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TRANSLATIONAL MEDICINE A NEW WAY FROM EXPERIMENTAL LABORATORY TO CLINICAL PRACTICE

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Abstract. The review article presents an analysis of modern problems in the development of medical science. The rationale for the need to develop a new direction in science - translational medicine, by creating conditions for the active transfer of the results of fundamental research to effective medical care is presented. To date, a colossal amount of information on molecular biology has been accumulated, subtle mechanisms of regulation of metabolic processes in the body, both under physiological and pathological conditions, have been revealed, and there are clear ideas on a number of pathologies, in particular, at the molecular and cellular levels. However, many aspects of such fundamental developments still remain at the level of theoretical material. The growing gap between understanding the causes of diseases and methods of their treatment is due to the fact that scientific developments and achievements are being introduced into practice for a long time or remain completely unclaimed in practical healthcare. The reason for this gap is related to the deepening specialization of theoretical researchers and experimenters, whose activities, with the amount of knowledge and time required for this, no longer allow them to combine scientific activity with medical practice. Translational medicine, as a young direction in medical science, is still at the level of its initial translational barrier, and the task is to introduce new biomedical scientific and theoretical provisions and methods to the field of clinical use as much as possible.

Keywords: translational medicine, medical science, molecular biology

On September 13, 1929, Alexander Fleming revealed for humanity his unique discovery - penicillin. Since then, for over a century now, biomedical research has been intensively developing. Unique discoveries in the field of genetics, molecular medicine and cell technology have opened up new possibilities for the fight against many diseases. Indisputable evidence has been obtained of the mechanisms of development of a number of pathologies, which for centuries were considered a mystery of nature [26].

Medical science has its own peculiarity, which consists in a large gap between the discoveries in fundamental research and the possibilities of applying the results in practical public health. Of course, the accumulation of theoretical information has its positive aspects - the creation of a knowledge base. Along with this, there is a need to reduce the distance between fundamental research and the possibilities of their application in practical public health. This served as the basis for the emergence of a new direction in science - translational medicine, that is, the creation of conditions for the active transfer of the results of fundamental research to effective medical care. At the same time, the specification of the direction of translation acquires a new variant in the form of personalized therapy. A clear relationship is created between the scientific laboratory and the patient's bedside in nature from theory to treatment and from treatment to theory ("Bench-to-Bedside" and "Bedside-to-Bench"). In other words, translational medicine is an interdisciplinary medicine based on the achievements of physiology, molecular biology, genetics and medicine and created to ensure high efficiency in the provision of medical services [1,3,8,11].

Initially, the term translational research was known, which was proposed in 1986 [11,12,15]. Subsequently, in the light of the development of the direction of development by the practical aspect of the introduction of theoretical developments into practical healthcare (new methods of diagnosis, prognosis, treatment, prevention, etc.), this direction acquired a more specific definition as translational medicine. At the same time, in 2010, the definition of translational medicine was already introduced as a method of applying experimental discoveries to clinical research.

As you know, the main goal of scientific and practical medicine is to improve the results of treatment of patients by conducting fundamental research, determining the biological patterns of the relationship between systems and structures of the body. It was the discoveries in the development of antibiotics and vaccines, understanding the mechanisms of restructuring of the body in complex biological situations, the invention of anesthesia, the

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principles of asepsis and antiseptics that made it possible to make a breakthrough in the medical industry. All this served as the basis for the formation of the direction of biomedical sciences, which cooperates in its foundation with such areas as molecular medicine, genetics, cell technology, genomics, metabolism, etc. [17,19,20,23].

Translational medicine is "a new field of knowledge that integrates elements of pathophysiology and approaches to the development of new therapeutic and diagnostic tools." It is "an evolving field of knowledge that focuses on using what is revealed in preclinical studies to bring ingenious and effective new steps in the clinic." Given the enrichment of theoretical knowledge through information from clinical observations, translational medicine is defined both as an all-encompassing scientific process that links basic research with clinical results, and as “a shift in the system of concepts in the tactics of new drug development, pharmaceutical economics and patient care” [28 , 29].

