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PHENOMENON OF DEMIKHOV

Status of the problem of organ transplantation in the USSR in 1970–1971 and ways to solve it (Yu.M. Lopukhin, A.G. Lapchinsky, V.P. Demikhov)

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Abstract

Aim. *The article examines and analyzes the state of the problem of organ transplantation in the USSR in the early 1970s and ways to solve it with the participation of three prominent transplantologists of the Soviet Union – Yu.M. Lopukhin, A.G. Lapchinsky and V.P. Demikhov, as well as some world achievements in this field.*

Material and methods. *Available printed works on the history of Russian and world transplantology in the 1970s, the analysis of which was carried out by historical-genetic and comparative-analytical methods.*

Results. *Developed by Yu.M. Lopukhin together with leading surgeons and immunologists of the country the Program of scientific research on*

the problem of transplantation of organs and tissues included three main areas: clinical problems of transplantation of organs and body parts (limbs), including ensuring the viability of organs and tissues outside the body, the ways to overcome biological incompatibility, and also the moral and ethical issues of transplantation, and donation issues. It is shown that the methods of overcoming biological incompatibility in organ and tissue allotransplantations, which had been used for many years by A.G. Lapchinsky and V.P. Demikhov (exchange transfusion of blood between organisms of different species, cross circulation between individuals of the same species), no longer corresponded to the state of medical science, which was represented by Yu.M. Lopukhin. However, scientists who had world-class priorities for the duration of survival of experimental animals with a transplanted limb (A.G. Lapchinsky) and an additional heart and lung transplanted into the chest (V.P. Demikhov) could help in the implementation of some provisions of the Lopukhin's Program. The preservation of organs and tissues before transplantation in a state of suspended animation was studied by A.G. Lapchinsky, and V.P. Demikhov worked at developing the methods for the extracorporeal connection of organs to the body of an intermediate host and using portable artificial hearts to maintain the vital activity of a cadaveric heart before transplantation.

Conclusions. *Pioneers of experimental transplantology in the USSR A.G. Lapchinsky and V.P. Demikhov, who began their research in the 1940s, still could have solved many issues of transplanting organs and body parts by the 1970s. But in presented in 1971 Program on the problem of organ and tissue transplantation, prepared under the guidance of Yu.M. Lopukhin, the emphasis was placed on immunological studies, while experimental surgeons played a minor role in it.*

Keywords: history of transplantation, organ and tissue transplantation in the USSR, scientific research program, Yu.M. Lopukhin, A.G. Lapchinsky, V.P. Demikhov, 1971

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AIK, heart-lung machine
CPC, cardiopulmonary complex
HBO, hyperbaric oxygenation

The state of the problem of organ transplantation in the USSR in 1971. Achievements and priorities of transplantology

In the early 1970s, world and domestic medicine approached a new stage of its development, an organ replacement therapy. The greatest successes have been achieved in the field of kidney transplantation. In 1971, 63 clinics around the world dealt with this problem, including 5 in the USSR (the Research Institute of Clinical and Experimental Surgery of the USSR Ministry of Health, the Research Institute of Maintenance and Technology of the USSR Academy of Medical Sciences, Urological Clinics of the 2nd Moscow State Medical Institute named after N.I. Pirogov and Kemerovo Medical Institute, a Urological Clinic of the Military Medical Academy named after S.M. Kirov). The main issues that transplantology was addressing at that time were the study of the nature and mechanisms of rejection of alien tissues, determination of the chemical composition and localization of transplantation antigens, which constituted the essence of the so-called non-infectious immunology. In

turn, these studies made it possible to continue the study of an important medical problem - allergic and autoimmune diseases.

In parallel with the development of transplantology, new methods - artificial circulation, controlled breathing, hyperbaric oxygenation (HBO), artificial liver and kidney - began to be developed to remove patients from life-threatening conditions. These methods formed the basis of another new area of medicine - the treatment of patients with temporary severe disorders of visceral organs. A major achievement in transplantology was the success in the field of temporary and long-term preservation of isolated organs and tissues [1].

As for the problem of organ and tissue transplantation, three main trends have been identified: (1) autotransplantation, (2) allotransplantation and (3) xenotransplantation[1]. Autotransplantation became the basis of plastic and reconstructive surgery; its origins went back to ancient times, and its progress depended on the development of new technical methods for moving tissue within the same body and preventing infectious complications. Allotransplantation, in addition to technical issues, raised the problem of overcoming the biological incompatibility of organs and tissues taken from unrelated animals of the same species. In the 1960s, while solving this problem, there has been a gradual transition from biological to pharmacological methods. The problem of xenotransplantation was discussed less frequently, but in the early 1970s, from a scientific point of view (in experiment) it was considered completely solvable. "*According to specialists' forecasts*," Yu.M. Lopukhin wrote in 1971, "*the problem of xenotransplantation will be solved within the next 15 years*" [1, p. 7][2].

[1] In the 1970s the old concepts of auto- (native), homo- (from a related species) and hetero- (from an unrelated species) transplantation were replaced by new ones: auto-, allo- and xenotransplantation.
[2] The first digit in square brackets means the source serial number, the second means the page in it.

Let's look at the key problems of allotransplantation, which solution should have ensured its success in the 1970s, as well as how they were seen at that time and what solutions were proposed by Professor Yu.M. Lopukhin[3] one of the leading specialists in the field of experimental surgery in the USSR, Corresponding Member of the USSR Academy of Medical Sciences, (Fig. 1).

Clinical problems of allotransplantation included preoperative preparation of patients, surgical technique and management of the postoperative period.

Fig. 1. Corresponding Member of the USSR Academy of Medical Sciences, Professor Yu.M. Lopukhin (1924–2016). 1970s. From the funds of the Museum of the Russian National Research Medical University named after. N.I. Pirogov (granted by V.A. Gorsky)

Important in preparing patients for surgery, according to Yu.M. Lopukhin, there was the presence of methods and devices for

[3] Lopukhin Yu.M. (1924–2016), a Soviet and Russian surgeon, 1965–1984. Rector of the 2nd Moscow State Medical Institute named after N.I. Pirogov; Laureate of the USSR two State Prizes, the State Prize of the RSFSR, two awards of the Government of the Russian Federation, holder of the Order of Lenin, October Revolution, Red Banner of Labor (three), Friendship of Peoples, Badge of Honor, "For Merits for the Fatherland" 2nd and 3rd Grade, Honored Scientist of the Russian Soviet Federative Socialist Republic, Academician of the Russian Academy of Sciences, Honorary Director of the Research Institute of Physical and Chemical Medicine of the Federal Medical and Biological Agency of Russia; Honorary Head of the Department of Operative Surgery and Topographic Anatomy of the Russian State Medical University named after N.I. Pirogov.

temporary support of the function of diseased organs with the help of their artificial analogues. The most difficult and least resolved issue was the development of effective methods for maintaining the function of a weakened heart. No less important aspects of the clinical problem of transplantology were the technical issues of internal organ transplants, where, according to Yu.M. Lopukhin: "*major merits... belong to... V.P. Demikhov. In 1947, he proposed a method of transplanting one lobe and a whole lung. In animal experiments, V.P. Demikhov described and tested dozens of options for heart and lung transplantation, single heart transplantation, kidney transplantation, head transplantation, limb transplantation, etc.*" [1, p. 13].

