends on their area of expertise. Gynecologists, surgeons, ophthalmologists, urologists are seen by such patients one or two times a year. Neurologists and physicians receive SPMS patients somewhat more often: 33–35% of the respondents said they paid visits to these medical doctors one or two times, but another 33–35% mentioned three or four visits a year. Another third of those who go to the clinic (31%) visit the mentioned medical professionals more than 4 times a year, with 11.5% of the respondents paying visits to their neurologists every month and 13.9% of the participating patients seeing their physicians as often.

A quarter of the respondents do not turn to a doctor specializing in the relevant field of medicine even when their condition worsens. Among SPMS patients, the main reason for refusal to seek assistance is the handicap on their ability to move. Over 40% of the participants that do not visit physicians noted that it was physically difficult for them to get to the clinic. Among other reasons behind refusal to seek medical assistance are the difficulties peculiar to the medical establishments, including the complexity of obtaining an appointment note (26.5%), long waiting time (long queues of patients in the clinic) (25.3%), lack of a neurologist in the clinic (9.5%). Twelve percent of the respondents have mentioned doubts about qualifications of the medical professional as a reason to not go to the clinic. Ten percent of the participating patients are not motivated enough to seek outpatient care, and

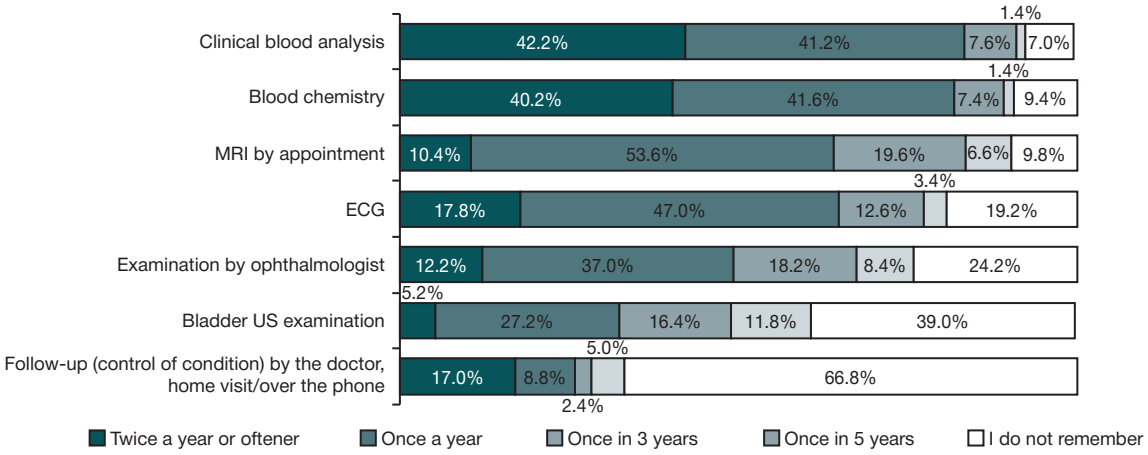

Diagram 6. Frequency of examinations

6.2% are too busy to to go the clinic. Diagram 6 shows the frequency of instrumental examinations underwent by patients with SPMS. (Diagram 6.)

The proportion of SPMS patients receiving care at home is 12.6% of the total number of respondents. Forty-one percent of the study participants have voiced unfulfilled need for such care, i. e., home medical assistance is unavailable to them. This is a significant share of SPMS patients who have difficulties with visiting the clinic and need patronage. The medical professionals that typically pay visits to SPMS patients are physicians (11.2% of the respondents) and neurologists (7.6%); the frequency of such home visits is once or twice a year. In individual cases, the patients are visited by a registered nurse, a massage therapist or an exercise therapy professional.

Treatment in regional MS centers and specialized departments of hospitals. In addition to outpatient medical care, patients with SPMS, as necessary, undergo treatment and rehabilitation in hospitals.

Currently, MS centers offer basic types of rehabilitation: exercise therapy, physiotherapy, massage (according to 80–87% of the neurologists interviewed). As stated by 74.4% of the participating medical professionals, patient organizations participate in the work of most MS centers. Sixty-two percent of neurologists highlighted the possibility of provision of psychological assistance at the MS centers. As for trips to health resorts, 41% of the respondents said that far from all MS centers offer them. According to the survey, 89.2% of patients diagnosed with SPMS are observed in specialized MS centers. A fifth of the participating patients (20.8%) are admitted to MS centers for inpatient care once a year, while 22% stay in the hospitals once every 2–3 years and 31% — less than once every three years. There are also patients that undergo inpatient treatment and rehabilitation in MS centers more often than once a year (12.2% of the respondents). SPMS patients take rehabilitation courses in an outpatient setting very rarely: over 75% of the respondents stated they have never done so.

In addition to treatment at the regional MS centers, MS patients are occasionally admitted to the neurological departments of hospitals. According to the survey, less than half of patients with SPMS received such inpatient treatment outside MS centers (43.8% of the respondents). In most cases (73.2%), the stay at the neurological department of a hospitals lasts up to two weeks.

The most common reasons for admission to a hospital are exacerbation of the disease (40% of the respondents) and its general aggravation (37%). Among other reasons, in isolated cases, the respondents mentioned the need to refine therapy, clarify the diagnosis or remedy the side effects of a previous therapy; 17.8% of the patients admitted to a hospital could not state the reason for admission clearly. Diagram 7 shows the reasons why 230 patients rarely seek inpatient care. (Diagram 7)

Specifics of drug therapy for SPMS. Evaluation of the drug component of therapy is the most important aspect in the analysis of quality of medical and social care. According to medical professionals, currently, regional MS centers offer courses of symptomatic, pathogenetic immunomodulatory or immunosuppressive therapies, and vascular-metabolic therapy. Seeking to analyze the role of drugs in SPMS therapy, we asked the participating patients to name the drugs that they are taking currently and have been taking before, and to indicate the duration of their intake and methods of obtaining them. The answers allowed making the following observations regarding the specifics of drug therapy for SPMS. Today, SPMS patients tend to take drugs from the following groups: Interferon beta-1b — 33% of patients, Interferon beta-1a — 14.6% of the respondents, Natalizumab — 10%, Glatimera acetate — 9.5%, Teriflunomide — 8.5%. Drugs that SPMS patients have been taking before: Interferon beta-1b — 73.3% of the respondents, Glatiramer acetate — 45.3%, Methylprednisolone and other glucocorticosteroids — 30.7%, Interferon beta-1a — 28%, Mitoxantrone — 14.4% of the participating patients. The vast majority of patients receive drugs free of charge. In isolated cases, patients independently purchased Interferon beta-1a s. c., Alemtuzumab, Methylprednisolone, Ocrelizumab.