To date, a colossal amount of information on molecular biology has been accumulated, subtle mechanisms of regulation of metabolic processes in the body, both under physiological and pathological conditions, have been revealed, and there are clear ideas on a number of pathologies, in particular, at the molecular and cellular levels. However, many aspects of such fundamental developments still remain at the level of theoretical material. The growing gap between understanding the causes of diseases and methods of their treatment is due to the fact that scientific developments and achievements are being introduced into practice for a long time or remain completely unclaimed in practical healthcare. The reason for this gap is related to the deepening specialization of theoretical researchers and experimenters, whose activities, with the amount of knowledge and time required for this, no longer allow them to combine scientific activity with medical practice. At the same time, the development of certain theoretical areas of biomedical knowledge, the accumulation of an increasing amount of scientific information makes it difficult to understand, perceive, and even more so the possibility of using this information by practitioners working “at the patient’s bedside” [5,26].

This implies the need to train specialists who combine the professional competence of a “clinician” and a “researcher”, in contrast to the classical model of medical education, which concentrated resources on training in a real clinical situation without recognizing the essential role of an integrated interdisciplinary approach. Awareness of this situation by specialists in many countries in the field of health care or, rather, in the field of organization of medical science, medical education and practical medicine led to the conclusion that it is necessary to transfer (translate) modern theoretical provisions of medicine to real medical care for a particular patient.

The definitions of the concept of translational medicine are somewhat different for different authors, which, in all likelihood, is due to its initial versatility and breadth, which makes it possible to predominantly focus on its various aspects. According to some authors, this concept is nothing but a new term. However, one cannot but agree that the practicing physician and the researcher in the field of medicine are now so far apart from each other that it has become necessary to create a special strategy aimed at building "crossings" between them. It is these tasks that translational medicine is designed to solve, the purpose of which, like medicine in general, is to increase the efficiency and effectiveness of therapy aimed at improving the quality of life and/or its duration.

It should be emphasized that the concept of translational medicine is broader than "translational research", since along with them, it also includes the organizational side: the introduction of changes in medical education, in the organization of the pharmaceutical industry, in the interaction and relationships of various, today largely disparate, medical and biomedical institutions [6, 30].

Translational medicine plays a leading role in optimizing the mechanisms for transferring the results of fundamental biomedical research into diagnostic, preventive and therapeutic technologies. Together with biotechnology and new imaging techniques, translational medicine will form the basis of progress in medicine. One of the main tasks of translational medicine in the creation of new biologically active substances is the coordination of research between research institutions, pharmaceutical and biotechnology companies, as well as the search for ways to improve the effectiveness of existing drugs and promote innovation in the pharmaceutical market [10,31].

Thanks to the development of molecular biology and molecular medicine, some progress has now been made in elucidating the pathogenesis of many

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diseases at the molecular and cellular level. An important place in this direction is occupied by the development of new diagnostic tools, the purpose of which is the timely detection of specific biomarkers that make it possible to personalize therapy, i.e. choose the most effective therapy strategy for a particular patient. Biomarkers are becoming an integral part of clinical research. The term "biomarker" was introduced by the US National Academy of Sciences for biological monitoring of the population. A biomarker is a system of indicators (markers) characterizing the functioning of an organism, its interaction with agents of different nature [26,32].

The discovery of specific biomarkers in combination with the introduction of new effective drugs and the analysis of the individual characteristics of their action serve as the basis for the development of personalized medicine. These activities should contribute to increasing the effectiveness of therapy, reducing the existing gap between theoretical and practical medicine.

Translational medicine covers almost all branches of medicine: oncology, cardiology, research in genomics, molecular biology, neuroscience, engineering biology, cardiovascular disease, drug delivery, cell culture, bioinformatics, and health policy. The importance currently attached to the development of translational medicine in the world is evidenced by the emergence of new specialized journals - « Journal of Translational Medicine ", " Science Translational Medicine ", " American journal of translational research ", which bring together scientists in the field of basic and clinical research in their quest to improve the quality of patient care, promote the exchange of information and ideas among practitioners and specialists in basic and clinical research [2,4,7,13,33].

Due to the scale of the tasks of translational medicine, much attention is paid to the training of relevant specialists, which is already being carried out in a number of medical colleges and universities, for example, in the USA and the UK, where a specialized course "Molecular and translational medicine" has been introduced. Centers for translational medicine have been created and are functioning, uniting and coordinating relevant research in various fields of medicine [34,40].

The emergence and development of translational medicine is aimed at improving the efficiency of diagnosis and treatment of diseases, predicting the course of the pathological process. At the same time, on the one hand, the most rapid translation of scientific achievements into clinical practice is assumed, and on the other hand, their personalized, that is, their individual application, taking into account the state of the molecular, biochemical and metabolic characteristics of a particular patient [9,24].