Further Yu.M. Lopukhin listed the priorities known to him at that time in the field of organ transplantation. According to his knowledge, the method of kidney transplantation to the pelvic area was developed by J. H. Harrison and J. E. Murray in 1954, the method of heart transplant was developed by N. Shumway in 1961, that of the liver by F. Moor in 1960, that of the lung by W. Neptune in 1951, that of the pancreas by W. Lillehei in 1966, spleen by T. Starzl in 1964.[4] Of the Soviet surgeons, the greatest contribution to the problem was made by I.D. Kirpatovsky, Yu.E. Berezov, N.A. Lopatkin, V.V. Kovanov, A.G. Lapchinsky and others.[5] Of all the features of the organ transplantation technique, Yu.M. Lopukhin highlighted the technique of suturing blood vessels, pointing to "*the widespread use of microsurgery in experimental work on organ transplantation (kidneys, liver, heart, etc.) on small laboratory animals: rats, mice, rabbits* " [1, p. 13].

[4] We do not provide actual priorities for organ transplantation, which differ from those listed. Let us repeat: this list was compiled in 1971 by Yu.M. Lopukhin according to sources available to him.
[5] The names are listed in the order, in which Yu.M. Lopukhin arranged them.

The main problem of the postoperative period, in Yu.M. Lopukhin opinion was the fight against an organ transplant rejection, defining that fight as "*selfless*" [1, p. 14].

The problem that determines the success of allotransplantation is ***the problem of ways and methods to overcome tissue incompatibility***. "*It has been firmly proven*," wrote Yu.M. Lopukhin, "*that any tissue taken from an unrelated organism of the same species or different species, and transplanted into another organism, after a certain period, equal to 7-12 days for allografts, 5-7 days for xenografts, dies, is destroyed, rejected*"[1, p. 16]. Let us pay attention to the period of allograft rejection accepted as an axiom in those years, equal to 7–12 days, which V.P. Demikhov overcame many times in his experiments; and let's see what ways to overcome tissue incompatibility were investigated in 1971.

The first was to rebuild the recipient's body so that it did not react to the transplanted tissue or organ (cultivating tolerance, immunosuppression). The second was to select a donor so that the antigenic properties of its tissues and organs were closest to the properties of the recipient's tissues and organs (donor selection, breeding). The third, "*still the least studied and, apparently, the least promising*," was to change the antigenic properties of the transplanted tissue and organ so that they would be identical to the properties of the recipient's tissues and organs (modification of the donor tissue or organ).

Our research has shown that V.P. Demikhov tried to solve all these problems. First, he "cultivated tolerance" through the so-called antigen load, using cross-circulation, exchange transfusion, or the method of immunological paralysis, that is, transplanting large amounts of tissue, for example, half of the torso. But his failures were also due to the fact that he used all these approaches *on adult animals*. Perhaps he should have tried to transplant a second heart into a newly born puppy with an

imperfect immune system (after all, he was well aware of the methods of "tolerance cultivation" of M. Hašek and P. Medawar). It could also be possible that in the future this animal would live happily with two hearts. But he did not conduct such experiments. He also tried pharmacological immunosuppression in the early 1960s, but the 6-mercaptopurine he had to use at that time was so toxic that V.P. Demikhov refused it. He had no less toxic immunosuppressants (methotrexate, imuran, azathioprine, corticosteroids), nor antilymphocyte serum.

Second, not being able to conduct complex immunological studies (for example, determine leukocyte antigens), V.P. Demikhov selected donor-recipient pairs either from related pairs of animals or from animals with the same blood type. In a number of observations this method did work.

Third, V.P. Demikhov tried to modify the donor organs by using purely biological methods: in his opinion, the inclusion of a transplanted organ in the recipient's circulatory system will change the heredity of this organ according to the type of vegetative hybridization in plants, and the transplanted organ would survive. The convergence of the immune systems of organisms was achieved through a cross-circulation and exchange blood transfusion. A.G. Lapchinsky, who proposed this method, believed that it was also possible to "nurture" donor tissue (for example, skin) or an organ (for example, a kidney) by exposing it to cold, V.P. Filatov preserved a cadaveric cornea with cold, and V.V. Kovanov preserved a cadaveric kidney with a weak solution of formalin [1, p. 30]. Next, we will show how Yu.M. Lopukhin proposed to solve these problems.

Problems in organ donation and preservation included the sources of tissue and organs (living donor or cadaver) and the problem of preservation of explanted organs. "*The problem of donation concerns a wide range of legal, moral, ethical and scientific-medical issues*," Yu.M. Lopukhin wrote [1, p. 31]. This was especially true for unpaired

organs, such as the heart. And here, the main thing was to establish the moment of death and the organ removing duration (warm ischemia). According to the legal criteria accepted at that time, a donor death was determined on the basis of: the absence of brain biocurrents for 2 hours, a “zero” ECG and the absence of breathing. The time criteria were as follows: after the cessation of blood circulation, irreversible changes begin after 5-7 minutes in the brain, after 15 minutes in the liver, after 45-60 minutes in the heart, after 60 minutes in the kidney, after 90 minutes in the lungs [1, p. 32].

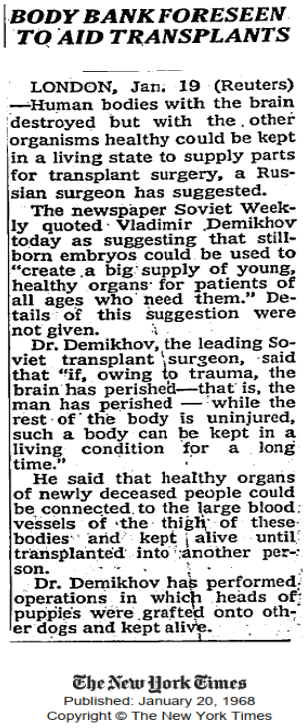
According to the views of that time, the most effective methods of maintaining organ vital activity before transplantation were the methods of cold perfusion or non-perfusion hypothermia at a temperature of +4°C. In this form, the organ could be preserved for several hours before transplantation. In 1971, Yu.M. Lopukhin believed that the best one was a combination of 3 methods: hypothermia (+4°C), perfusion with antienzymes (chlorpromazine), and HBO (up to 3 atmospheres) [1, p. 33].

Perfusion of an isolated organ with oxygenated blood using a cardiopulmonary bypass pump (AIK heart-lung machine) under normothermia was also promising. Similar experiments with isolated hearts were conducted by A.A. Vishnevsky and V.F. Tailor at the A.V. Vishnevsky Institute of Surgery in the 1970s (Fig. 2).

Fig. 2. Model of the unit for isolated cardiac perfusion, designed by V.F. Portnoy. A.V. Vishnevsky Institute of Surgery of the USSR Academy of Medical Sciences, 1970s. Exposition of the Museum of A.N. Bakulev National Medical Research Center for Cardiovascular Surgery. 2023

But there was one more way that deserves special mention. In 1905 A. Carrel proposed preserving organs in a viable state as a single block in a special chamber, calling this method visceral organism. The lungs were inflated with special bellows, and blood circulation was provided by the native heart. "*Unfortunately*," Yu.M. Lopukhin wrote, "*such a preparation can work for no more than an hour*" [1, p. 34]. And further:

> "The famous Soviet experimenter V.P. Demikhov, developing the idea of A. Carrel, proposed a system he called a "living organ bank." A set of organs, each of which is placed in a plastic box, is connected to the vessels of a "revitalized" corpse, whose cardiac activity is artificially resumed, and the lungs are ventilated by the respiratory apparatus. According to V.P. Demikhov, in this way it is possible to preserve isolated organs for a long time and "give them out" at the surgeon's request" [1, p. 34] (Fig. 3).