The most common active agents in doctors' prescriptions are: interferon beta-1b, interferon beta-1a, methylprednisolone, ocrelizumab, mitoxantrone.

As for the interviewed medical professionals, currently they prescribe the following drugs to patients with an established diagnosis of SPMS: Interferon beta-1b (90.2% of the respondents), Methylprednisolone and other glucocorticosteroids (60.8%), Interferon beta-1a (43.1%), Ocrelizumab (41, 2%), Mitoxantrone (39.2%), Natalizumab (25.5%), Teriflunomide (19.6%), Alemtuzumab (19.6%), Glatiramer acetate, fingolimod and pegylated interferon (17.6% each name), Dimethyl fumarate (9.8%). (Diagram 8)

Throughout the length of their practice, the participating doctors have been prescribing: Interferon beta-1b (84.4% of respondents), Methylprednisolone and other glucocorticosteroids (77.8%), Mitoxantrone (62.2%), Interferon beta-1a (57.8%), Glatiramer acetate and pegylated interferon (37.8% each), Natalizumab (33.3%), Fingolimod (31%), Teriflunomide (26.7%), Alemtuzumab (22.2%), Dimethyl fumarate (17, 8% of respondents). The primary guides for doctors in prescribing drugs to SPMS patients are the clinical

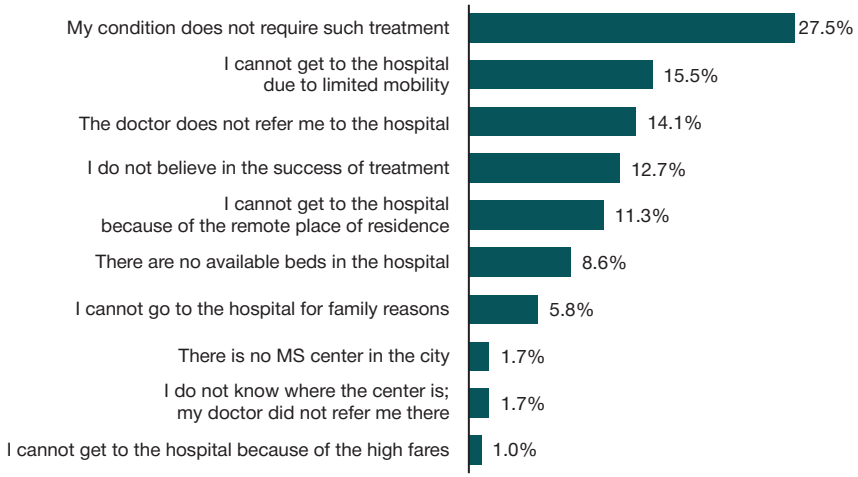

Diagram 7. Reasons for refusal to undergo hospital treatment, % of those who answered the question

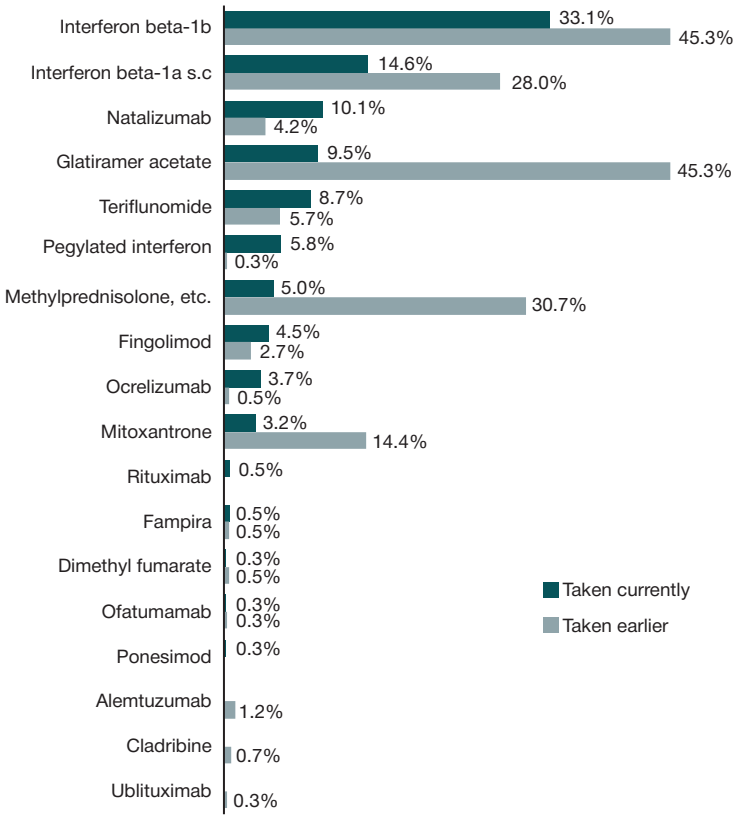

Diagram 8. Drugs taken by SPMS patients at different times

picture and the specifics of the course of the disease, as well as the existing standards and recommendations of the specialized federal government body. (Diagram 9)

Interviewed neurologists mentioned that, selecting drugs to prescribe, they perform a comprehensive assessment of the patient's condition, factor in comorbidities, patient's psychophysiological condition, including the degree of his/her cognitive and emotional impairments. A dynamic assessment of the patient's condition based on examination supports the doctor's opinion about the need to change the treatment regimen and prescribe drugs. The responses given by the participating medical professionals indicate that they monitor patient's condition based on the laboratory blood tests and MRI data. Dynamic observation allows evaluating the efficacy of the previously followed therapy in order to select the most appropriate treatment regimens while factoring in individual reactions of the patient.

The success of therapy largely depends on the motivation of patients, their adherence to therapy, awareness of the desired result and willingness to follow doctor's recommendations. When the patient feels comfortable in treatment, the chances of his/her adherence to the therapy throughout go up, which is why medical professionals, when prescribing drugs, also pay attention to the convenience of using them (how easy it is to dilute them, dose and administer).

