https://doi.org/10.23873/2074-0506-2021-13-4-398-416

PHENOMENON OF DEMIKHOV

At N.V. Sklifosovsky Institute (1960–1986).

V.P. Demikhov and world transplantology in 1968-1969

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Abstract

The article has reviewed the advances of Soviet and world Transplantology in the field of heart and other organ transplantation achieved by the end of the 1960s. It is shown that there were several groups of doctors and scientists who worked in the USSR dealing with the problem of experimental organ transplantation and trying to bring this experience into clinic. The group of surgeons and urologists (B.V. Petrovsky, Y.M. Lopukhin, etc.) from the Research Institute of Clinical and Experimental Surgery and the 2nd MOLGMI named after N.I. Pirogov, which had the greatest administrative resources and technical capabilities, was successfully implementing kidney

transplantation into clinic. The staff of the Faculty Surgery Department (V.S. Savelyev and others) of the 2nd MOLGMI named after N.I. Pirogov developed experimental approaches to heart and liver transplantation. Surgeons from the Tuberculosis Research Institute (N.I. Gerasimenko and others) were dealing with in lung auto- and homotransplants in experiment. All those studies were conducted in close contact with the Department of Operative Surgery and Topographic Anatomy of the 2nd MOLGMI named after N.I. Pirogov (G.E. Ostroverkhov) and the Research Laboratory for Organ Transplantation established at that Department (Y.M. Lopukhin). The leading position in heart transplantation in the country belonged to the Vishnevsky Institute of Surgery (A.A. Vishnevsky, etc.). Surgeons of the MMA named after S.M. Kirov (I.S. Kolesnikov, etc.) rendered a great assistance to the Institute. Apart from these institutions, the Organ Transplantation Laboratory (headed by V.P. Demikhov) worked at N.V. Sklifosovsky Research Institute for Emergency Medicine; it had gained a huge experimental experience, but had very modest opportunities to purchase equipment and pharmaceuticals, to conduct laboratory and morphological studies, having practically no prospects for introducing the results of its research into clinic. Meanwhile, the world clinical Transplantation continued to develop successfully, which was reflected in the materials of the 2nd International Symposium on Heart Transplantation held in 1969 in Montreal (Canada).

Keywords: V.P. Demikhov, Soviet transplantology, world transplantology, 1968-1969

Conflict of interests Author declares no conflict of interest

Financing The study was performed without external funding

For citation: Glyantsev SP. Phenomenon of Demikhov. At N.V. Sklifosovsky Institute (1960–1986). V.P. Demikhov and world transplantology in 1968–1969. *Transplantologiya. The Russian Journal of Transplantation.* 2021;13(4):398–416. (In Russ.). https://doi.org/10.23873/2074-0506-2021-13-4-398-416

CPB pump, cardio-pulmonary bypass (pump)/heart-lung machine

ALS, anti-lymphocytic serum

MMA, Military Medical Academy named after S.M. Kirov

SVC, superior vena cava

EC, extracorporeal circulation (assisted blood circulation)

PA, pulmonary artery

IVC, inferior vena cava;

ECG, electrocardiography

ECP, electric cardiac pacemaker

EEG, electroencephalography

The first clinical heart transplantation in Czechoslovakia and the "wait-and-see" approach of Soviet surgeons

From December 3, 1967 to July 2, 1968, a total of 24 heart transplants were performed worldwide. But all of them were performed in the so-called capitalist countries. Finally, on July 9, 1968, the first heart transplant outside the Iron Curtain and the 25th one in the world was performed. But it was not in the Soviet Union, but in Czechoslovakia.

The Pittsburgh Post-Gazette was the first to respond to this event. On the evening of July 9, 1968, in the article entitled "Czech widow received a new heart", subtitled "the First heart transplant in Eastern Europe" and with reference to the United Press International News Agency (UPI, USA), the

author reported that a group of Czech surgeons transplanted the heart of the 40-year-old men to a 50-year-old woman by the name Horvathova admitted in the clinic in critical condition with severe heart disease. The operation lasted for more than 6 hours. The transplanted heart functioned normally. At the end, the newspaper item reported that last week the condition of P. Blaiberg, the second patient of C. Barnard, worsened, and that surgeons decided to give him a second heart transplant, possibly combined with his lungs. [1] However, the next day, in an article entitled "Czechoslovak citizen with heart transplant is dying" with the subtitle "Widow was the first *red* recipient (italics ours. – Auth.), the same newspaper reported on the death of 49-year-old Helena Horvathova. It was also mentioned that a group of surgeons led by K. Šiška (Fig. 1) had been preparing for that operation for a long time. During the previous 2 months, 3 patients were waiting for a heart transplant, but all of them died without waiting for a donor [2].

Fig. 1. Professor Karol Šiška (1906-2000), a Full Member of the Czechoslovak Academy of Sciences, a Foreign Member of the USSR Academy of Sciences and the USSR Academy of Medical Sciences, a pioneer of heart transplantation in Eastern Europe. Available at: http://isaran.ru/?q=ru/person&guid=A876E54B-7D75-B4D3-1E01-F1A1FF332BAC

More detailed and accurate information about the operation was published in the Schenectady Gazette Gazette, which reported on July 10 that a group of surgeons from the Cardiology Clinic of Bratislava University Hospital performed the first heart transplant in the socialist camp countries the day before:

"The recipient, a 54-year-old woman from Bratislava, suffered from such severe heart failure due to a valvular defect that surgeons decided that a heart transplant would be less dangerous for her than valve surgery.

The donor was a 46-year-old man who fell from the balcony of his own house on the morning before the operation. On the night of July 8 to 9, his brain stopped working, his heart stopped, but the doctors "started" it artificially.

The group of 22 surgeons who performed the transplant was headed by Academician Karol Šiška. It included Dr. Ladislav Kuzela, one of the most famous cardiac surgeons in Czechoslovakia. The donor's heart was harvested by Professor Vladimir Haviar.

For 5 hours after the operation, the woman remained in the operating room. She was unconscious, but the EEG showed that her brain was functioning normally, and the graft contracted without electrical stimulation. However, the woman soon died from bleeding.

"The transplanted heart was contracting well, but we had a problem with bleeding from the sutures, so the prognosis was disappointing," said Ivo Sobiesky, Head of the Anesthesiology team.

The most interesting thing was contained further in this material. The newspaper's reporter, as if to justify the fact that the first heart transplant in a socialist country was performed by Slovak rather than by Soviet doctors, tried to smooth the situation:

"Doctors from the Soviet Union, the nominal leader of the Eastern Bloc countries, apparently have refused (literally: *are shying away*. - *Auth.*) from human heart transplantation, although we have conducted many experiments with various types of transplants on animals.

Shortly after Dr. Christiaan N. Barnard performed the world's first successful operation, and then he and other surgeons performed three more, the USSR Health Minister Boris Petrovsky expressed his doubt that these patients would survive.

"Soviet surgeons are developing the problem of transplanting a living human heart systematically and very carefully," he said in January 1968[1]." Since the problem of immunological incompatibility has not yet been solved, our further efforts will be directed at creating an artificial heart."