BODY BANK FORESEEN TO AID TRANSPLANTS

LONDON, Jan. 19 (Reuters) —Human bodies with the brain destroyed but with the other organisms healthy could be kept in a living state to supply parts for transplant surgery, a Russian surgeon has suggested.

The newspaper Soviet Weekly quoted Vladimir Demikhov today as suggesting that stillborn embryos could be used to "create a big supply of young, healthy organs for patients of all ages who need them." Details of this suggestion were not given.

Dr. Demikhov, the leading Soviet transplant surgeon, said that "if, owing to trauma, the brain has perished—that is, the man has perished — while the rest of the body is uninjured, such a body can be kept in a living condition for a long time."

He said that healthy organs of newly deceased people could be connected to the large blood vessels of the thigh of these bodies and kept alive until transplanted into another person.

Dr. Demikhov has performed operations in which heads of puppies were grafted onto other dogs and kept alive.

Fig. 3. An item from The New York Times (USA) about the views of V.P. Demikhov on the possibility of growing the healthy organs from non-viable embryos and V.P. Demikhov's creating the bank of healthy organs for their subsequent transplantation. January 20, 1968

We should note that Yu.M. Lopukhin mentioned the method that V.P. Demikhov had described in 1969 in the *Experimental Surgery and Anesthesiology* journal [2]. However, Yu.M. Lopukhin did not comment on the possibility of its use in clinical settings. "*In some situations*," Yu.M. Lopukhin wrote, "*you can use a method of temporarily connecting an isolated organ to the vessels of a patient [human] awaiting a transplant, or to another organism, the so-called "intermediate host"* [1, p. 34]. Here, Yu.M. Lopukhin again mentioned the experiments of V.P. Demikhov with temporary connection of the heart and lungs to the femoral vessels of the recipient with their subsequent transplantation into the chest cavity in the absence of a rejection reaction [2]. But

Yu.M. Lopukhin discussed no moral, ethical, medical, or any other problems associated with implementing these methods into the clinic.

He further described a method for temporarily connecting a donor kidney to the so-called Scribner shunt and, if its function was satisfactory, transplanting the organ to this or another patient. And that was also a modified idea of V.P. Demikhov, who in the 1970s conducted experiments with the Scribner shunt. However, as further emphasized by Yu.M. Lopukhin, Yu.A. Pytel found that a kidney attached to a shunt at the level of the radial artery does not function for long due to the small diameter of the vessel. And this method was abandoned. Two more links to the works of V.P. Demikhov without indicating his last name. (1) "*In experiments, the isolated kidneys and livers connected to the animal's blood vessels functioned well for 24–48 hours*." (2) "*To temporarily preserve the heart, attempts were made to connect it to the vessels of a baboon monkey, whose blood had previously been completely replaced by human blood*" [1, p. 34]. Thus, V.P. Demikhov left his mark, as well, in the development of methods for temporary preservation of isolated organs. But true was here that in the absence of technical capabilities (for example, equipment for organ perfusion), he used biological approaches ("visceral organism" by A. Carrel; temporary transplantation of organs to the femoral vessels, etc.). But, as we will show at the end of the article, by the beginning of the 1970s, these biological approaches had been replaced by technical ones (assisted circulation devices), and the "visceral organism" of Carrel–Demikhov was forgotten.

Considering the problem of long-term preservation of tissues and organs, Yu.M. Lopukhin described a method of freezing tissues after they had been treated with special "*cryostatic protective solutions*" containing glycerin and sugars, with which the cells were pre-impregnated and gradually frozen. "*Unfortunately*," Yu.M. Lopukhin wrote, "*all attempts*

to apply this method for long-term preservation of entire organs have not yet led to any success" [1, p. 35]. Let us note a method that has turned out to be promising over time, which Yu.M. Lopukhin casually mentioned: "*You can freeze, dry (lyophilize), and store skin, bones, blood vessels, nerves, fascia. When transplanted, such tissues serve as a temporary framework on which the recipient's own tissues regenerate*" [1, p. 35]. Today, the method of tissue decellularization is being developed with the aim of creating bioprostheses that are similar in their biological properties to the recipient's own tissues, for example, heart valves.

Speaking about the criteria for the viability of a transplanted organ, Yu.M. Lopukhin pointed to three periods: the period of warm ischemia (no more than 30–45 minutes should pass from the moment of death to the start of preservation), the period of preservation (hypothermia for 1–2 hours), the period of the second warm ischemia (from the moment of warming to inclusion in the bloodstream, 30–45 min). Total from 2 to 3.5 hours [1, p. 36]. But let us emphasize that V.P. Demikhov was not worried about these problems: he transplanted a viable organ - either a beating heart, or a heart stored under conditions of biological perfusion using a "visceral organism".

Next time Yu.M. Lopukhin mentioned the name of V.P. Demikhov in the "Experimental data" section of the chapter devoted to heart transplantation: "*Special merits in the development of various methods of heart transplantation belong to Vladimir Petrovich Demikhov. He proposed and tested many types of operations in animal experiments in 1951: transplanting a heart to the site of a removed one, transplanting a second heart into the chest cavity along with one lung, etc.* "[1, p. 44].

These words require a comment. We especially note the first sentence: the author named the only scientist in his book with a circulation of 85,600 copies *by name and patronymic*. But the next

sentence raises more questions than it answers. What does "*he proposed many types of operations*" mean if Yu.M. Lopukhin cited only two: an additional heart transplant and a heart and lung transplant? What does 1951 have to do with it, if V.P. Demikhov began his experiments in 1946? Indeed, he first performed an isolated heart transplant on a dog in 1951, but he was able to complete this operation by removing the animal from the operating table only 4 years later, that is, in 1955. And then: "*many types of operations*" is not an achievement, *but* means only that V.P. Demikhov was looking for only one type, but the optimal one[6]. Finally, and this is the most important thing: why Yu.M. Lopukhin, repeatedly citing foreign and domestic sources on the problem of organ transplantation, did not refer to the book by V.P. Demikhov "Experimental transplantation of vital organs" published in 1960. After all, it describes the results of heart transplants (additional and isolated), transplantation of cardiopulmonary complex, lobe and whole lung, kidneys, liver, head to torso, halves of the torso [3]. This suggests a conclusion: only few serious scientists, including Yu.M. Lopukhin, were interested in the research by V.P. Demikhov, who in the 1970s continued actively working in the field of organ transplantation.