The duration drug therapy courses varies. Glatiramer acetate and interferon beta 1-b are often taken for a long time: 52.6% of the respondents said they have been taking glatiramer acetate for over 4 years, and 36.2% of the patients stated the same about interferon beta 1-b. The estimations given by doctors and patients in this connection are quite similar. As for interferon beta 1-a, the duration of its intake is different: from several months (26.9%) to more than 4 years (22.7%). Teriflunomide and

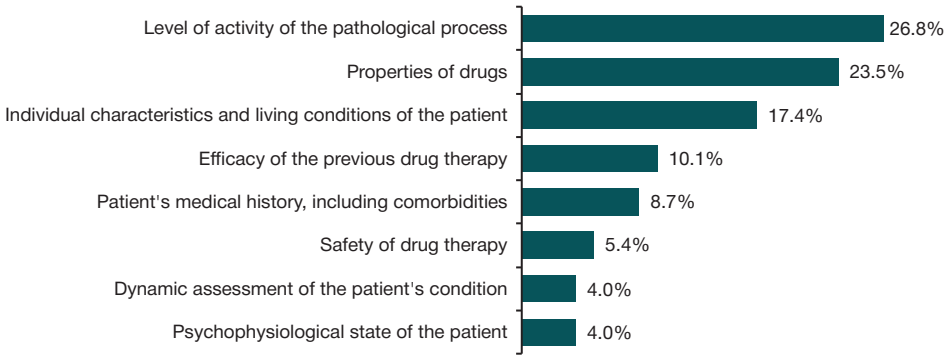

Diagram 9. Criteria of selection of therapy for SPMS patients (answers from neurologists)

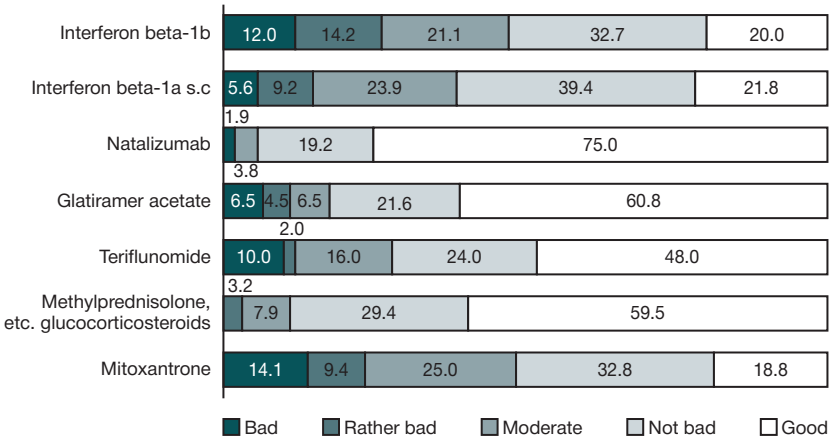

Diagram 10. Tolerability of drugs by patients with SPMS, in % for each drug

Natalizumab are taken for a relatively short period, only up to 2 years (97% and 69% of the participating patients, respectively). Pegylated interferon is also among the drugs that are taken mainly for up to a year (13 patients out of 15 mentioning this drug). Fingolimod was noted by 75% of respondents as a drug they have been taking for up to 3 years. Diagram 10 shows the tolerability of drugs by SPMS patients. (Diagram 10)

Evaluation of the efficacy of SPMS therapy. Patient satisfaction with the medical care they receive is a relative subjective indicator of its efficacy, which, nevertheless, can influence the further course of the disease, determining the quality of life with a chronic condition. The opinions of SPMS patients about the efficacy of drugs they take differ. Almost half of the respondents (48%) believe that drugs help. Sixteen percent of the respondents report no effect from drugs. Another 28% of the study participants rated the efficacy of drugs they take neutrally.

Patients' opinions of the effectiveness of treatment and rehabilitation in MS centers are mostly positive: the share of positive assessments is 2.5 times higher than that of negative assessments (47.4% versus 17.6%). According to the surveys conducted by the All-Russian Public Organization of Disabled People with Multiple Sclerosis, the dissatisfaction of patients with therapy is often associated with accumulated fatigue from the manifestations of the disease and disbelief in the success of subsequent manipulations.

Neurologists have differing opinions about the quality of medical care for patients with SPMS. Less than 15% of them are of very low opinion, while 24% believe the quality of care is "mediocre". Sixty-two percent of the interviewed medical professionals believe the level of care provided to SPMS patients is above average. The majority of interviewed neurologists (68%) believe that the quality of medical assistance to MS patients is better in their region than generally in the country. It should be noted here that such appraisals may be attributed to the fact that many of the neurologists that participated in the study are practicing in large MS centers in Moscow, St. Petersburg, Samara and Kazan.

The overall opinion of MS DMDs therapy for SPMS expressed by the participating neurologists cannot be called high. Negative appraisals significantly outweigh positive ones: only 12% of the interviewed medical professionals had a positive opinion about pharmacotherapy received by patients with SPMS. The vast majority of doctors — 76% — consider it insufficiently effective, and 12% believe it is completely ineffective. Neurologists also think that the problem of provision of MS centers with effective drugs is quite acute. Seventy-five percent of the doctors surveyed indicated a high need for effective drugs for SPMS seen at such centers. Despite the high demand for effective drugs, medical professionals also point out the potential problems that may arise as effective SPMS therapy becomes available. The first problem is legal registration of the new drugs. Doctors (83.7% of the respondents) believe that if the new drug is not part of the federal list of "14 nosologies", its registration will be a complicated matter. Other reasons for concern are the facts that the new drugs are not mentioned in the list of Vital and Essential Drugs (opinion shared by 53% of the respondents) and in federal clinical guidelines (45% of the respondents). There is another aspect that makes provision of drugs a complicated matter in the context of change of prescriptions: 43% of the participating doctors point to difficulties associated with diagnosis revision from latent RRMS to SPMS, and 22.4% mention complications arising in the process of identifying the patients that need therapy. According to the doctors, the main problems with treating patients in MS centers arise from the lack of effective drug therapy and clinical SPMS management guidelines.