However, of the 24 transplants performed before this operation, 7 patients survived, including 59-year-old Dr. Philip Blaiberg from Cape Town, South Africa, whose life span is the longest" [3, p. 7][2].

Thus, the first heart transplant in Eastern Europe was performed by Slovaks, and Slovak journalists explained their priority by the "caution" of their Soviet colleagues. In addition, the primacy of foreign doctors in Soviet medicine at that time was not welcomed, as it seems. The so-called struggle against cosmopolitanism in science, which took place in the 1950s, was still fresh in the minds of doctors. Here, for example, is how Professor S.A. Kolesnikov, the Director of the Cardiovascular Surgery Institute of the USSR Academy of Medical Sciences, reflected this opinion in spring of 1966 in a report at the Anniversary Session of the Cardiovascular Surgery Institute of the USSR Academy of Medical Sciences:

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1 Apparently, the date is not accurate, since the 4th heart transplant operation in the world was performed by Shumway on June 1, 1968.

2 The number after the comma in square brackets indicates the page number in the source.

"It should be recognized as a sign of bad taste statements that, they say, this or that "first" operation was performed. The first operations are not so many, they are more repeated. We consider it more important to develop an operation in which, along with the demonstrated skill of the surgeon, thorough physiological, biochemical and pathomorphological studies were carried out, making the understanding of the disease pathology and therapeutic measures accessible to a wide range of specialists" [4, XLI].

Given the fact that the session was attended by a large number of surgeons from other medical institutions, it is obvious that the majority of Soviet doctors shared the same opinion. Who disputes the importance of conducting "thorough physiological, biochemical, and pathologic studies" both before and after the first operation, and then developing it so comprehensively and thoroughly that it will be accessible to "the general public"?

But no operation can be implemented in clinic until it has been performed by someone. So someone has to go first. Why did the largest Soviet breast surgeons A.N. Bakulev, P.A. Kupriyanov, A.A. Vishnevsky, B.V. Petrovsky, E.N. Meshalkin and others not manage to transplant the heart first in the world or, for example, before their Slovak colleagues, preferring "planned and careful" development of the problem? The question is rhetorical.

Development of the problem of heart and other organ transplantation in the Organ Transplantation Laboratory of the N.V. Sklifosovsky Research Institute for Emergency Medicine (1962-1968)

Recall that V.P. Demikhov was appointed an Acting Head of the Organ Transplantation Laboratory at the N.V. Sklifosovsky Institute in September 1960. In 1962, he was elected to this position. Five years passed. On January

31, 1968, at the Meeting of the Institute's Academic Council, V.P. Demikhov was re-elected for a new 5-year term; 22 members of the Academic Council voted for it. There were no "black balls" [5, pp. 47-54]. According to the staff schedule in his laboratory at that time, in addition to the Head, the staff included: L.L. Gugushvili, Candidate of Medical Sciences, a Senior Researcher, who collected material for a doctoral dissertation on liver transplantation, 3 Junior Researchers (including V.S. Nepomnyashchaya, Candidate of Medical Sciences), a Laboratory Physician V.M. Goryainov, a Senior Nurse, 4 Laboratory Assistants and an Orderly. A total of 12 people (although it was not the fact that all positions were taken) [6]. And on March 27, 1968, at the Meeting of the Academic Council, presentations were made by the Head of the Organ Transplantation Laboratory (V.P. Demikhov), the Head of Anesthesiology Laboratory (B.V. Chetverushkin), and the Head of the Intensive Care Unit (L.L. Stazhadze).

V.P. Demikhov briefly spoke about his work before joining the Institute and about the research he conducted from 1960 to 1968, namely: experimental transplantations of the heart, lungs, kidneys, liver, sternum, duodenum, head, etc. He illustrated his presentation with drawings, diagrams and demonstration of V.F. Gudov-designed vascular stapling device (Fig. 2). The questions he was asked by I.I. Sokolov, E.N. Popov, D.A. Arapov, T.A. Malyugina and other participants of the Meeting were about immunological studies, determining the future trends of research, possibility of organ transplantation in clinic, detailed preparation for heart transplantation surgery and the transplant surgical technique, which four months earlier had been performed by C. Barnard.

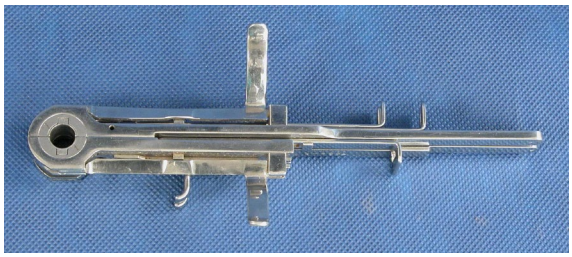


Fig. 2. The ASC-20 vascular circular stapling device designed by V.F. Gudov. 1950s. [From the collection of the Museum of A.N. Bakulev National Medical Research Center of Cardiovascular Surgery]

After V.P. Demikhov answered the questions, the debate began. E.N. Popov spoke about the importance of research in the field of organ transplantation, the importance of home-land priorities in this area, recommended this work to be continued within the walls of the Institute and advised to help V.P. Demikhov in their implementation.

Professor I.M. Grigorovsky, emphasizing that the report on the work of the Laboratory was delivered for the first time since 1960, noted that it would help the Institute's employees to get better acquainted with the work of the Laboratory. Special attention, according to I.M. Grigorovsky, should be paid to the fact that the Head of the Laboratory is a biologist, rather than a doctor, so the implementation of the results of his research in practice requires the involvement of clinicians. Moreover, the speaker stressed that the topic of organ transplantation "is being brought to the forefront of medical science", the N.V. Sklifosovsky Institute, having great opportunities to solve this problem, should become "one of the pioneers in the implementation of the tasks set for medicine".

Director of the Institute M.M. Tarasov told about the path that V.P. Demikhov took before joining the N.V. Sklifosovsky Institute, and what he managed to do in the Institute. But what M.M. Tarasov reported further is doubtful. First, he said that C. Barnard not only came to Moscow (which corresponds to reality), but also worked in the Laboratory of V.P. Demikhov (we were not able to document this fact [7]). Second, M.M. Tarasov claimed that in previous years the attitude of the Institute's scientists towards V.P. Demikhov's Laboratory "had become more favorable". But if for 7 years the Academic Council had never taken an interest in V.P. Demikhov's research, and the main reason for rejecting him the title of a Corresponding Member of the USSR Academy of Sciences in 1966 was the ignorance of the members of the Academic Council of what research he was making, M.M. Tarasov's statement about the "favorable" attitude of the Institute's scientists to V.P. Demikhov's work, in our opinion, was exaggerated.

The Academic Council Resolution on the topic that was being "brought to the forefront of medical science" was brief: "Take the reported presentation into account" [5, pp. 96-98]. At the same time, I.M. Grigorovsky was absolutely right: without the participation of clinicians, V.P. Demikhov alone could not have introduced anything into practice. But none of the leading surgeons of the Institute (B.A. Petrov, D.A. Arapov or P.I. Androsov) spoke in the debate.