Further, Yu.M. Lopukhin, answering the question "Who needs a heart transplant?", listed the conditions for which surgeons performed heart transplants in 1968–1969. As a rule, these were patients with severe lesions of the coronary vessels, multiple myocardial infarctions, and complex congenital and acquired defects. It seemed that replacing a diseased heart with a healthy one could solve all problems. But it was not there. It turned out that with severe heart failure, irreversible changes in other organs created serious problems for the donor heart: it could not

[6] By 1969 V.P. Demikhov, choosing the best method, had developed more than 40 types of heart transplantation.

cope with its function, and the patient died. Another problem was the damage to the vessels of a healthy heart by atherosclerosis in a relatively short period of time after transplantation, the phenomenon of the so-called “relapse of the underlying disease.” Therefore, the question naturally arose: could a person live longer with a diseased heart than with a transplant? In this case, a heart transplant, instead of prolonging the patient’s life, could shorten it, and this was contrary to the basics of medical ethics. Thus, as early as in 1971, surgeons (Yu.M. Lopukhin referred to A.A. Vishnevsky and M. DeBakey) agreed: clinical heart transplantation is permissible only if it is the only chance to save patient’s life [1, p. 47].

But the most difficult problem that the first cardiac transplantologists faced was not the problem of immunology, but acute postoperative heart failure, which was briefly mentioned above. According to Yu.M. Lopukhin, 24% of all those operated on in 1968 died from acute cardiac weakness on the 1st day after heart transplantation, and in 41%, due to poor heart function in the postoperative period, kidney, liver and lung failure developed, which led to their death. Biological incompatibility was the cause of death in only 20% of recipients. Therefore, the experience of the first years of cardiac transplantation showed that methods of maintaining the function of the transplanted heart in the first days after surgery should be put in the foreground rather than methods of immunosuppression. And for this purpose, according to Yu.M. Lopukhin, it was necessary to create devices that “*temporarily relieve the work of the transplanted heart, the so-called. unloading circulatory systems. According to calculations by the US National Heart and Lung Institute, if the problem of circulatory support devices were solved, the number of heart transplants could increase by 220 times"* [1, p. 47]. Let us recall that V.P. Demikhov wrote back in 1947

[4], and all of his "*many types of operations*" were dedicated to the development of a method of assisted circulation by transplanting a second, additional heart into the chest (Fig. 4).

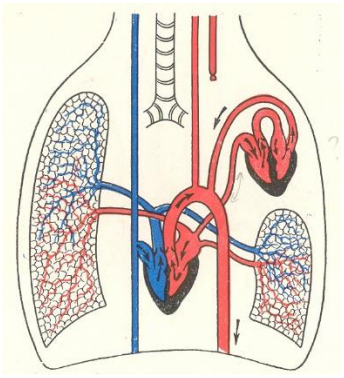


Fig. 4. Scheme of bypassing the left heart using a second isolated heart transplanted into the place of the upper lobe of the left lung. V.P. Demikhov, 1960 [3]

We can see another mention of V.P. Demikhov in the Section "Lung transplantation. Experimental data". Yu.M. Lopukhin wrote: "*After V.P. Demikhov's first 6 experiments (in 1947) on lung lobe transplants in dogs with an average postoperative lifespan of 7 days, many thousands of experiments were performed*" [1, p. 55]. It is clear that "*many thousands of experiments*" refers not so much to V.P. Demikhov, as to all experimental surgeons (in the USSR, for example, N.I. Gerasimenko was involved in experimental lung transplantation at the Research Institute of Tuberculosis of the USSR Ministry of Health, and J. Hardy of the University of Minneapolis performed more than 1,000 animal surgeries before deciding to perform a human lung transplant on April 18, 1963). But for some reason, only 6 operations made by V.P. Demikhov in 1947 with a survival period of 7 days were mentioned. After all, the vast majority of second additional heart transplants were accompanied by transplants of a lung lobe or a whole lung (Fig. 5). For example, the dog

Grishka lived with an additional heart and *a transplanted lung lobe* for 142 days in 1962.

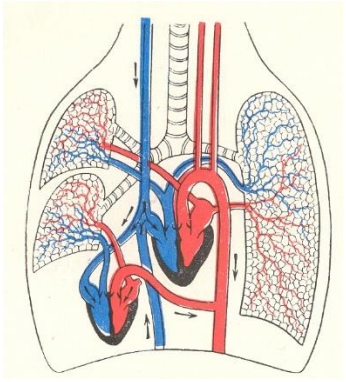
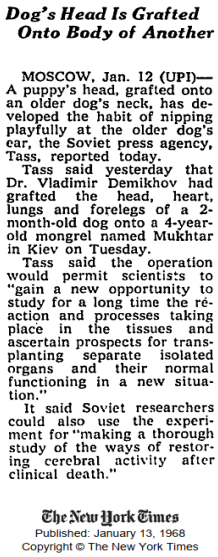


Fig. 5. Scheme of a complete cardiac bypass using a second additional heart transplanted together with the upper lobe of the lung. V.P. Demikhov, 1960 [9]

It is interesting Yu.M. Lopukhin's mentioning about the temporary connection of an isolated lung to the blood vessels of a sick person for assisted breathing both in severe lung diseases and after allotransplantation of the lung, which respiratory function acutely decreases immediately after transplantation [1, p. 56]. So, V.P. Demikhov proposed solving the problem of cardiorespiratory failure in the 1960s. Today this problem is solved using extracorporeal membrane oxygenation.

Let's summarize. Yu.M. Lopukhin mentioned, although very respectfully, the works of V.P. Demikhov only in sections devoted to experimental heart and lung transplantation. And even then very briefly. In the sections on kidney, liver, pancreas, and spleen transplants, V.P. Demikhov was not mentioned. In the short chapter “Transplantation of other organs” it was said about him as follows: “*V.P. Demikhov conducted a series of amazing experiments with transplanting a second head into a dog, which remained alive for several days*" [1, p. 60]. That's

all. But why "*several days*", if the maximum survival period of the 2nd head in 1959 was 26 days? And why, according to Yu.M. Lopukhin: "*the brain replacement with an allograft does not seem possible even in experiment*" [1, p. 60], if, according to V.P. Demikhov, it was possible to transplant not only the head, but also the entire front half of the body? (Fig. 6). Indeed, in 1971, the problem of restoring the conductivity of the spinal cord during its intersection had not yet been raised.



Dog's Head Is Grafted Onto Body of Another

MOSCOW, Jan. 12 (UPI)— A puppy's head, grafted onto an older dog's neck, has developed the habit of nipping playfully at the older dog's ear, the Soviet press agency, Tass, reported today.

Tass said yesterday that Dr. Vladimir Demikhov had grafted the head, heart, lungs and forelegs of a 2-month-old dog onto a 4-year-old mongrel named Mukhtar in Kiev on Tuesday.

Tass said the operation would permit scientists to "gain a new opportunity to study for a long time the reaction and processes taking place in the tissues and ascertain prospects for transplanting separate isolated organs and their normal functioning in a new situation."

It said Soviet researchers could also use the experiment for "making a thorough study of the ways of restoring cerebral activity after clinical death."

The New York Times
Published: January 13, 1968

Fig. 6. An item from The New York Times (USA) about the half the body (head, heart, lungs and front legs) transplantation performed by V.P. Demikhov from a 2-month-old puppy to a 4-year-old dog. The purpose of the experiment was to find ways to restore the brain activity after clinical death. January 13, 1968

Why do we ask all these rhetorical questions? In our opinion, they once again confirm that the leading transplantologists of the USSR either did not know V.P. Demikhov's research at all, or knew them but didn't analyze them, or analyzed them but didn't take them seriously. At the same time, Yu.M. Lopukhin was aware of the experimental research of American authors with results that were much worse even in conditions of immunosuppression and not comparable in terms of survival time with

the results obtained by V.P. Demikhov. And these, too, are the components of the “Demikhov phenomenon”. Apparently, after the start of clinical heart transplants, he was already perceived as a dreamer, and not as a serious researcher.