Appraising the efficacy of rehabilitation measures, medical professionals believed the best options were psychological

assistance, assistance from a patient organization and exercise therapy. Treatment at health resorts, massage, and physiotherapy scored lower. Answering an open question about the problems in organizing rehabilitation for SPMS patients, neurologists revealed different aspects:

1. Lack of a full-fledged rehabilitation system and its regulatory framework, which is a basic general problem from which many particular ones follow. There are no rehabilitation programs, rehabilitation rooms and departments, day care departments, health resorts offering relevant treatment. The doctors interviewed pointed to the fact that rehabilitation is not in the list of services covered by the compulsory medical insurance, and it is difficult to book a course through a doctor. Rehabilitation as activity is in the scope of the Ministry of Social Protection, which puts it out of competence of RS centers. Moreover, there are no codes and regulations governing establishment of rehabilitation centers offering a complex of medical and social services. There are also no regulatory documents on the standards of rehabilitation and patient referral. Treatment standards for MS do not provide for rehabilitation measures. In reality, the rehabilitation of MS patients often takes form of arresting exacerbations in MS centers.
2. Physical inaccessibility of MS centers for people with restricted mobility is the second most pressing problem voiced by neurologists. Such centers typically operate in regional capitals, and frequent regular visits (once every three months) thereto is a difficult task for people living in remote areas. Today, there is no established procedure facilitating trips to an MS center, it is not possible to bring the patients there. There are no mobile teams at the centers nor outreach services that would perform diagnosing and basic rehabilitation activities at home. Currently, outpatient rehabilitation activities are non-existent. In remote areas, there are no rehabilitation opportunity available in any form.
3. Lack of effective drugs designed specifically for treatment of SPMS is the third most frequently mentioned problem. In this connection, the respondents spoke about the "14 nosologies" list and that there are no SPMS-specific MS DMDs there with proven efficacy. The lack of effective therapy designed specifically for SPMS, according to the medical professionals interviewed, raises concerns of both neurologists and their patients, who stop visiting the doctor when RRMS transforms into SPMS because they know their current therapy can be canceled, which is what they are afraid of.
4. Administrative problems in the work of MS centers stem, as mentioned by the doctors, from the lack of a regulatory framework governing their operations. In a number of regions, such centers exist as departments of hospitals, and in some cases, there are either no or too few job positions under them, which translates into overloaded neurologists who work part-time and are often driven by their enthusiasm exclusively. Another manifestation of this problem is the limited number of beds and low capacity of MS centers, which complicates admittance for the patients.
5. There is a problem that is common for all MS centers: the rehabilitation programs offered there are too focused, and there are no clinical guidelines covering rehabilitation of patients with MS and SPMS. According to the doctors working at such centers, today they do not have a license for rehabilitation activities. The interviewed professionals mentioned lack of facilities for neurorehabilitation, general unavailability of equipment for rehabilitation of neurological patients, mechanotherapy, yoga therapy, aquatic procedures, psychological assistance. SPMS as a condition imposes its own limitations on the possibilities of rehabilitation. In some centers, exercise therapy physicians refuse to work with SPMS patients because they are convinced such patients have no rehabilitation potential.
6. Insufficiency of the physical infrastructure (materials and equipment) of RS centers. Addressing this issue, the respondents spoke about lack of necessary equipment, both medical and common, including specialized beds and bathroom aids. Auxiliary care products and mobility aids were mentioned as available in insufficient quantities.
7. Lack of a clearly defined SPMS treatment algorithm: a single diagnostic algorithm, clear clinical guidelines for patients with SPMS.
8. Problems encountered by SPMS patients in the clinics: first line neurologists know little about MS (and SPMS in particular) and side effects of MS DMDs, MS patients do not receive proper attention from the staff and have to make two "stops" before they get an appointment with an MS center neurologist (physician — neurologist of the clinic — neurologist of the MS center).

Measures needed to improve the quality of therapy and rehabilitation of SPMS patients, according to medical professionals. The interviewed neurologists state that in order to solve the problems existing in the system of rehabilitation of patients with SPMS it is necessary to update regulatory documents governing rehabilitation of patients (71.7% of the respondents), purchase new rehabilitation technologies (61%), adopt better patient referral patterns (39%), train staff (24% and 32.6%), optimize the approach to registration of SPMS patients (24%). As for the quality of medical care offered to patients with SPMS its improvement calls for additional trainings for clinic neurologists, cooperation between regional healthcare systems and regional MS patient organizations, involvement of federal centers in the differential diagnosis procedures, budget-supported MRI examination of the spinal cord in debatable cases, organization of work with relatives of patients.

In general, neurologists see the optimization of the system of medical care for MS patients reflected in the following steps:

- Update of the regulatory documents governing rehabilitation of MS patients.
- Development of regional programs designed to help people with MS.
- Expansion of the list of drugs for MS: inclusion of new effective drugs in the federal list of "14 nosologies", federal clinical guidelines and the list of Vital and Essential Drugs.
- Improvement of the patterns of prescription of MS DMDs in SPMS cases.
- Establishment of specialized MS centers where they currently do not exist.
- Improvement of the physical infrastructure (materials and equipment) of the MS centers.
- Procurement of the new rehabilitation technologies.
- Training staff for RS centers to cover the current shortage.
- Advanced training of neurologists working at outpatient clinics to have them detect the disease at earlier stages.
- Introduction of the proper MS patient referral patterns.

CONCLUSION

The study revealed a significant variability in the social status and living conditions of patients with SPMS. According to the authors, the problems associated with provision of medical care to this group of patients are vivid to the medical professionals

surveyed. The measures proposed by the doctors to eliminate the problems of providing medical care to patients with SPMS are, in the opinion of the authors, relevant and appropriate, and their list is quite complete. The authors believe that the matter of registration of highly effective drugs for SPMS in the Russian Federation is one of the most important steps. At the same time, the results of this study suggest the high significance of the patients' own motivation and adherence to therapy. These parameters directly depend on how clear and convincing the arguments in favor of the treatment sound for the patient, how convenient the MS DMDs are to use and how comfortable the therapy is in general.

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THE DYNAMICS OF QUALITY OF LIFE INDICATORS DURING SURGICAL REVASCULARIZATION OF MYOCARDIUM

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Coronary heart disease (CHD), being one of the most common cardiovascular diseases, has a negative impact on patients' quality of life. The purpose of the work was to study the dynamics of quality of life indicators in patients with CHD during surgical revascularization of myocardium depending on the presence or absence of old myocardial infarction. 68 patients with CHD were examined, including 57 (83.8%) patients with old myocardial infarction (old MI) and 11 (16.2%) patients in the absence of old MI. There was a statistically significant improvement in quality of life, both in the physical and psychoemotional spheres, in patients with stable coronary heart disease including those with a history of myocardial infarction. No effect of old MI on quality of life in patients after myocardial revascularization surgery was observed.