Were there any conditions in N.V. Sklifosovsky Institute for clinical heart and other organ transplants at that time? Unfortunately, this question has to be answered in negative. In addition to the lack of interest of surgeons, this can be indirectly judged by the presentation from the Intensive Care Unit, which was made at the same meeting after V.P. Demikhov's presentation. It turned out that the Unit was established in September 1967

on the basis of the Anti-shock Unit at the Emergency Room. The great organizational and clinical work of the Intensive Care Unit was covered in the presentation, but the first questions asked by V.P. Demikhov put L.L. Stazhadze in a dead end. They were like that. Did the Unit carry out work on revitalizing organs for transplantation? Does the Unit plan to purchase a cardio-pulmonary bypass (CPB) pump (a heart-lung machine)? The answers to both questions were negative, after which V.P. Demikhov summarized that without a CPB pump, it was impossible to revitalize organs and transplant the heart and lungs. That summary did not raise any objections among the participants. At the same time, taking into account the need for joint work of anesthesiologists and intensive care physicians, it was decided to establish an Anesthesiology and Critical Care Department to replace for the Anesthesiology Laboratory and the Intensive Care Unit. The new Department was headed by B.G. Zhilis who was elected its Head on May 22, 1968 [5, p. 180-181].

On September 11, 1968, the new Director of the N.V. Sklifosovsky Institute, Professor B.D. Komarov, took part in the meeting of the Academic Council of the Institute for the first time [8, p. 97].

Nevertheless, V.P. Demikhov's Laboratory worked and even achieved certain results. The 1968 Report on the Scientific Activities of N.V Sklifosovsky Institute named 4 main Research Programs that defined the "scientific profile" of the institution: (1) Hypertension disease, Atherosclerosis, Coronary and Heart Failure; (2) Trauma and Traumatism; (3) Abdominal Surgery; (4) Acute Poisoning and its Control [9, p. 7].

We found the Research Reporting Sheets of the Organ Transplantation Laboratory in Research Program 2 "Trauma and Traumatism" among the Research Reporting Sheets on the topic "Transplantation and preservation of

organs and tissues". There were four Research Reporting Sheets. Here are their contents.

"Reporting Sheet No. 44.

Topic: Experimental heart and lung transplantation and anatomical development of heart and lung transplantation methods on human corpses.

Supervisor: V.P. Demikhov.

Investigators: V.P. Demikhov, L.L. Gugushvili.

Start: transferred from previous years.

End date: December 1968

Type of investigation: experimental, laboratory, morphological.

Type of work: article.

Abstract: Experimental organ transplantation approaches the human clinic. There is a need for anatomical development of various heart and lung transplantation options on human corpses that can be used for clinical application. In total, more than 40 methods of heart and lung transplantation were developed in the experiment. For clinical use, a heart and lung transplant option (this is 2-stage transplantation. – *Auth.*), developed on corpses, can be applied in the appropriate conditions.

Results: scientific and practical recommendations" [9, p. 81].

"Reporting Sheet No. 45.

Topic: ECG studies in heart homotransplantation.

Supervisor: V.P. Demikhov.

Investigators: V.M. Goryainov.

Start: previous years.

End date: December 1968

Type of investigation: experimental.

Type of work: article.

Abstract: in numerous experiments on heart transplantation, more than 1000 ECGs were taken, which were processed and studied.

Results: will be presented in press " [9, p. 82].

"Reporting Sheet No. 46.

Topic: Liver transplantation in an experiment.

Supervisor: V.P. Demikhov.

Investigators: V.P. Demikhov, I.M. Grigorovsky, L.L. Gugushvili[3].

Start: previous years.

End date: December 1968

Type of investigation: experimental.

Type of work: article, report.

Abstract: new liver transplant options were developed in an experiment. The results were reported at the Moscow Surgical Society Session. Details of liver transplantation in dogs (orthotopic and heterotopic transplants) are highlighted [9, p. 83].

Results: article (published in the journal "*Klinicheskaya Khirurgia*" [Clinical Surgery] [10].

"Reporting Sheet No. 47.

Topic: Physiological method of preserving revitalized organs for human transplantation.

Supervisor: V.P. Demikhov.

Investigators: V.P. Demikhov (together with the Intensive Care Unit).

Start: previous years.

End date: December 1969

Type of investigation: experimental.

Type of work: article.

Part of the research was performed in 1968: creating physiological conditions (blood circulation, respiration, nutrition) to maintain the function and preserve revitalized organs for human transplantation.

Abstract: in an experiment dated back to 1948, we developed a method for preserving revitalized organs under physiological conditions. Similar conditions can be

3 In 1965, L.L. Gugushvili defended his doctoral thesis on: "Surgical venous anatomy and liver circulatory pathology issues".

created for the preservation of revitalized organs extracted from human corpses in the first hours after death. The conducted research suggests that it will be possible to create a stock of revitalized organs for human transplantation.

Results: The research will be continued in 1969" [9, p. 84].

The Reporting Sheets in other topics from V.P. Demikhov's Laboratory were missed. The topic of Kidney Preservation was developed by the Cadaveric Blood Transfusion Laboratory (G.A. Paphomov) and the Pathology Department (N.K. Permyakov), but the issue of kidney transplantation was not raised in the clinic [9, p.85].

In the 1st Therapy Clinic, 172 patients with myocardial infarction (32 of them or 15% died), 207 with angina pectoris (all survived), and 63 with coronary cardiosclerosis (12 patients or 17% died) received treatment during a year. However, there was no talk of introducing the surgical treatment method for coronary insufficiency by applying a mammary-coronary anastomosis, which V. P. Demikhov had been talking about for almost 15 years [11].

Thus, in 1968, when more than 90 human heart transplants had been performed using biatrial Lower–Shumway technique, including the first heart transplant in Czechoslovakia; and the surgeons in many hospitals around the world began to transplant lungs, kidneys and liver, V.P. Demikhov was still trying to overtake the world transplantation, or at least keep up with it. He developed an anatomical method of heart transplantation on a human cadaver, studied the heart function during homotransplantation using electrocardiography (ECG), transplanted liver in an experiment, and continued to improve the physiological system, which he invented in the late 1940s for preserving revitalized organs. As we will show below, all these areas were still quite relevant at that time.

Development of the issue of heart and other organ transplantation in a Problem Laboratory for Organ Transplantation of the 2nd MOLSMI named after N.I. Pirogov of the RSFSR Health Ministry, the Research Institute of Clinical and Experimental Surgery of the USSR Health Ministry, at the Faculty Surgery Department of the 2nd MOLSMI named after N.I. Pirogov and the Research Institute of Tuberculosis of the USSR Academy of Medical Sciences (1960s)

On January 30, 1969, "the first book in our country", as its annotation put, which "based on the own material of a large team of authors" covered "the most important issues of organ transplantation" was submitted for publication to the *Meditsina Publisher's* (Fig. 3) [12]. The book was written by a team of surgeons and scientists who worked in the Problem Laboratory for Organ Transplantation (headed by Yu.M. Lopukhin) or together with that Laboratory. The Laboratory was established in 1966 at the Department of Operative Surgery and Topographic Anatomy (headed by G.E. Ostroverkhov) of the 2nd MOLSMI named after N.I. Pirogov of the RSFSR Health Ministry.