In addition to V.P. Demikhov, another patriarch of experimental transplantology worked in the USSR A.G. Lapchinsky, who headed the Laboratory of Experimental Grammatology and Orthopedics at National Medical Research Center for Grammatology and Orthopedics named after N.N. Prozorov (CITO). The main difference between A.G. Lapchinsky from V.P. Demikhov was that A.G. Lapchinsky was a doctor. And he even defended his dissertation for the degree of Doctor of Medical Sciences. True, in a specialty of Traumatology-Orthopedics. However, as far as we know, he did not work in clinic. What did he do as an experimental surgeon?

Exchange blood transfusion as a way to biologically overcome organ incompatibility during homotransplantation

Earlier we wrote that a certain part of V.P. Demikhov’s research he conducted in the late 1960s-early 1970s, included experiments on replacing blood in animals of one species with the blood of animals of another species, and even replacing blood in animals (dogs or monkeys) with human cadaveric blood. So, there were 9 such experiments in 1969–1970, [5], and 9 more in 1972 [6]. But why did V.P. Demikhov, who developed and applied the method of cross blood circulation in the 1960s in order to overcome the incompatibility of organs during homotransplants, took up a new problem for himself: an exchange blood transfusion into animals of different species?

Let us turn to A.G. Lapchinsky's doctoral dissertation he defended in February 1970 on the topic: “Experimental autotransplantation and homotransplantation of a limb” (Fig. 7). The research was conducted at

the Central Research Institute of Traumatology and Orthopedics of the USSR Ministry of Health, where A.G. Lapchinsky worked. Let us note that the opponents of the dissertation were the Academician of the USSR Academy of Medical Sciences N.N. Blokhin, Professors V.N. Blokhin and I.D. Kirpatovsky[7].

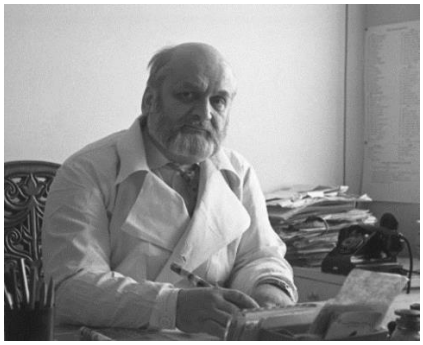


Fig. 7. Doctor of Medical Sciences A.G. Lapchinsky (1908–1982). 1970s

As early as in the "Introduction", the author, pointing at the difference in the results of autotransplantation (replantation) and homotransplantation of organs, known since the beginning of the twentieth century, with reference to A. Carrel (1912), argued that " *for acceptance of homografts, it is not enough to perform a technically correct operation; it is necessary to overcome the biological incompatibility of tissues of different organisms, to avoid the recipient's reaction against donor tissues that are foreign to him*" [7, p. 4]. In what ways did the author propose to overcome this incompatibility? Talking about his experiments in 1939–1940 on successful homotransplantation of limbs in rats, A.G. Lapchinsky, citing the achievements of the American biologist J. Schwind (1938), pointed out that one of the methods to overcoming this was parabiosis, i.e. a temporary (up to 20

[7] All opponents, including N.N. Blokhin, at their time were engaged in auto- and homotransplantations of limbs with varying success.

days) connection of the donor and recipient with each other by creating a single circulatory system[8] [7, p. 17]. Moreover, after limb homografting, the recipient rats[9] lived after surgery for up to 2 years or more before their natural death [8]. However, with reference to M. Hašek (1953), A.G. Lapchinsky noted that his experiments with the acceptance of homolimbs were successful because he used for his experiment 15–25-day-old rat pups, rather than adult animals, that is, the method of postembryonic (embryonic by M. Hašek) parabiosis. In 1953, P. Medawar and his colleagues experimentally proved the possibility of acquiring immunological tolerance in the antenatal period. Thus, A.G. Lapchinsky was one of the first in the world to empirically observe the phenomenon, for which P. Medawar and F. Burnet received the Nobel Prize in 1960[10]. Having set out to investigate the role of age in such experiments, in 1963–1964, A.G. Lapchinsky and his colleagues began to transplant large flaps of skin with mammary glands from unrelated rats using the method of temporary parabiosis, and achieved both a stable acceptance of homo-skin, and also functional restoration of the morphologically intact mammary glands [7, p. 19].

However, it turned out to be difficult to apply the parabiosis method in dogs, and then A.G. Lapchinsky came up with another option: in experiments of 1963–1966, in the first days after birth, the future recipient puppy underwent a subtotal blood replacement with blood taken from the intended limb donor. After the puppies prepared in this way grew up, in "*five [of them] the survival of a homotransplanted limb exceeded the time limits described that in the world literature*" [7, p. 20]:

[8]These experiments were made at the Institute of Experimental Biology of the USSR Academy of Sciences (now the N.K. Koltsov Institute of Developmental Biology of the Russian Academy of Sciences).

[9]The animals were demonstrated by the author at a Meeting of the Surgical Society of Moscow and the Moscow Region on February 13, 1940.

[10]In the literature of the 1960s. There are opinions that the third Nobel Laureate should have been the Czech scientist M. Hašek. There was no mention of the Soviet scientist's work.

in 3 dogs the transplanted limbs were rejected on the 25th, 29th, and 36th days after transplantation, and in 2 dogs stable graft acceptance was observed. One dog died of pulmonary embolism on the 335th day, and a dog named Bratik, whose homotransplantation was performed on January 9, 1964, had already lived for 6 years by February 1970. The data obtained were superior to those, including those of foreign authors, where immunosuppression was performed with cortisone or radiation.

> "The method of one-time replacement of blood in a newborn recipient with donor blood," concluded A.G. Lapchinsky, can be considered as the introduction of a massive dose of antigeneic material (immunocompetent cells) during the immunoadaptive period of the body. It entails a large immunobiological restructuring and causes persistent tolerance ... in homotransplantation of limbs from a blood donor." At the same time, the author came to the conclusion that "the method of subtotal blood replacement in the first days after birth, as well as the similar method of temporary parabiosis between donor and recipient, cannot currently be directly used in clinic. But they are of great theoretical significance <...> and show the fundamental possibility of performing an operation to replace an amputated limb in people, when simpler, more reliable and safe ways to overcome the incompatibility of donor and recipient tissues are developed" [7, p. 23–24].

Note that, while developing biological methods for overcoming incompatibility, A.G. Lapchinsky, first, followed global trends in creating immunological tolerance through parabiosis or replacement blood transfusion *in the early postnatal period*; second, he was aware of the relative safety of biological methods compared to the unsafe methods of pharmacological immunosuppression in those years; third, that the use of "*unsafe immunosuppressive agents is indicated only when transplanting vital organs (heart, kidneys, liver, etc.) to those patients whose lives cannot be saved by other methods*" [7, p. 25]. Thus, using the methods of

parabiosis and replacement of the recipient’s blood with the blood of the intended donor during transplantation, A.G. Lapchinsky confirmed their efficacy, although pointing out their unacceptability in clinical practice.