Keywords: CHD, quality of life, myocardial revascularization

Authors contribution: Shereshneva MV — conducting a survey, collecting materials, tables creating and description, writing a text. Ilyin MV — consulting on research, statistical calculations, writing a text.

Compliance with ethical standards: this study was approved by the Ethics Committee of the Yaroslavl State Medical University. Voluntary informed consent was obtained for each participant. The survey for the adult population was conducted on a voluntary basis.

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ДИНАМИКА ПОКАЗАТЕЛЕЙ КАЧЕСТВА ЖИЗНИ ПРИ ПРОВЕДЕНИИ ХИРУРГИЧЕСКОЙ РЕВАСКУЛЯРИЗАЦИИ МИОКАРДА

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Ишемическая болезнь сердца, будучи одним из самых распространенных кардиоваскулярных заболеваний, оказывает негативное влияние на качество жизни пациентов. Целью работы было изучение динамики показателей качества жизни больных ИБС при проведении хирургической реваскуляризации миокарда в зависимости от наличия или отсутствия постинфарктного кардиосклероза. Обследованы 68 больных ИБС, в том числе 57 (83,8%) пациентов с постинфарктным кардиосклерозом (ПИКС) и 11 (16,2%) больных в отсутствие ПИКС. У пациентов со стабильной ишемической болезнью сердца, в том числе при наличии инфаркта миокарда в анамнезе, наблюдалось статистически значимое улучшение качества жизни, как в физической, так и в психоэмоциональной сферах. Установлено отсутствие влияния ПИКС на качество жизни пациентов после операции реваскуляризации миокарда. Пациент должен активно быть вовлечен в поиск оптимальной в его индивидуальном случае стратегии улучшения прогноза и качества жизни, что сопряжено с определенными этическими проблемами выбора.

Ключевые слова: ИБС, качество жизни, реваскуляризация миокарда

Вклад авторов: Шерешнева М. В. — проведение опроса, сбор материалов, формирование таблиц и их описание, написание текста; Ильин М. В. — консультирование по вопросам проведения исследования, статистические расчеты, написание текста.

Соблюдение этических стандартов: данное исследование было одобрено Этическим комитетом ФГБОУ ВО ЯГМУ Минздрава России. Добровольное информированное согласие было получено для каждого участника. Обследование для взрослого населения проводилось на добровольной основе.

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Cardiovascular diseases are not only the leading cause of death worldwide. They also significantly worsen the quality of human life. Being one of the most common cardiovascular diseases, coronary heart disease significantly limits mobility of patients including limitations of self-service. Comorbidity makes a certain negative contribution to quality of life in patients with CHD [1]. Depressive and anxiety disorders occur more commonly in patients with CHD than in a population [2]. Meanwhile, increased anxiety provokes angina attacks and intensifies ischemia.

Quality of life means a wide specter of parameters associated with physical activity, capacity for labor, social interactions, self-service, emotional stability, absence or presence of discomfort, including the one associated with the disease. To reflect common satisfaction, the term HRQoL (health-related quality of life) assessing the effect of a disease or disability on a human well-being is used in clinical practice. To study patients' quality of life as the subjective parameter, the survey method is applied. Short-Form 36 (SF-36) is a standard survey reflecting general well-being in the physical (physical health, PH) and psychoemotional (psychic component, MH) spheres. Complexity and non-specificity, i. e., the capacity to assess parameters in different pathologies, belong to its advantages.

It is demonstrated that coronary artery bypass grafting (CABG) does not only improve the prognosis and decrease

Table 1. Dynamics of mental (MH) and physical (PH) health indicators in patients with CIHD (*n*=11)

Indicator	V1	V2	*p*
MH, scores	39.2 (34.7; 42.6)	49.3 (37.8; 52.9)	0.004
PH, scores	31.4 (25.2; 38.3)	41.1 (36.1; 49.9)	0.0001

Table 2. Dynamics of mental (MH) and physical (PH) health indicators in patients with IHD and old MI (*n*=57)

Indicator	V1	V2	*p*
MH, scores	39.3 (36.2; 44.7)	48.4 (38.9; 53.2)	0.0017
PH, scores	34.6 (26.4; 39.1)	41.1 (36.1; 48.2)	<0.0001

Table 3. Influence of the presence of old MI on the values of mental (MH) and physical (PH) health parameters in patients with CHD (*n*=68)

	Multiple-R	Multiple–R^2	Adjusted–R^2	F	*p*
B1 SF36 (MH)	0.13	0.017	-0.003	0.84	0.36
B1 SF36 (PH)	0.24	0.058	0.038	2.96	0.09
B2 SF36 (MH)	0.0028	0.01	-0.020	0.0003	0.98
B2 SF36 (PH)	0.105	0.01	-0.009	0.53	0.46

a number of anginal attacks, but also results in a significant improvement of overall quality of life, both short-term and long-term [3].

Though revascularization by means of CABG is currently a routine intervention, it is accompanied with certain risks of post-operative complications and mortality [4]. The factors influence on the subjective perception by a patient of relevant intervention and potential improvement of quality and life expectancy, and promote development of anxiety in perioperative period. Some patients have difficulties after a surgery as well; they mention their dissatisfaction with life quality [5].

The purpose of the study was to examine the dynamics of life quality parameters in patients with CABG while performing surgical myocardial revascularization depending on the absence or presence of old MI.

MATERIALS AND METHODS

68 patients with CABG aged 38 to 76 years old (58.7±8.8 years in average) were examined, including 55 men and 13 women, who were admitted to the department of heart surgery of the Yaroslavl Regional Clinical Hospital to perform coronary artery bypass surgery. The diagnosis of CHD is confirmed by the results of a clinical study, stress tests, coronary angiography.

The patients were divided into groups depending on whether there was a history of acute myocardial infarction: 57 (83.8%) patients had old myocardial infarction (old MI), 11 (16.2%) of patients had no old MI (CIHD or chronic ischemic heart disease).

The SF-36 survey was used to examine the parameters of quality of life. It was designed to capture general well-being and degree of satisfaction with life activity influenced by the state of health. The SF-36 has 36 items grouped in dimensions: physical functioning, role activities, bodily pain, general health, vitality, social functioning, emotional condition and mental health. The higher is the index (from 0 to 100), the better is the estimate according to the selected scale. The indices are used to provide the mental (MH) and physical (PH) health components [17]. Considering the decrease of life quality during the postoperative period, the examination was done prior to the surgery (V1) and at 6 months (V2).