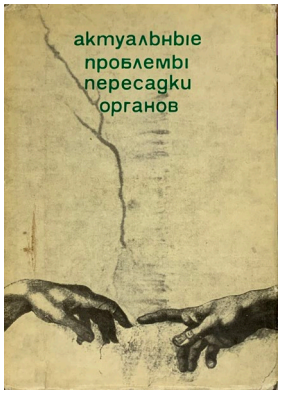


Fig. 3. Lopukhin Yu.M. (ed.) *Actual issues of organ transplantation*. Moscow: Medicine Publ.; 1969. Book dust jacket

Chapter 10 on heart transplantation is preceded by an extensive introduction to the history of experimental heart homotransplantation starting from the studies of F.C. Mann et al. (1933) in donor heart transplantion onto the vessels of the neck and graft survival up to 8 days, and ending with orthotopic heart transplants under conditions of extracorporeal blood circulation (EC), and immunosuppression undertaken by R. Lower and N. Shumway from 1963-1965 with a dog survival for from 21 to 250 days. Among the pioneers who studied this problem, V.P. Demikhov was mentioned, but only as the creator of three (!? – *Auth.*) options of heterotopic second heart transplantation. Against the background of numerous data on the survival of animals by other authors, V.P. Demikhov's data on the survival of his dogs were not given [13].

"Own material" was as follows. During 1967, a group of surgeons led by V.S. Savelyev performed 43 heart homotransplantation operations using the Lower–Shumway biatrial method (1960). Before the operation, the donor and recipient were not examined for biological compatibility, that is, the choice of pairs was random. All operations were performed under normothermal EC conditions using *AIK-63* CPB pump. The investigation covered the following: the methods of donor anesthesia, removal and perfusion of an isolated graft, its preservation in a cold solution under high oxygen pressure in a specially designed pressure chamber (Fig. 4), methods of recipient anesthesia, implantation ("stitching") of the heart and restoration of its activity; impairments of acid-base balance during the recipient perfusion; the management in the postoperative period, including temporary resumption of IC to unload the transplanted heart for the period of its adaptation to new conditions. It should be noted that, first, all the above-

mentioned methods were applied after a thorough study and analysis of literature, mainly foreign, reports and without references to V.P. Demikhov's works. Second, the authors did not use immunosuppression, since the purpose of their experiments was to work out the heart transplant technique and identify its "weak" links. In addition, in their opinion, the global trend was to create artificial tolerance in the recipient's body not by pharmacological immunosuppression, but by using the so-called antigenic load (immunological paralysis), which V.P. Demikhov once had written a lot about, but which was no longer relevant in the world of transplantation.

Fig. 4. TBSh-1 pressure chamber for the isolated heart preservation under increased oxygen pressure conditions [12]

In the transplantation period, various ECG-related cardiac disorders were observed: extrasystole, atrioventricular block, atrial and ventricular tachycardia, and cardiac arrest. The causes of animals' death named were bleeding, technical errors and cardiac weakness at early stages, atelectasis, inflammation and purulent lung damage, empyema and graft rejection ("immunological conflict") at later stages. Morphological and histochemical

studies of the myocardium of the transplanted hearts were performed. Survival data were not provided.

Despite no special selection of dogs for the experiments, it was concluded that "the success of heart transplantation depended primarily on selecting the graft that would have the most in common by its properties with the recipient." The second conclusion was that the problem of preserving [graft] preservation had been solved, although the world experience showed the futility of this direction. Finally, the third conclusion concerned solving the "problem of compensation for early circulatory failure of the recipient". As a priority, it was decided to create a "mechanical heart" capable of supporting the activity of the transplanted organ in the early postoperative period (by analogy with an" artificial kidney") [13].

It is clearly seen that V.P. Demikhov went through the technical and partly theoretical chapter of what V.S. Savelyev group was engaged in, independently, without regard for world surgery. So, to overcome biological incompatibility, he practiced cross-blood circulation, which in a certain sense can be attributed to the "antigenic load". Without applying EC, he transplanted a beating heart. To create an "organ bank", he did not preserve the cadaveric organ, but proposed to keep it in a working state under physiological conditions. To maintain the function of the transplanted organ, he had his originally developed "mechanical heart", which V.S. Savelyev was going to create.

In addition to surgical solutions to the problem, P.V. Sergeev's group (V.I. Kostrykin, V.A. Chistyakov, and others), working under the guidance of Yu.M. Lopukhin, detected a systemic reaction of the body to homotissue, which was manifested by intima alteration, platelet aggregation, and arterial thrombosis. The important role of thrombosis in the pathogenesis of

rejection was proved by K.M. Lapkin's group. V.P. Demikhov observed this phenomenon many times, considering it a violation of the vascular anastomosing technique.

Let us name the groups that developed other areas of transplantation within the walls of this Laboratory: N.A. Lopatkin, I.N. Kuchinsky, Yu.A. Pytel, and others were engaged in kidney homotransplantation in clinic; G.E. Ostroverkhov, Yu.E. Berezov, V.R. Anakhasyan, E.F. Malyugin and others were dealing with experimental ortho- and heterotopic liver transplantation; N.I. Gerasimenko, M.M. Averbakh, E.M. Kogan, G.V. Latsis and others investigated experimental auto- and homotransplantation of lungs. They were all big scientists and surgeons who headed powerful research teams. Moreover, as Yu.M. Lopukhin wrote in the Preface to the book, "our own and foreign experimental data indicate that homotransplantations of the liver, heart, and lung is quite possible and technically feasible in humans" [12, p.7]. Starting in 1947, when V.P. Demikhov joined the Vishnevsky Institute of Surgery, he pursued exactly the same goal. But over the course of 20 years, none of the leading Soviet surgeons and clinicians had been able to use his achievements, vast experience, and intuition.

Development of the heart transplantation problem at the A.V. Vishnevsky Institute of Surgery of the USSR Academy of Medical Sciences of the (1963-1968)

At the beginning of 1969, for the first time in the Russian literature, the entire issue of one of the USSR leading surgical journals, the journal "Experimantalnaya Khirurgia i Anesteziologia" [*Experimental Surgery and Anesthesiology*], was devoted to homoplastic heart transplantation. The

journal issue was opened with the article by V.P. Demikhov entitled "Transplantation of the heart, lung, and other organs". The article *dedicated to the memory of A.V. Vishnevsky* became a kind of the scientist's report on the work V.P. Demikhov had done since 1940, and then, with a break for the war, from 1946 to 1968. V.P. Demikhov emphasized that he was the first who performed transplantation of the second, additional heart into the chest cavity. The development of 40 variants of the anatomical connection of the donor and recipient main vessels for over 20 years was due to the complexity of the cardiovascular system of higher animals, including the dog. Depending on which recipient's vessel the donor heart vessel was connected to, different conditions of its functioning were created. For example, when it was connected in parallel, both organs worked synchronously, receiving blood from the lungs and pushing it into the common aorta (Fig. 5). In this case, the second heart took on half the volume of circulating blood, unloading the biological heart. The more blood the donor heart pumped, the easier it was for the recipient's heart to work. This idea of V.P. Demikhov, he was also the first to have implemented, forms the basis of the today concept of auxiliary blood circulation, when the role of the second heart is performed by a mechanical ventricle. V.P. Demikhov called the first cardiopulmonary complex transplant he performed on October 20, 1946, another major global achievement. The next invention by V.P. Demikhov concerned heart and lung transplantation in clinic. Well aware of the homograft possible rejection, he suggested transplanting the cardiopulmonary complex in two stages: first, on the vessels of the thigh (according to the principle of connecting the EC), placing the organs in a transparent case to monitor their activity; and in case of satisfactory function and the absence of a negative reaction from the new body, transplanting in