This is exactly what V.P. Demikhov began doing when conducted a total blood replacement in animals of different species. We emphasize, however, that in none of his research did he quote A.G. Lapchinsky. For his part, publishing his dissertation report in 1970, A.G. Lapchinsky mentioned V.P. Demikhov's works in only one place, pointing to his research in 1946, that is, 15 years ago.

Eight years passed. Had anything changed in the problem of limb transplantation during that time? In his Act Speech delivered in CITO named after N.N. Priorov on December 14, 1978, A.G. Lapchinsky, citing the results of experiments of 1960s, reported on successful *replantations* of limbs in the USSR and abroad conducted in the 1970s. Noting that the pioneer of a new direction in the USSR was the Research Institute of Clinical and Experimental Surgery of the USSR Ministry of Health (Director: the Academician of the USSR Academy of Sciences B.V. Petrovsky, Head of the Department: Professor V.S. Krylov), A.G. Lapchinsky complained that neither the Institute of Organ and Tissue Transplantation of the USSR Academy of Medical Sciences (Director: Professor G.M. Solovyov, a Corresponding Member of the USSR Academy of Medical Sciences), nor the Laboratory for Organ and Tissue Transplantation of the USSR Academy of Medical Sciences at the Department of Operative Surgery and Topographic Anatomy (Head of the Department: Academician of the USSR Academy of Medical Sciences V.V. Kovanov) of the 1st MMI named after I.M. Sechenov were dealing with limb replantation. Further, he covered in detail the technique of limb replantation after traumatic amputation. A.G. Lapchinsky pointed out possible complications and ways to overcome them. Unfortunately, he

confirmed that no progress had been achieved in the field of limb allotransplantation over the past 8 years. A.G. Lapchinsky cited only one foreign work, the authors of which carried out immunosuppression with pharmacological drugs and antilymphocyte serum, removing the thymus and spleen. The results included 7 survived dogs with transplanted paws and life spans from 24 to 300 days [5].

Let us repeat, however: a dog named Bratik, to whom A.G. Lapchinsky transplanted a limb from another dog in 1964 lived with the transplanted paw for more than 6 years. This situation is reminiscent of what happened with V.P. Demikhov's dog Grishka that lived for 141 days without immunosuppression in 1962. As the media wrote then, the dog of V.P. Demikhov “placed an atomic bomb under immunity.” Obviously, the same can be said about the achievement by A.G. Lapchinsky. However, these observations, which refuted all immunological postulates, were not subjected to any analysis by leading Soviet immunologists.

On the Scientific Research Program on the problem of organ and tissue transplantation

What “*ways of scientific research development*" did Yu.M. Lopukhin see "*on the problem of organ and tissue transplantation*” related to “*one of the rapidly developing areas of contemporary medical and biological science*”? For the purpose of a “*reasonable coordination of the efforts of a large army of scientists, a scientifically based distribution of material resources and in accordance with the most important areas of scientific research*” [1, p. 61]. R.V. Petrov, a surgeon and immunologist, was authorized to submit the all-Union Scientific Research Program on the problem of organ and tissue transplantation (Fig. 8). The Problem Commission on Organ and Tissue Transplantation

of the USSR Academy of Medical Sciences (chaired by Professor G.M. Solovyov, a Corresponding Member of the USSR Academy of Medical Sciences), individual scientists, as well as the Commission on the Problem Prediction (chaired by B. V. Petrovsky, the Academician of the USSR Academy of Sciences) were involved in working up this Program [1, p. 62]. Let's see if it was possible to assign some role to A.G. Lapchinsky or V.P. Demikhov and their research in this Program?

The problem of organ preservation implied an improvement of the methods for storing grafts from the moment they were taken from the donor to the moment of their transplantation to the recipient, and it was planned to solve the problem in the ways presented in diagram A (Fig. 9).

Let us pay attention to the Section “Preservation of organs and tissues in suspended animation” and its Subsections “Preservation of organs and tissues in a state of deep freezing” and “Preservation of organs and tissues in a state of reduced metabolism”. Paragraphs No. 1 and No. 2 "Preservation of organs and tissues in a state of deep freezes", and No. 4 "The use of moderate hypothermia for the preservation of organs and tissues" were directly related to the issues that had been developed by A.G. Lapchinsky.

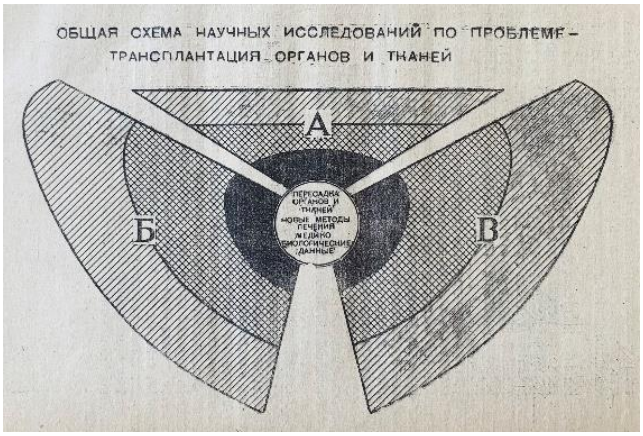


Fig. 8. General scheme of scientific research on the problem of organ and tissue transplantation. Yu.M. Lopukhin, 1971 [1, p. 70]

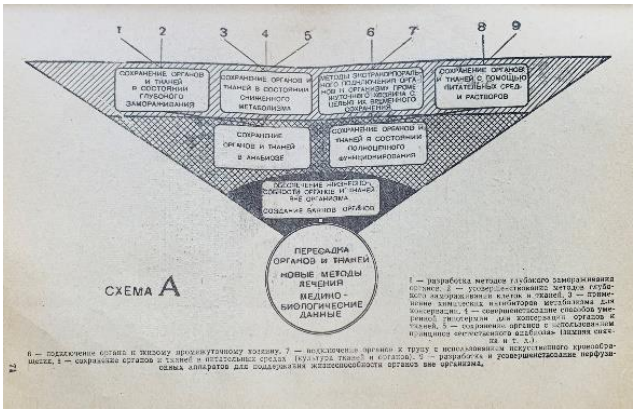


Fig. 9. Scheme A. Ensuring the viability of organs and tissues outside the body. Creation of an organ bank. Yu.M. Lopukhin, 1971 [1, p. 71]

And the paragraphs of the Section “Preservation of organs and tissues in a state of full functioning” and Subsection “Methods of extracorporeal connection of organs to the body of an intermediate host for the purpose of their temporary preservation” No. 6 "Connection of an organ to a living intermediate host" and No. 7 "Connection of an organ to a corpse using an AIK" could only be embodied into practice by V.P. Demikhov, since no one else in the country mastered those methods. He could also take part in the implementation of paragraph No. 9 "The development and improvement of perfusion devices to maintain the viability of organs outside the body", since he was interested in such devices.

Ways to solve clinical problems of transplanting the heart, kidneys, liver, limbs and other organs are presented in diagram B (Fig. 10). Let us note that the heart was mentioned the first organ among others, which transplantation V.P. Demikhov was dealing with; and limbs mentioned the last, which transplantation was the problem developed by A.G. Lapchinsky.