We analyzed the results of determining the role and place of non-respiratory lung functions in the pathogenesis of the development of surgical sepsis against the background of severe forms of purulent-inflammatory diseases of soft tissues. Taking into account the fact that the earliest violations of the non -respiratory function of the lungs in the pathogenesis of the development of surgical sepsis were attributed to the barrier-filtration function of the lungs, in the form of endothelial dysfunction in the lungs, it is this side of the changes that should form the basis of methods for predicting the generalization of the inflammatory process.

The translational study of the experimental block was transferred to 27 patients with sepsis against the background of severe forms of purulent-inflammatory diseases of soft tissues. In order to move to the third block of the translational study, a study was made of the level of specific metabolites characterizing the barrier-filtration function of the lungs. The conducted studies confirmed their identity to the revealed mechanisms of development of changes in this organ in experimental animals, namely, a direct correlation was found between the volume of lung tissue damage, the degree of change in the morphological substrate with deviations in the biochemical parameters of the blood. At the same time, a separate analysis of indicators of non-respiratory lung functions revealed changes that were personalized and can be combined into 2 subgroups.

The first group consisted of patients with severe forms of purulent-inflammatory soft tissues, in whom, after surgical treatment of a purulent focus, no more than 2 clinical criteria for systemic inflammatory response syndrome (SIRS) were noted. In the second subgroup, patients with 3-4 signs of SIRS were identified. The nature of the revealed changes in this group was identical in all patients. The personalization of translational medicine is characterized by the regularity of the pathogenesis of the disease under study. An example of

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personalization can be the following observation.

Patient R.I., 1953 ə.b., (No. i/b 1031/790), was transferred to the multidisciplinary clinic of the Tashkent Medical Academy from the proctology department of the regional hospital of the Jizzakh region on 12.01.21 in a serious condition with a referral diagnosis "Condition after opening the ischiorectal paraproctitis. Sepsis. Diabetes mellitus type II . Complaints at admission to pain and the presence of a purulent wound in the perineum, an increase in the size of the scrotum, fever, shortness of breath, weakness, sweating, dizziness. From the anamnesis: sick for 2 weeks. Operated on for ischiorectal paraproctitis in the clinic at the place of residence. Due to the deterioration of the condition on 07.01.21, he was hospitalized in the proctology department at the place of residence. The antibacterial and detoxification therapy performed had no effect, the patient's condition worsened, from 01/09/21 edema and hyperemia appeared in the scrotum, groin and anterior abdominal wall, fibrilitic hyperthermia was replaced by hectic one. The patient's condition is grave. Tachypnea up to 28 times in 1 min. In the lungs on both sides, against the background of many different-sized moist rales, there is sharply weakened vesicular respiration. In the lower segments, breathing is not audible. Percussion - dullness of sound in the lower lateral sections on the left. BP 90/70 mm Hg, pulse 110 beats. in 1 min. Locally: in the area of the perineum and scrotum, there are several longitudinal wounds with scanty purulent discharge, around there are large areas of hyperemia of the skin without clear boundaries, the inflammatory infiltrate was not of the correct form. Palpation around the wound and in the area of infiltration revealed subcutaneous crepitus and tenderness. Plain roentgenoscopy of the thoracic organs dated 01/12/21 showed a slight increase in the vascular pattern of the lungs with signs of finely looped cellular deformity of the lung root. The results of a non-blood culture test were negative. The diagnosis was made: "Synergic necrotizing fasciitis of the perineum, inguinal regions and anterior abdominal wall. Fournier's gangrene. SIRS4 . _ severe sepsis. Syndrome of multiple organ dysfunction". On January 12, 21, after preoperative preparation, surgical treatment of the purulent focus was urgently performed with excision of necrotic tissues of fascial structures and fatty tissue. Incisions were made in the inguinal regions with excision of necrotic tissues of the anterior abdominal wall. On the same day, catheterization of the aortic arch was performed through the right femoral artery. Samples of mixed venous and arterial blood were taken. Analyzes in a sample of mixed venous blood - total protein - 46 g / l, total lipids - 2.9 g / l, albumins - 43%, lactoferin - 1649 ng / ml; procalcitonin - 1 ng / ml; IL-1b - 46.3 pg/ml; IL-6 - 31.3 pg / ml; TNF-α - 23.8 pg/ml; NO -21.9 μmol/l; eNOS - 2.1 μmol/min/l; iNOS - 0.2 μmol/min/l; peroxynitrite -1.9 μmol/l; von Willebrand factor -5.4 μmol/l; In the arterial blood sample - total protein - 30 g/l, total lipids - 2.1 g/l, albumins - 23%; lactoferin - 2429 ng / ml; procalcitonin - 0.5 ng / ml; IL-1b - 32.4 pg/ml; IL-6 - 8.2 pg/ml; TNF-α - 16.8 pg/ml; NO - 24.2 μmol/l; eNOS - 4.3 μmol/min/l; iNOS - 0.07 μmol/min/l; peroxynitrite - 0.52 μmol/l; von Willebrand factor - 4.3 μmol / l. Started regional infusion according to the scheme. The noted positive dynamics from 19-20.01.21 was characterized by a decrease in hyperthermia to 37.5 °C and tachypnea to 22 times per 1 min. Repeated samples of mixed venous and arterial blood were taken. In analyzes in mixed venous blood - total protein - 49 g / l, total lipids - 2.4 g / l, albumin - 33%; lactoferrin - 1243 ng / ml; procalcitonin - 0.5 ng / ml; IL-1b - 22.3 pg/ml; IL-6 - 27.4 pg / ml; TNF-α - 22.7 pg/ml; NO - 18.3 μmol/l; eNOS - 3.1 μmol/min/l; iNOS - 0.2 μmol/min/l; peroxynitrite - 1.8 μmol/l; von Willebrand factor - 3.2 μmol/l; In the arterial blood sample - total protein - 32 g/l, total lipids - 2.2 g/l, albumins - 28%, lactoferrin - 374 ng/ml; procalcitonin - 0.2 ng / ml; IL-1b - 12.8 pg/ml; IL-6 - 4.2 pg/ml; TNF-α - 14.5 pg/ml; NO - 22.5 μmol/l; eNOS - 7.2 μmol/min/l; iNOS - 0.05 μmol/min/l; peroxynitrite - 0.6 μmol/l; von Willebrand factor - 2.1 μmol/l. On the control fluoroscopy, confluent shadows are visible on both sides, diffuse interstitial edema with abundant spotted shadows, varying degrees of decreased transparency of the middle and lower lung fields. The symptom of "air bronchography" is noted, enlightenments are visible along the large and medium bronchi.