the chest (Fig. 6). Finally, from 1947, from V.P. Demikhov's words, he began to develop an experimental method of preserving revitalized organs before transplantation (USSR Copyright Certificate No. 410342 of January 10, 1950) (Fig. 7). He believed that, first, using such long-term preserved organs, immunological, physiological, pathophysiological, pharmacological and other experiments can be performed that cannot be performed in humans, and second, such organs can be transported both from one clinic to another, and also from one city to another, where they need to be transplanted. At the end of the article, V.P. Demikhov mentioned that "our heart transplant experiments were attended and mastered by many surgeons, including C. Barnard, who later transplanted a human heart." [14]

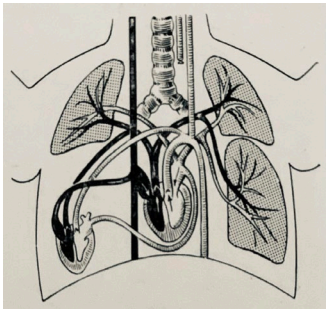


Fig. 5. The scheme of the second heart parallel inclusion into the blood circulation system of a dog [14]

Fig. 6. The scheme of a two-stage heart and lung transplantation surgery in a human [14]

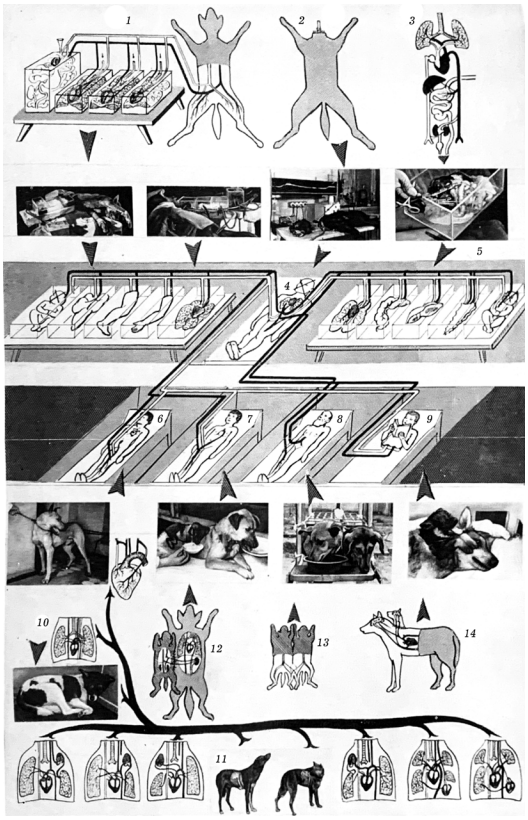


Fig. 7. An experimentally based scheme for the preservation of revitalized organs for transplantation and the use of cross-circulation for therapeutic purposes (further, the author-edited V.P. Demikhov's text is used to describe the figure):

(1) 4 working hearts with lungs are connected to the dog's femoral vessels in 4 transparent plastic cases by using prostheses and the heart and lungs together with the abdominal organs are in the marginal (left) case. Below there are two photos from the documentary popular science film "The Word of Life" (1965); (2) a scheme for preserving a headless body alive in an experiment on a dog; (3-4) a complex of visceral organs (3) or a whole body after an irreversible destruction (damage) of the brain can be kept alive in order the organs from the deceased to be connected to them in cases (5) in the first minutes and hours after death; blood vessel prostheses are used for connection; thermostats, absolute humidity of the environment, artificial respiration, artificial nutrition and special care are required to maintain the life of these organs; blood circulation will be maintained by the connected revitalized hearts; (5) stillborn children can be connected to the complex of revitalized organs when their brain revival turned impossible, but the body revived; in such cases, the organs can be grown for patients of all ages in need; (6) blood vessel prostheses may be diverted from the revived organs preserved for transplants to the adjacent operating room, where open-heart operations or transplantations will be performed by means of cross-circulation rather than by using a heart-lung machine; in some cases, the cross-circulation can be maintained until a complete recovery; (7) the cross-circulation can be used to maintain the life of people who had visceral organs removed due to cancer metastases invasion; In this case, the patient will live without visceral organs until young and healthy organs have been transplanted (this surgery can be effective if there are no metastases in the spinal cord and brain); (8) it is known that tissue cultures staying in artificial conditions get aged, but the periodic addition of embryonic tissue extracts leads to their rejuvenation, and these tissues live many times longer than in natural conditions; <...> a periodic connection of an elderly human to revitalized young organs should lead to his rejuvenation and slowing down the aging process; for periodic connection, the same "taps" can be used as for connecting to an artificial kidney; (9) if cancer metastases have sprouted into the spine, and all other visceral organs are affected by cancer (or as a result of injury), except for the head, then the head and the hands can be connected to prostheses coming from the complex of visceral organs; in this case, the head will live, think, control hands and do everything by using them, as before the surgery; (10) the dog with the replaced heart and lungs; (11) the dog with two hearts; (12) the dog without the heart and lungs is drinking water; (13) cross-circulation between two dogs; (14) the dog with two heads [14, the insert]

The second article was devoted to the development of methods to preserve the functional ability of the donor heart during the period from its removal to completing its implantation [15]. It follows from the article that employees of the Experimental Surgery Laboratory of the Vishnevsky Institute of Surgery of the USSR Academy of Medical Sciences under the leadership of V.F. Portnoy began studying circulatory disorders and circulation typical features in conditions of "brain death", as well as regional EC of the brain and heart[4] in the mid-1960s. The results obtained made it possible to develop a technique for an isolated perfusion of a donor heart (Fig. 8), which was used in the preparation and implementation of the first heart transplant in the USSR [16].