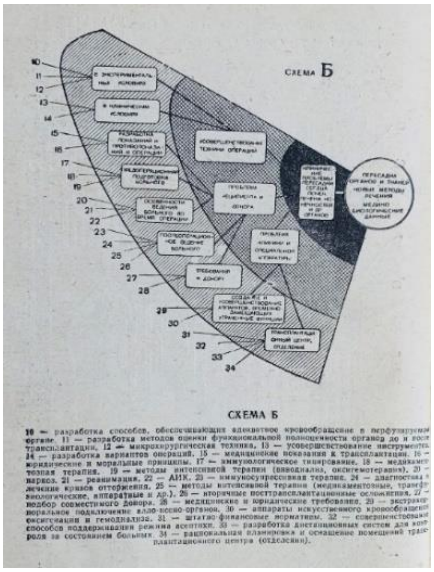


Fig. 10. Scheme B. Clinical problems of heart, kidney, liver, limb, and other organ transplantation and ways to solve them.
Yu.M. Lopukhin, 1971 [1, p. 72]

Here we turn our attention to the Section “Improving surgical techniques” and the Subsections “In experimental conditions” and “In clinical conditions”, in which all five paragraphs could well be realized by V.P. Demikhov and his collaborators: paragraph No. 10 "Development of methods to ensure adequate blood circulation in the perfused organ" (by V.P. Demikhov for heart, by L.L. Gugushvili for liver); paragraph No. 11 "Development of methods for assessing the functional usefulness of organs before and after transplantation" (V.M. Goryainov for heart; L.L. Gugushvili for liver); paragraph No. 12 "Microsurgical technique (V.P. Demikhov would also have been able to cope with this problem, because the talk was about suturing small-diameter vessels, which he encountered when developing the method of mammary-coronary bypass surgery); paragraph No. 13 "Improvement of instruments (suturing of vessels using M.M. Razgulov device); paragraph No. 14 "Development of options for operations (as for the heart, V.P. Demikhov had no equal in the

development of options for transplanting it; the same can be said about transplanting a kidney, liver and other organs).

As for other paragraphs, in the implementation of which V.P. Demikhov could take part, we can point out paragraph No. 29 "Extracorporeal connection of allo-xeno-organs" and paragraph No. 30 "AIK creation". We should note, however, that the creation of devices that "*temporarily relieve the work of a transplanted heart*" (as mentioned earlier), as well as the development of methods of assisted circulation, for some reason were not included in scheme B. A.G. Lapchinsky and the Laboratory he headed at the CITO named after N.N. Priorov could also take part in the development of techniques for operations on small-caliber vessels and in solving many clinical issues of allotransplantation of organs and limbs.

The problem of overcoming tissue incompatibility during transplantation and ways to solve it are depicted in diagram B (Fig. 11). Several areas are considered in this problem: the immunogenetic basis of transplantation, nonspecific methods of immunosuppression, the creation of specific tolerance and donor selection. Of these, the following ones can be attributed to V.P. Demikhov's research and developments: paragraph No. 44 "Methods of creating chimerism (barely, cross blood circulation); paragraph No. 58 "Study of the cellular and humoral factors of immunity (there were models, but there were no methods for studying them) and paragraph No. 60 "Study of the graft-versus-host reaction (there were models, but no methods). Let us draw the attention to the fact that there was not a single biological method of overcoming incompatibility (in particular, exchange blood transfusion, which V.P. Demikhov was actively involved in) in the scheme (and, therefore, in the plans). There was no place for A.G. Lapchinsky's approaches in solving this problem

with his methods of “cultivating tolerance” by transplanting limbs from newborn animals.

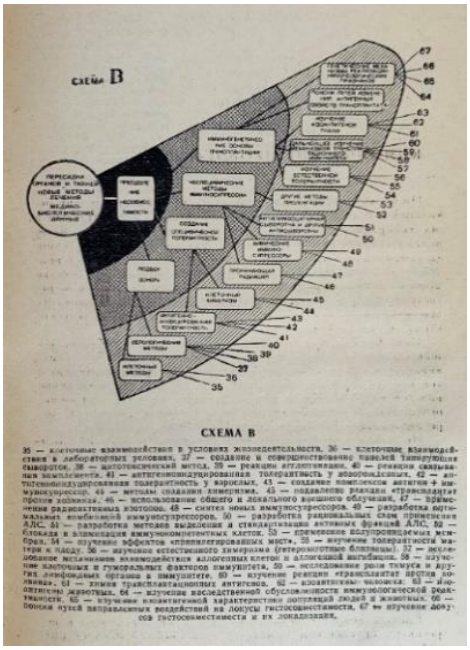


СХЕМА В

Fig. 11. Scheme B. Ways to overcome biological incompatibility of tissues in organ transplants. Yu.M. Lopukhin, 1971 [1, p. 73]

Thus, of 67 items for solving the problems of organ transplantation in the USSR in 1971, V.P. Demikhov and his employees could really take part in almost every fifth. So could the staff, perhaps in a smaller number, of the Laboratory headed by A.G. Lapchinsky, since he was not involved in organ transplants. However, in the conclusion of stated plans, Yu.M. Lopukhin dedicated only two lines to experimental surgeons: “*Experimental surgeons master the technique of kidney, liver, heart and other organ transplants, and study many issues of allotransplantation in animal experiments. Not everything is still clear in transplantation immunology, not all issues have been resolved in experimental surgery*" [1, p. 76]. And although the issues of limb transplantation were included in Scheme B, they were hardly considered promising. It turned out that

neither A.G. Lapchinsky, nor V.P. Demikhov fitted into contemporary schemes for the development of transplantology any longer.

Now let's see what issues of the assisted circulation and artificial heart, the problems posed by Yu.M. Lopukhin were discussed at the XXIV Congress of the International Society of Surgeons held in conjunction with the X International Congress on Cardiovascular Diseases.

X International Congress on Cardiovascular Diseases. Moscow, August 26–28, 1971

At the Congress, which was chaired by Academician B.V. Petrovsky, the USSR Minister of Health, held for the first time in the Soviet Union, almost all the main areas of surgery for the diseases of the heart, great and peripheral vessels were discussed. Many Soviet surgeons took part in the work of the Congress, including the main personalities of our article: 47-year-old Yu.M. Lopukhin, 55-year-old V.P. Demikhov, and 63-year-old A.G. Lapchinsky (Fig. 12).

Fig. 12. At the X International Congress on Cardiovascular Diseases (from left to right): V.P. Demikhov, A.G. Lapchinsky, Yu.M. Lopukhin. Moscow, August 27, 1971

At the Session "Assisted circulation and artificial heart" there were presentations on:

- Issues of development and application of venous-arterial bypass with extracorporeal oxygenation and arterio-arterial counterpulsation in experiment (V.I. Shumakov et al., Moscow), in experiment and in clinic (R.A. Deterling et al., Boston, USA), in clinic (E.I. Chazov et al., Moscow);
- Development and use of ventricular assist devices and orthotopic heart replacement in experiments[11] (V.I. Shumakov et al., Moscow);
- The use of long-term normo- and hypothermic perfusion using AIK in experiment (A.L. Mikaelyan et al., Yerevan, Armenian SSR);
- The use of venous-arterial perfusion to unload the right heart, and ventricular assist devices to support the left heart function in experiment and in clinic (S.I. Skorik et al., Leningrad);
- The use of complete, parallel and regional artificial circulation using heart-lung machines of various designs in experiment and in clinic (G.L. Ratner and V.D. Ivanova, Kuibyshev);
- The use of AIK ISL-2, ISL-4 and AIC-60 in experiments and in clinic in the injuried with severe combined trauma and traumatic shock (V.P. Radushkevich et al., Voronezh);
- The use of left-side bypass by using ventricular assist devices full cardiopulmonary bypass with a Heart-Lung machine and counterpulsation in clinic (C. Dennis et al., Brooklyn, USA);
- The use of a Heart-Lung machine to prepare the patients in end-stage cardiopulmonary failure for surgery (J. Kennedy, Houston, USA) [10, p. 187–214].