Statistical data were processed using STATISTICA 10.0 pack of programs (StatSoft Inc., USA). The normality of distribution of qualitative parameters was checked using the Kolmogorov-Smirnov test with Lilliefors' amendment and Shapiro-Wilk test. Due to log-normal distribution of attributes, the cited data are presented as a median and percentiles (25.0% and 75.0%). A Mann-Whitney U test was utilized to compare two independent groups by one attribute. The study of an attribute dependence type on one or several other attributes was done based on the logistic regression analysis. The critical value of statistical significance level was at 5.0%.

RESULTS AND DISCUSSION

When analyzing the results of quality life parameters obtained during research using the SF-36 survey (table 1), it was established that in the group with CIHD, MH and PH were 39.2 and 31.4 scores, respectively, prior to the surgery, and 49.3 and 41.1 scores, respectively, at 6 months ($p = 0.004$ and $p = 0.0001$).

In patients with IHD and old MI (table 2), MH and PH were 39.3 and 34.6 scores, respectively, prior to the surgery, and 48.4 and 41.1, respectively, at 6 months after the coronary artery bypass grafting ($p = 0.0017$ and $p < 0.0001$).

A statistically significant improvement of life quality, both in physical, and psychoemotional spheres, was observed in patients with stable ischemic heart disease, including those with a history of myocardial infarction. No statistically significant differences were obtained during comparison of physical and psychoemotional health parameters in patients with or without a history of myocardial infarction.

The logistic regression analysis showed a lack of old MI influence on quality of life in patients after myocardial revascularization (table 3).

Coronary artery bypass grafting is performed under cardiopulmonary bypass (on-pump CABG) or under the beating heart (off-pump CABG). The results of a large multi-center clinical study revealed no advantages of any surgery neither for prognosis and rate of revascularization, nor for quality of life or cognitive functions [4]. The subsequent studies showed no difference between ONCABG and OPCABG for the effect produced on life quality [6], including in the need of recurrent intervention [7].

The method of revascularization (PCI or coronary artery bypass), performed in accordance with indications, also produces no influence on life quality parameters [8]. Based on the results of a small prospective randomized study, a greater improvement of life quality according to the SF-36 was noted at 3 months after the surgery as compared to those who

underwent an intervention under standard cardiopulmonary bypass [9].

According to Pačarić S et al., in the remote period, coronary artery bypass grafting is followed by a significant improvement of life quality over all domains of the SF-36 survey with the greatest difference for the pain syndrome. The best outcome was observed at one year after the intervention, whereas at one month after the surgery quality of life was not satisfactory [10]. Grazulyte D. et al. showed that within five years after surgical interventions on the heart (the study also included the patients who underwent a surgery on the valvular heart apparatus) a significant improvement of physical and social functioning, mental health and vitality was noted.

Among the analyzed factors (dyslipidemia, arterial hypertension, low ejection fraction, high scoring according to EuroScore II, cardiac rhythm disorders), only arrythmia was a significant prognostic factor for lower parameters of vitality and social functioning [11]. High level of anxiety for myocardial infarction in patients with CHD and diabetes was associated with a greater rate of occurrence of new areas of myocardial ischemia [14]. In patients with CHD, who underwent rehabilitation, bad quality of life was related to a greater fatigue and decreased tolerability of physical load irrespective of psychoemotional stress and CHD severity [15].

A large prospective study was conducted in Netherlands. The purpose was to study quality of life and potential factors with an influence within one year after a cardiosurgical intervention. 2 basic groups of patients were identified (with and without improved physical functioning) based on the scoring in the SF-36 survey physical functioning domain. The last ones accounted for 21.9% of all the participants. Lower scores in the domain of physical functioning were observed in patients with improvement at one year after the surgery.

The patients with a lack of improvement after the surgery had a more frequent history of myocardial infarction. The factors associated with a lack of improvement were identified during the subsequent analysis: infectious complications following the interventions and need in recurrent PCI. 23.2% of patients who underwent coronary artery bypass grafting had no improvement in the physical domain at one year following the intervention. The factors associated with the lack of improvement were the same. A surgery type produced no effect on life quality [12].

A prospective study involving 272 patients who underwent coronary artery bypass grafting was conducted based on the university clinics of cardio- and thoracic surgery in France. Prior to the surgery and within 10 years after it, the patients were surveyed using the SF-36. At 5 years, the cumulative indicators of both the physical, and mental components were significantly higher than the primary ones. At 10 years, PH was significantly lower than at 5 years. However, it was still significantly higher than the primary one. Diabetes and dyspnea made the greatest contribution into the worsening of a physical condition. At 10 years, the mental component parameter was higher than prior to the surgery [13].

Østergaard B. et al. made an emphasis on the population elder than 70 years old and subsequently examined their life quality at 3, 5 and 8 years after the intervention. Statistically significant differences were noted only for the social functioning with a higher scoring for the patients who underwent a surgery using cardiopulmonary bypass. At eight years, a significant improvement of role functioning due to an emotional condition was found in the general population. On the contrary, the parameters of physical functioning that were the best at 12 months were gradually decreased at eight years after the intervention. This was probably associated with the peculiarities of inclusion criteria [16].

CONCLUSION

The coronary heart disease materially produces a negative influence both on the physical, and psychoemotional health of patients. Myocardial revascularization due to coronary artery bypass grafting improves the prognosis and life quality in patients with CHD irrespective of a history of myocardial infarction.

The patient needs to be actively involved into the search for an optimal individual strategy of improving the prognosis and quality of life. This is associated with certain ethical issues of choice. It is important to find a correct decision, considering the balance of benefit and risk and using the weighted assessment of prognosis and quality of life priorities. Though the benefit of revascularization in relation to ischemia therapy was convincingly proved, in some cases, optimal drug therapy is a reasonable alternative, which is not less effective than a surgery and has no associated risks. Thus, a patient with a stable CHD must be explained all possible types of treatment and their potential negative consequences associated with some kind of intervention in an easily understandable and clear way, both in the nearest, and remote time.

The patient who is currently satisfied with life quality, can underestimate the risks of great unfavorable cardiovascular events in the future. On the contrary, the patient who suffers from angina pectoris, can ignore the fact that in certain clinical situations a drug therapy and modified way of life help avoiding bad symptoms and improve the outcomes just like revascularization does. In his turn, a cardiovascular surgeon must be driven not by professional ambitions and objectively assess his skills while choosing a method of coronary artery bypass grafting: technically, an off-pump surgery is a more complicated procedure that must be performed by an experienced surgical team only. When revascularization is an option, a decision on its optimal method must be jointly taken by a cardiologist, heart surgeon and specialist in X-ray endovascular diagnostics.