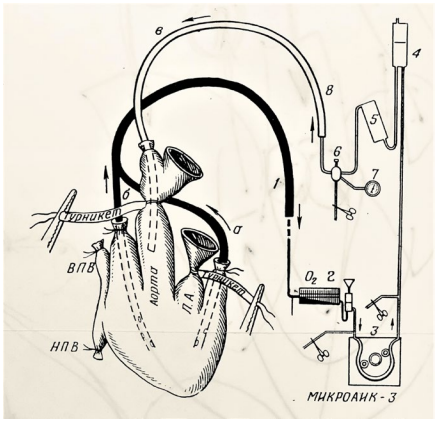
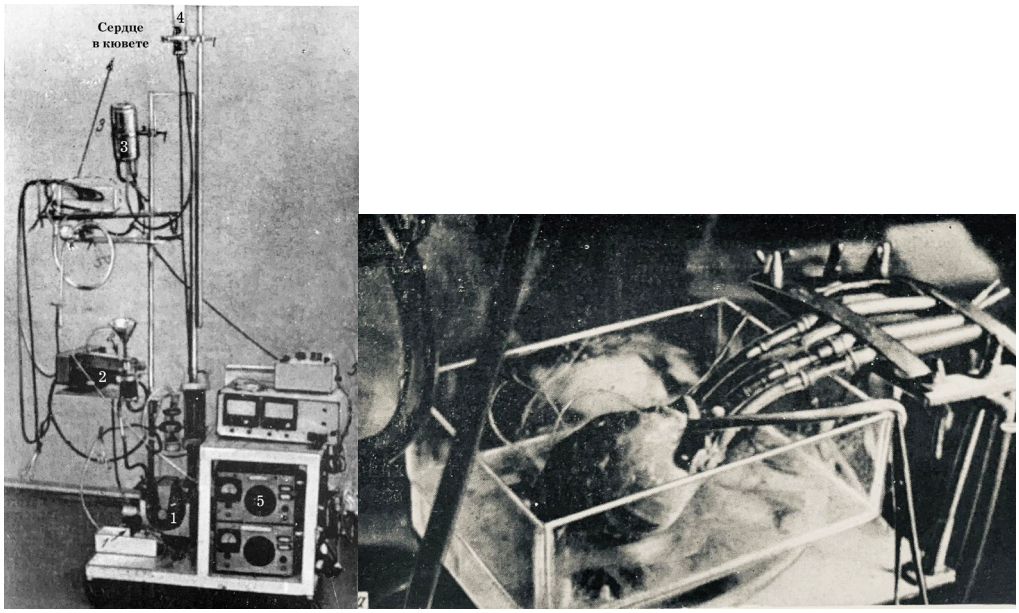


Fig. 8. Connection and the scheme of microAIC-3 CPB pump for an isolated perfusion of a donor heart (the technique by A.A. Vishnevsky, V.F. Portnoy, G.K. Vandyaev): (1) the venous line draining blood from the cavities of the heart through catheters "a" and "b" inserted through the left and right atrial auricles into the ventricles; (2) oxygenator; (3) pump; (4) stabilizing cylinder; (5) heat exchanger; (6) bubble trap; (7) arterial pressure gauge; (8) arterial line connected via "b" catheter to the stump of the ascending aorta; SVC and IVC, superior and inferior vena cava; PA, pulmonary artery [16]

4 V.P. Demikhov worked in this laboratory in 1947-1953; in 1953-1955, he headed a self-standing Laboratory for Organ Transplantation of this Institute. V.F. Portnoy became the Head of the Laboratory of Experimental Surgery in 1965.

Several options for maintaining blood flow in an isolated heart were developed, one of which with using a cardiopulmonary drug was first developed by V.P. Demikhov. However, for practical purposes, it turned out to be more appropriate to use an autonomous EC by means of the device designed in the Laboratory and manufactured at the Leningrad Plant named after M.I. Kalinin (Fig. 9a, b). During the Great Patriotic War, this plant belonged to the USSR People's Commissariat of Ammunition and became famous for producing field rocket artillery systems ("Katyusha").



a b

Fig. 9. Machine for a long-term perfusion of an isolated heart:

a) General view of the device: (1) pump; (2) oxygenator; (3) heat exchanger; (4) a pressure-stabilizing cylinder; (5) control panel and measuring instrumentation; b) perfused heart in a cuvette [15]

A noteworthy article is devoted to the legal aspects of tissue and organ transplantation [18]. According to M.I. Avdeev the author of that article:

"The statement of the French State Medical Academy that a person whose heart is still beating can be considered dead if it is decided that his brain cannot control his vital

functions" is not true, because "in this case, we are not talking about a corpse, but about a person who is legally incapacitated; his life is protected by law. Organs can only be taken from a corpse; there can be no two opinions in this regard." [18, p. 24]

But in this case, the question arose about the time, procedure and method of ascertaining biological death, after which irreversible changes occur in the brain, and which was not regulated in the USSR at the beginning of 1969.

We should recall that for the first time, the moral and ethical issues of organ transplantation were raised by the German press in spring of 1959 after V.P. Demikhov's stay in Germany and his demonstration of operations on heterotopic transplantation of an additional heart and transplanting the puppy's head onto the neck vessels of an adult dog [18]. But no one had considered the issue of death ascertaining for organ harvesting at that time. The public was much more concerned with the question of the legitimacy of the surgeon's right to change a human created in the image and likeness of God. Ten years had passed since that time.

"If in relatively recent times the determination of the onset of death was not particularly difficult, and cardiac arrest was taken as the time of death, at present the diagnosis of death is much more complicated, especially with the possibility of restoring vital functions of the body, the so-called resuscitation <...> It goes without saying that no matter how hopeless the patient or such a resuscitated person returned to life without consciousness, there can be no question of taking an organ from him before his death there can be no question of taking an organ from him before his death. But such consequences of resuscitation involuntarily force us to raise the question of the need for strict indications and contraindications to it. Resuscitation should not be performed for the sake of resuscitation" [17, p. 24].

M.I. Avdeev believed that

"The exceptional complexity and social significance of the problem of tissue and organ transplantation, its specific moral, ethical, legal and medical aspects require a strict regulation. Such operations should be allowed only in certain medical institutions. The Forum of Specialists should determine, and the Ministry of Health should approve the range of institutions and specialists allowed to perform organ transplantation operations" [17, p. 25].

It is obvious that such views were fully shared by the pioneer of heart transplantation in the USSR A.A. Vishnevsky, the Editor-in-Chief of the journal "Experimantalnaya Khirurgia i Anesteziologia" [*Experimental Surgery and Anesthesiology*], and other Soviet surgeons, including employees of the USSR Health Ministry, who were asked to "approve the range of institutions and specialists allowed to perform organ transplantation operations". We should also note that the legal documents presented in the article concerning the legal basis of "individual organ transplantation" were dated 1937, and the "Rules for Forensic Autopsy of a corpse" were approved even earlier, in 1928.

Be that as it may, this is the first article in the Russian literature on the forensic medical foundations of organ transplantation, which, according to the Editorial Board of the Journal, "can serve as the material for an appropriate decision" [17, p. 21].

The article published by the Department of Forensic Medicine of the S.M. Kirov Military Medical Academy (MMA) examines the forensic issues of determining the death of a donor in connection with the subsequent removal of his heart [19]. The matter was that for heart removal at that time, the corpses of people who died from mechanical trauma were usually used.

Meantime, according to the USSR Health Minister Order No. 166 of April 10, 1962, it was forbidden to perform any intervention on a corpse, subject to forensic medical examination without permission and in the absence of a forensic medical expert. In addition, there was a rule according to which a forensic autopsy could not be performed earlier than 30 minutes after the statement of death. In the event of making a decision to remove the heart, the forensic doctor was required to describe all injuries inflicted on the donor during resuscitation or the heart removal. The article presented the "Protocol of ascertaining the fact of death" developed by the authors, and it was proposed to work out an instruction "which would reflect all the issues related to this problem" [19, p. 28].