The last three presentations at that Session concerned experimental transplantology. One of them, entitled “Orthotopic heart-lung transplantation in rats,” was prepared by a group of New York surgeons

[11] By that time, the Research Institute of Clinical and Experimental Surgery of the USSR Ministry of Health (Director: Academician of the USSR Academy of Sciences B.V. Petrovsky) had developed more than 20 models of ventricular assist devices.

led by C. W. Lillehei, a pioneer in open-heart surgery. There were several goals in their study: reducing the cost of experiments by eliminating heart transplants in dogs, developing a method of heart and lung transplantation in rats using microsurgical techniques, developing a method of electrodiaphragmatic stimulation of transplanted lungs, evaluating the methods for controlling an allograft rejection, elucidating the role of chemical mediators of the hypersensitivity reaction in acute and chronic rejection, and improving the results of cardiopulmonary complex transplantation in clinic [10, p. 215–216].

Another presentation on the topic "Cardiopulmonary autotransplantation in primates (baboons)" was made by a group of surgeons from the University of Minneapolis under the leadership of A.R. Castaneda, no less famous than C.W. Lillehei. The objective of their study was to achieve longer survival times than in dogs after *autotransplantation of* cardiopulmonary complexes. Of the 23 animals, 3 survived, with only one baboon living for a year. However, the authors of the presentation came to the conclusion that denervated heart and lungs are capable of providing circulatory and breathing functions for a long period of time [10, p. 217–218].

One more presentation "On new methods of connecting a transplanted natural and artificial heart to create additional blood circulation," was made by V.P. Demikhov, M.N. Anichkov, I.V. Vigdorchik, M.M. Razgulov, and N.M. Anichkov. V.P. Demikhov and M.M. Razgulov were representatives of the N.V. Sklifosovsky Research Institute for Emergency Medicine, the other co-authors were from the Surgical Service of the Moscow Military District (MVO), whose Chief Surgeon was Professor M.N. Anichkov. The presentation covered the development of methods for temporary support of blood circulation and respiration in life-threatening cases by connecting the patients with severe

cardiopulmonary failure or heart transplant recipients to: (1) the human cardiopulmonary complex (CPC) (at the same time, as the authors stated, “the natural heart and lungs, accounting the compatibility of blood groups, can support extracorporeal blood circulation for several days and even weeks”; the authors said nothing of what the patient would feel during that time, being next to the beating heart and breathing lungs, who would care for them and how); (2) CPC of a pig or monkey after preliminary washing it with human donor blood of group I (0) or blood compatible with the recipient’s blood group.

But if the CPC of an animal can be extracted in a functioning condition, then in a human this is possible only after death. Therefore, to revitalize cadaveric organs, the authors improved direct cardiac massage and designed a portable artificial heart. Finally, to provide an assisted blood circulation, the authors developed the methods of transplanting an additional heart into the chest of animals with one (Fig. 13) or two lungs and creating a parallel blood circulation; and in order to reduce the surgery duration, they used a vascular stapling device designed by M.M. Razgulov [10, p. 219–221] (Fig. 14).

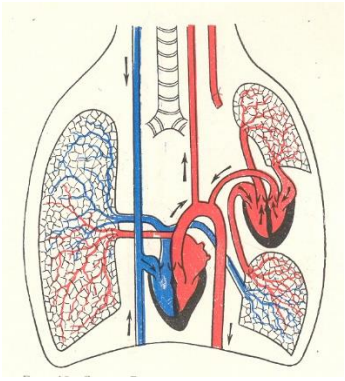


Fig. 13. Scheme of bypassing the left heart using a second additional heart transplanted together with the upper lobe of the lung.

V.P. Demikhov, 1960 [3]

Fig. 14. M.N. Anichkov (left), the Chief Surgeon of the Moscow Military District, Professor, the Colonel of Medical Service; V.P. Demikhov (in the center); and I.V. Vigdorchik (right), the Colonel of the Medical Service, are discussing vascular stapling devices designed by M.M. Razgulov. Moscow, 1971

If we comment on these presentations from the perspective of today, then the first two methods proposed by V.P. Demikhov (using the CPC of a corpse or an animal), even at that time were clearly not suitable for use in clinic and sounded archaic against the background of other reports, as, indeed, was the transplantation of a second additional heart into the chest cavity against the backdrop of reports on the heart bypass using ventricular assist devices, an artificial hearts and portable AIKs. And even mentioning a “portable artificial heart” invented by V.P. Demikhov once for the first time in the world, raised neither surprise, nor admiration: too many in the USSR and abroad were already actively engaged in this subject both in experiment, and in clinic.

Conclusion

We have analyzed the state of the organ transplantation problem in the USSR in the early 1970s and the ways to solve it, as well as some world achievements in this area. The Program of Scientific Research on the problem of organ and tissue transplantation developed in 1971 by leading surgeons and immunologists of the Soviet Union headed by the

Corresponding Member of the USSR Academy of Medical Sciences Yu.M. Lopukhin included three main objectives: resolving clinical problems of transplantation of organs and body parts (limbs), ensuring the viability of organs and tissues ex vivo and the ways to overcome biological incompatibility, including moral and ethical issues of transplantation and donation issues.

During those same years, two leading world-famous experimental surgeons A.G. Lapchinsky and V.P. Demikhov actively worked in the USSR. However, methods for overcoming biological incompatibility in allotransplantations of organs and tissues, which they had developed over many years (exchange blood transfusion between organisms of different species, cross-circulation between individuals of the same species, etc.), no longer corresponded to the state of medical science, which was represented by Yu.M. Lopukhin. Meantime, having world-class priorities for the survival duration in experimental animals A.G. Lapchinsky (and his dog Bratik with a transplanted limb), and V.P. Demikhov (and his dog Grishka with an additional heart and lung transplanted into the chest) possessed methods that could have helped in implementing some provisions of Yu.M. Lopukhin's Program. The organ and tissue preservation in a state of suspended animation (anabiosis) before transplantation was studied by A.G. Lapchinsky, and the development of methods for extracorporeal connection of organs to the body of an intermediate host and the use of portable artificial hearts to maintain the vital activity of a cadaveric heart before transplantation was undertaken by V.P. Demikhov. These scientists could also have solved many technical issues of organ and body part (limb) transplants. But in the Program of Scientific Research on the problem of organ and tissue transplantation, which was focused on immunological research, the experimental surgeons were assigned a minor role.

Thus, once ahead of time and all his colleagues, V.P. Demikhov gradually began losing momentum and lagged further and further behind world and homeland transplantology, and his fantastic methods began fading into history. Why did it happen? But this is the “Demikhov phenomenon” that we have in store to formulate.

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