Comparison of data on the barrier-filtration function of the lungs with other clinical and instrumental data of surgical sepsis makes it possible to bring this information closer to the real conditions of the course of the pathological process under study.

Statistical processing of the information data array formed in this way made it possible to determine the most characteristic indicators, which formed the basis for constructing linear integral data in surgical sepsis. The conducted experimental studies created the conditions for translating data into clinical conditions. The continuity of these conditions also made it possible to personalize the method for predicting the development of surgical sepsis against the background of severe forms of purulent-inflammatory diseases of soft tissues.

Translational medicine, based on the achievements of molecular biology and medicine, which ensures high efficiency in the provision of medical services, uses the accumulated arsenal of modern fundamental knowledge about the mechanisms of basic metabolic processes and their disorders to provide effective medical care to a particular patient, i.e. for personalized therapy. Personalized therapy is a new quality of medical services [34,37].

It is impossible to overestimate the role of translational medicine in oncology. The deciphering of the human genome and the development of genomics have made it possible to obtain information about the association of individual genomic and proteomic disorders with the likelihood of certain diseases [14, 21, 22, 25, 35, 36].

Despite the increase in life expectancy in European countries, diseases of the cardiovascular system are among the main causes of death. At the same time, for various forms of heart failure, a correlation

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was established with the expression of a group of protein genes involved in many cellular, including signaling, processes. It has been shown that in these patients there are changes in hundreds of genes involved in transduction, in energy-dependent metabolic processes, apoptosis, transmembrane ion transport, maintenance of the structure of the cytoskeleton and extracellular matrix [38, 39]. The clinical application of these data obtained in population studies can be based on them a detailed classification of cardiomyopathies and the prediction of response to appropriate therapy [16, 18, 27].

Thus, translational medicine, combining the success of scientific research, the informativeness of diagnostic approaches and data from clinical studies, is designed to improve the efficiency and effectiveness of therapeutic intervention, and, consequently, improve the quality of life. Thus, when discussing ways to combat high mortality from cardiovascular diseases, many researchers note the need to overcome the existing gap between the available scientific and clinical data, on the one hand, and health policy, on the other, which can only be done through translational medicine - by sequentially passing through the above-mentioned translational barriers. Translational medicine, as a young direction in medical science, is still at the level of its first translational barrier, and the task is to introduce new biomedical scientific and theoretical provisions and methods to the field of clinical use as much as possible.

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