A group of staff members from the Military Field Surgery Clinic of the MMA proposed the following criteria for statement of "brain death" of the donor before the removal of the heart: (1) the absence of corneal reflexes, (2) the lack of the eye pupils reaction to light, (3) the absence of spontaneous breathing or its extreme disorder; (4) "electric silence" of the cerebral cortex or the individual pathological "splashes" on the EEG. Meantime, "to determine brain death, it is necessary that this combination of symptoms being recorded within 2 hours" [20].

A team of surgeons, anesthesiologists and critical care physicians from the Transplantation Department established on the basis of the Intensive Care Unit of the MMA Hospital Surgery Clinic, and Surgical Department No. 1 of A.V. Vishnevsky Institute of Surgery, presented the results of maintenace therapy in 8 casualties who were diagnosed with "brain death" after the injury. These were the patients who were being prepared for the country's first heart transplant as donors [21].

EC specialists from the MMA, the A.V. Vishnevsky Institute of Surgery, the Leningrad Clinical Military Hospital named after Z.P. Solovyov, and the Krasnogvardeyets Production Association reported on the design peculiarities of the ISL-4 device used for the first clinical heart transplantation (Fig. 10), and the perfusion specific features, noting the possibility of implementing the perfusion during the entire period of the heart exclusion from circulation. At the beginning of the article, the authors mentioned V.P. Demikhov's method of working heart transplantation, but pointed out its futility [22]. In the next article, L.S. Smirnov from the A.V. Vishnevsky Institute of Surgery described an original device for cooling the donor's body before removing the heart (Fig. 11) [23].

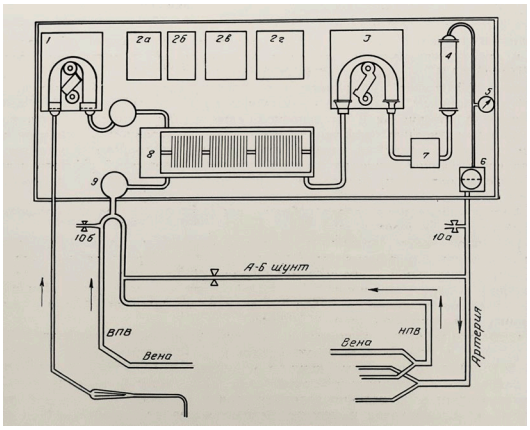


Fig. 10. Switching diagram of the ISL-4 apparatus units: (1) coronary suction unit; (2 a–d) recording units of measuring devices (manometers, H–O_2-meter, thermograph, flow meter); (3) an arterial pump unit; (4) heat exchanger; (5) an arterial pressure gauge sensor; (6) trap-filter; (7) flow meter sensor; (8) a disk oxygenator unit; (9) H–O_2-flow-meter sensor; (10) the sites of connecting arterial (a) and venous (b) lines of the isolated cardiac perfusion system; SVC and IVC, vena cava [22]

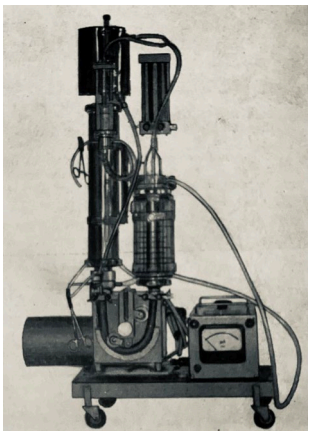


Fig. 11. An overall view of the unit for hypothermic perfusion of the donor's body before the heart is removed for transplantation [23]

Immunological issues of clinical organ transplantation (in particular, the use of anti-lymphocyte sera, ALS) were discussed by immunologists from the A.V. Vishnevsky Institute of Surgery and the Central Institute of Hematology and Blood Transfusion. They pointed out that the first method for obtaining ALS and the scheme for using them were described in 1967 by T. Starlz; ALS were first used in heart homotransplantations by D. Cooley in 1968, which made it possible to significantly reduce the dose of imuran and corticosteroids; and that A.A. Vishnevsky was the first in the USSR to use this drug on November 4, 1968 [24].

The series of these publications by Soviet authors was completed with the translated into Russian C. Barnard's article "Human Heart Transplant" written by him after his 2nd heart transplant operation [25]. The article briefly described the donor heart perfusion technique, which conceptually coincided with the technique of the A.V. Vishnevsky Institute of Surgery and was provided with drawings of the technique of orthotopic biatrial heart transplantation. There were no other data in the article [26].

Development of the heart transplantation problem in surgical clinics around the world. Based on the Proceedings of the 2nd International Symposium on Heart Transplantation (June 6-8, 1969, Montreal, Canada)

Meanwhile, the problem of clinical organ transplantation in the world was gaining momentum. In June 1969, at the initiative of Canadian cardiologists and cardiac surgeons, the 2nd International Symposium on Heart Transplantation was held in Montreal (Canada) (Fig. 12) [27]. The Symposium was directly organized by the Heart Transplant Group of the Montreal Institute of Cardiology under the leadership of P. Grondin. The symposium was attended by representatives of 30 (among 45) clinics that had performed at least one heart transplant by the summer of 1969. Honorary guests of the Symposium who opened its Meetings were the pioneers of transplantation of the human heart J. Hardy (USA) and C. Barnard (South Africa). Among the participants there were D. Cooley, W. Lillehei, N. Shumway (all from USA), C. Dubost (France), W. Bigelow (Canada), D. Ross (Great Britain), etc. A.A. Vishnevsky participated in the work of the Symposium from the USSR, and K.S. Šiška, a pioneer of heart transplantation in the countries of people's democracy, from the Czechoslovak Republic.

Fig. 12. The emblem of the 2nd International Symposium on Heart Transplantation (June 6-8, 1969, Montreal, Canada) [27]

A total of 134 heart transplants had been performed worldwide by June 1, 1969, with about 20% of patients still alive and 17% of them being active; 13 people had been alive for more than six months, two (P. Blaiberg and D. Boulogne) for more than a year[5]. Two patients of Drs D. Cooley and M. DeBakey underwent a second heart transplant. One patient of Dr D. Cooley performed a cardiopulmonary complex transplant. The largest number of operations (20) was performed by D. Cooley at Saint Luke's Hospital (Houston, Texas, USA). The cost of one operation in the United States reached 50,000 dollars, which was comparable to the training of 4 doctors.

At the breakout sessions the following issues were discussed: the selection of donors and recipients, preservation of isolated hearts before transplantation and techniques of their transplantation, biological incompatibility, development of clinical and laboratory methods for diagnosing rejection reactions, infectious and other complications of

5 The "long-livers" among the first 25 patients with transplanted hearts were: No. 3. P. Blaiberg, aged 58 years (South Africa) who lived 592 days (surgeon S. Barnard); No. 9. E. Thomas, aged 47 (USA), 205 (D. Cooley); No. 14. D. Boulogne, 57 (France), 523 (C. Dubost); № 15. J.L. Fierro, 54 (USA), 146 (D. Cooley); No. 22. Pt. of 24 y.o. (Chile), 132 (J. Kaplan); No. 24. Pt of 46 (USA), 268 (D. Cooley) [28].

immunosuppressive therapy, pathogenesis, prevention and treatment of rejection reactions, as well as the immediate and long-term results of heart transplantation.