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TRUTH IN MEDICINE

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Truth must be the starting point of any definition in medicine and therefore in medical ethics. The space-time definition of the human body and the continuity of the process in it is the first obstacle in medicine on the path to truth, and we immediately encounter this when we try to determine the state of health of patients. The second obstacle lies in the very definition of the concepts of health and disease, which in the end mutually define each other. The desire to penetrate into the continuity of processes in the body is in fact the desire for absolute truth. That which provides existence has an insider (internal, representative) approach to truth. The need to have complete control over the truth in medicine must sometimes end in faith or self-evidence. Philosophy accepted this a long time ago and for the sake of ethics, in the light of a scientific approach to medicine, it is necessary to constantly revise our views.

Keywords: truth in medicine, correspondence, pragmatism, consistency, conventionality, induction, deduction, insider (representative) truth, state of health

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ИСТИНА В МЕДИЦИНЕ

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Истина должна быть отправной точкой любого определения в медицине и, следовательно, в медицинской этике. Пространственно-временное определение человеческого тела и континуальность процесса в нем — первое препятствие в медицине на пути к истине, и мы немедленно сталкиваемся с этим, когда пытаемся определить состояние здоровья пациентов. Второе препятствие содержится в самом определении понятий здоровья и болезни, которые в конечном счете взаимно определяют друг друга. Желание проникнуть в континуальность процессов в организме на самом деле является стремлением к абсолютной истине. То, что обеспечивает существование, имеет инсайдерский (внутренний, репрезентативный) подход к истине. Потребность иметь полный контроль над истиной в медицине иногда должна заканчиваться верой или самоочевидностью. Философия приняла это уже давно и ради этики, в свете научного подхода к медицине, необходимо постоянно пересматривать наши взгляды.

Ключевые слова: истина в медицине, соответствие, прагматизм, согласованность, условность, индукция, дедукция, инсайдерская (репрезентативная) истина, состояние здоровья

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In this article, an attempt was made to determine the problems that shape the path to truth in medicine. Every problem is interdisciplinary to the extent that modern science is interrelated.

First, the problems we come across due to the nature of a human body itself will be enumerated by way of analysing its space-time specificity. Then the definition of 'health' and 'a disease', the issue of a language and logics, and, finally, the issue of a disease classification and use of modern technologies will be analyzed. All this is considered from the point of view of philosophy as the cradle of science and medicine itself and the influence of other sciences and primarily physics and mathematics.

THE ISSUE OF SPACE-TIME DETERMINATION OF A HUMAN BODY

The first question which a patient asks his/her doctor concerns the condition of health. It takes some time to think the question over. A human body is a complex and hence dynamic system with many undergoing processes. To present data about all parameters of the complicated system, for the sake of absolute truth, it's necessary to consider all constituents. As it is impossible, we appeal to propositional and the so-called pragmatic truth.

Let's provide some facts that explain the issue of space-time definition. The first is the continuity of a human body, and according to the second one, all laws of physics apply in all inertial reference systems.

The continuity is determined both in time, and space. When it comes to a human body, the importance of space-time determination can be clarified by mentioning the special theory of relativity by Albert Einstein (1871–1955.), and Werner Heisenberg's uncertainty principle (1901–1976.). No absolute knowledge of any bodily process results can be obtained; there is still a hope that the knowledge can be approached as close as possible.

In ancient times, the philosophical thought was avant-garde and made breakthrough in understanding the world. As science developed, it was followed by philosophy and agreed its view of world with it. Philosophy couldn't define

the relationship between matter and spirit. Descartes gave unequivocal expression that it was not possible to correct the gap for a long time (res extensa, res cogitans). I. Kant made three synthetic a priori judgements such as the immortality of the soul, the human freedom and the unity of the world (The Kingdom of aims).

The condition of spirit at the end of the XIX century and beginning of the XX century gave birth to existentialism, a school of thought, stating that 'what' (I am) can't define 'who' (I am) (Shelling, Kierkegaard, Nietzsche, Bergson, Scheler, Jaspers, Heidegger, Sartre, Camus) [1, 2]. This allows to interpret the existence of the reality we come across. If something continuous exists in space and time, then something that controls the existence, has an idea of its condition at the continuous level. For the person with today's level of knowledge, we suggest it to be the endocrine and vegetative nervous systems. They at once react to the change of parameters in the body. Thus, we can state that they have a privilege for truth, let's call it 'internal truth', 'representative truth; or, according to a widely applied expression, 'insider truth'. Impossibility to obtain absolute knowledge as it is used in science doesn't mean that the fact of existence lacks the truth if we follow the ideas of existentialists, as it is not an assertion, but the existence itself.

THE ISSUE OF DEFINING THE NOTIONS OF 'HEALTH' AND 'A DISEASE'

The terms 'health' and 'a disease' are opposed. As both terms result from an agreement, a patient with a serious and incurable disease can be declared healthy and vice versa.

As well-being is a relative notion, no reliable basis is provided for independent assessment of health. It is based on the personal judgement of the one whose health is estimated and on our belief in what he or she is saying.

To understand what health is we need to know what a disease is. On the contrary, a disease is defined as a deviation from the state of health based on several parameters. The cycle defining the state of health and illness makes us a good judge of the ways used to comprehend truth in medicine to avoid its relativization.

THE ISSUES ASSOCIATED WITH A LANGUAGE, LOGICS AND SCIENTIFIC APPROACH TO TRUTH IN MEDICINE

The human ability to differentiate between the body and the environment by means of self-consciousness is important for comprehension of truth in medicine. Kant mentioned that at the level of mind, the notions are considered from the point of view of categories (quality, quantity, relations and modality). It is where all possible data obtained by the organs of sense are sorted [3, 4].

Laws of identity, contradiction and excluded middle and other fundamental 'laws of thought' determined by logics enable us to understand the gender and the difference [5]. Thus, according to Aristotle, 'we study the existence as the existence' [6]. Based on the abovementioned data, 'the logical principles are formal and universal' [7]. This means that they are not independent from truth.

Induction doesn't go beyond premises, i. e., the conclusion is already contained in assumptions. That's why they say that induction 'can't be both true and useful' [3]. It could be thought that deduction is a non-reliable way of conclusion, as giving one hypothesis and achieving premises, it is not always possible to come back using the same way. However, an advantage of checking premises in the empiric sense and their measurement using the competing hypothesis premises and, thus, their adoption or denial, is present. According to Popper [8], this allows science to be an open system and constantly progress as technical and other possibilities develop. A simple set of analytical data can facilitate inspection, but doesn't lead to epochal discoveries. The discoveries require a brilliant mind. It has certain metaphysical elements.

That's why we make premises using deduction. Then, inducing the premises in the opposite direction, the starting point can't be reliably reached, i. e., this is possible in the statistically significant degree, but not to the absolute extent.

The fundamental judgements woven into the language of the discussed science are considered obvious and there is no need to prove them. We need a belief in self-evidence to accept them. For biology and medicine, it is about birth, growth, nutrition, reproduction, ageing and death. Evolution taken in science as a proven fact and having a status of theory is quite different. It is not something fundamental and self-evident, though it is currently an essential part of any scientific approach in biological sciences.

Something we start with by way of induction or something we achieve by way of deduction can be a thing marked with a property determined using a descriptive term or any fact [8]. Including a language into the process of cognition, we actually get a mediator who provides the first verification, because the notion should correspond to a thing, property or fact. Intersubjectivity is actually the first place where we come across truth as the concept of correspondence.

How the notions are named is decided in a collaborative way. It is rather simple if things are meant. However, when speaking about conditions (properties), the agreement is commonly the question of pragmatism and thus our knowledge about these conditions belong to pragmatic true facts. It can be said that agreement is a product of our wish to have an absolute cognition.

THE ISSUES ASSOCIATED WITH THE USE OF MODERN TECHNOLOGIES TO ACHIEVE TRUTH IN MEDICINE

If, analysing how the sensory organs work, the possible illusions used to be discussed in the past, we are now fighting a vast amount of data provided by machines. When making conclusions withing daily medical procedures, it is necessary to analyze and check the obtained data every day and be attentive when conclusions are made.

To avoid any abuse in treatment in countries with developed medicine, the procedural behaviour is required. This prevents us from making unnecessary mistakes. The only objection is represented by one-sided approach to pragmatic truth by weighing the correlation of the expected benefit and afflicted damage. It occurs when a lower level of diagnostics (primary care) is required to make a diagnosis in some cases as compared to some other situations demanding a higher level of diagnostics due to a larger potential danger (secondary or tertiary care). This is more associated with a rational use of resources than with truth.

THE ISSUES ASSOCIATED WITH A CLASSIFICATION OF DISEASES IN MEDICINE

The WHO developed the International Classification of Diseases at the international level. It establishes a unique system of conceptual marking of diseases and conditions. In this case, truth is of a very pragmatic type. This is reflected in a unique definition of notions (language-code) used in all countries and

hence allows to avoid various designations of national medical data, as medical issues are related to the entire humanity. A list of participants represented by our best and outstanding specialists who took part in printing of a joint collection in 1997 proves that the matter is important and needs to be concentrated on.

INSTEAD OF CONCLUSION

Areas of preventive medicine present a special problem in relation to truth in medicine because it must be sought in the interdisciplinary approach. The relations between a human being and his surrounding are finely balanced and consist of mutual actions. The evolutional theory and extensive knowledge about genetics made the truth evident. It's been a long-time experience that such things as boomerang can turn against those who cause changes in nature.

It is of special significance that prevention requires to assess the risk for human health in the first place. As any assessment in medicine, it is very ungrateful due to a highly unpredictable nature of a living organism, especially when it is required to assess the risk in relation to one or another group of people. We mainly link our possible failures with a risk of statistical research, which can be justified in many cases, and, to the less extent, with an uncomplete comprehension of a problem occurring due to our limited cognitive abilities.

A special problem is medicine is represented by truths inside psychiatry. The definition given by Dr. Bogdan Drakulich [9] stresses complexity of the issue: 'Considering the philosophical idea of integrity, a mental disturbance is defined as predominance of particularity (irrationality) escaping from the iterative function of the personality'.

FINAL CONSIDERATION

It can be concluded that cognition of truth in medicine, just like in other sciences, including philosophy, is based on the same principles. It includes (I) our beliefs that basic terms, properties and facts are obvious, (II) justification of beliefs achieved by way of induction and deduction during the actions taken to approach the truth and, finally, (III) respecting 'externalism of principles and internalism of reasons' [10] used to take a decision about the nature of the truth required to perform certain procedures. Why is externalism of principles mentioned? Because we'll make less mistakes when the procedures are followed. Why does the internalism of reasons occur? Because the approach to truth in medicine is of a nuanced type. Apart from the multidisciplinary type of the problem, it denotes the presence of experience and all other psychological factors that determine our activity.

Sometimes we accidentally save a person when trying to find the truth. And sometimes we lose a person, even when we know the truth. Truth is something we can't do without in any science, including medicine. But in accordance with the principles of existentialism, existence (of a human being, in this case) is the greatest truth, as no medicine can exist without it.

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COMMENTARY ON THE ARTICLE “TRUTH IN MEDICINE” BY MIKHAILO LUKOVICH, KATARINA MAJSTOROVICH, DUNI KNEZHEVICH

TRUTH IN MEDICINE: EXPERIENCE OF A STUDY OF BIOETHICS

Consistency of reasonable pragmatism of decisions and strive for ‘truth’ in the widest sense is one of the most important theses of V. R. Potter’s concept of bioethics. Humanistic rationalism and civilizational optimism translated by him belong to the integrating grounds for the research in the wide register of theoretical and practical problems of modern bioethics, including pressing applied issues of medical science and deontology.

The work by the Serbian researchers ‘Truth in medicine’ updates the problem of axiological grounds for the scientific paradigm. Considering ‘truth’ as an immanent basis of human existence and referring to historical experience of philosophical and naturalistic world view development, the authors repudiate the failure of a stereotype about the conceptual discordance of philosophical and common cognition with common ground in functional redundancy and thus non-obviousness of the immanent relation between separate formalized logical procedures and the fundamental laws of life.

The approach allows authors to translate optimism in relation to solution of the problem repudiating its immediacy following the best traditions of V. R. Potter’s bioethics. ‘Truth’ is brought to life as ‘wisdom’ providing the increasing knowledge with an actual and truly humanistic value.

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