Since three-quarters of the recipients suffered from severe coronary insufficiency, indirect myocardial revascularization operations with a mortality rate of 15% were suggested as an alternative to heart transplantation (A. Vineberg). In extensive post-infarction aneurysms, a number of surgeons excised cicatricial areas of the myocardium under cardiopulmonary bypass conditions (P. Grondin) or performed aneurysm repair by plicating the affected muscle areas (J. Kay).

Less favorable results than in coronary disease were obtained in heart transplants for cardiomyopathies. High-grade pulmonary hypertension was identified as a contraindication for heart transplantation.

Most surgeons preferred to transplant the heart under normothermal perfusion with single-use bubble oxygenators and followed the Lower-Shumway technique with minor modifications. Electric cardiac pacemakers (ECPs) were used in a number of patients. A novelty was the report on experimental developments of ECP with radioactive power sources.

In opinion of the Symposium participants, the issues of preserving a functioning donor heart outside the body, especially for the purpose of it transportation, issues of ascertaining donor's death, determining the optimal time for heart removal, the legal basis for donation, issues of recipient postoperative management, prevention of infectious and other complications remained unresolved.

The main problem was called the overcoming tissue incompatibility. Prednisolone, ALS, and azathioprine were administered for the prevention of rejection reactions; and less frequently, X-ray irradiation of the heart area

was used; a complex of clinical, instrumental, and laboratory methods was developed for early detection of rejection.

As a casuistic example, A.A. Vishnevsky cited the case of kidney transplantation in a patient with renal insufficiency from a donor after a preliminary session of cross-circulation. The transplanted kidney functioned for 3 years, which A.A. Vishnevsky considered a consequence of the use of this method. Interesting was the opinion expressed by some Symposium participants that heart transplantation, without eliminating the underlying disease, is a palliative operation (H. Selye, C. Barnard).

It is difficult to say post factum to what extent, for example, V.P. Demikhov's presentation made by him at a Meeting of the Scientific Council of N.V. Sklifosovsky Institute, would be relevant at such a symposium, but it is safe to say that it would have been listened to with great attention. V.P. Demikhov's opinion on assisted cross-circulation, his physiological system of preserving revitalized organs before transplantation, and also his experience in creating a mechanical heart could have been particularly interesting. New to the participants of the Symposium could have been his anatomical technique of transplanting a *working* heart and transplanting an *additional* heart to unload an ill biological organ. The fact is that no one spoke about the concept of assisted blood circulation at the Symposium, perhaps not even thought about it. For the time of this trend in the treatment of heart failure had not yet come.

Conclusion

Analysis of the studied material showed that in the 1960s several groups of surgeons, urologists, anesthesiologists-critical care physicians, perfusiologists, experimental researches, hematologists, and immunologists

worked in the USSR, dealing with the problem of organ transplantation in experiment and trying to transfer this experience to clinic[6].

The group of surgeons and urologists from the Institute of Clinical and Experimental Surgery (B.V. Petrovsky, G.M. Soloviev, V.I. Shumakov, etc.) and of the 2nd MOLSMI named after N.I. Pirogov (N.I. Lopatkin, Yu.M. Lopukhin, I.N. Kuchinski, Yu.A. Pytel, etc.), which had the largest administrative resources and technical capacity developed so successfully the clinic kidney transplantation operation that it was it was implemented in clinic in1965.

Employees of the Faculty Surgery Department of the 2nd MOLSMI named after N.I. Pirogov (V.S. Savelyev, I.V. Stupin, Yu.E. Berezov, V.R. Anakhasyan, etc.) worked out the issues of heart and liver transplantation in experiment, but it did not reach clinical implementation. Thoracic surgeons from the Research Institute of Tuberculosis of the USSR Academy of Medical Sciences (N.I. Gerasimenko, M.M. Averbakh, etc.) were engaged in auto - and homoplastic lung transplants in the experiment, but the clinic did not perform a lung transplant.

All these studies were carried out in close contact with the Department of Operative Surgery and Topographic Anatomy of the 2nd Pirogov Moscow State Medical University (G.E. Ostroverkhov) and the Problem Organ Transplantation Laboratory (Yu.M. Lopukhin) established at this department, where the stages of organ transplantation in the experiment were worked out and immunological and morphological studies were conducted. The Organ Transplantation Laboratory of the USSR Academy of Medical Sciences

6 It is known that in parallel with Russian scientists, this problem was experimentally developed by a group of Ukrainian surgeons from F.G. Yanovsky Kiev Research Institute of Thoracic Surgery and Tuberculosis headed by N.M. Amosov and they even tried to transplant a heart in clinic in 1968, but they failed to do so [29].

(I.D. Kirpatovsky), which had been working since the mid-1950s at the Department of Operative Surgery and Topographic Anatomy of the 1st Sechenov Moscow State Medical Institute (V.V. Kovanov), developed methods for tissue and endocrine organ transplantation after V.P. Demikhov left it in 1955.

Two institutes of the USSR Academy of Medical Sciences were also involved in the developments on the topic of heart transplantation: the A.V. Vishnevsky Institute of Surgery (A.A. Vishnevsky, A.D. Arapov, A.N. Kaidash, etc.) and the A.N. Bakulev Institute of Cardiovascular Surgery (V.I. Burakovsky, G.E. Falkovsky, etc.), where both experimental (V.F. Portnoy, G.E. Falkovsky) and immunological (L.L. Khundanov, M.A. Frolova) studies were conducted. A distinctive feature of these Institutes was that they had extensive experience in heart surgery under CPB conditions and had a well-developed intensive care service.

However, the leading position in heart transplantation in the country belonged to the A.V. Vishnevsky Institute of Surgery. This was evidenced by the fact that V.F. Portnoy, the closest student of A.A. Vishnevsky, studied the feasibility of long-term coronary perfusion of an isolated heart for its transplantation as early as in 1963 [15, p. 11], and in 1967 he defended the first doctoral dissertation in the country on this topic [15]. In addition, military therapists (N.S. Molchanov) and the staff of the Department of Hospital Surgery of the MMA named after S.M. Kirov (I.S. Kolesnikov, F.V. Ballyuzek, N.V. Putov, etc.), who had well-equipped perfusion service (F.V. Ballyuzek, N.K. Dzutsov, etc.), the anesthesiology and resuscitation services (Yu.N. Shanin, G. N. Tsybulyak, etc.) provided great assistance and support to the Institute. That is why the group of A.A. Vishnevsky-I.S. Kolesnikov performed the first heart transplant in the country in clinic.

The first heart transplant was performed by surgeons led by V.I. Burakovsky at the A.N. Bakulev Institute of Cardiovascular Surgery only in 1983.

It is clearly seen how isolated from these institutions, departments and clinics was the Organ Transplantation Laboratory at the N.V. Sklifosovsky Research Institute of Emergency Medicine that worked having very modest resources opportunities to purchase equipment and pharmaceutical agents, conduct laboratory and morphological studies. However, V.P. Demikhov was the only one who had experience in transplanting the heart, lungs, kidneys and liver, as well as the head, trunk, intestines, sternum and other organs in experiment. In the absence of assisted blood circulation, he was perfect technically and able to transplant *working* organs, which no one else did. When it was impossible to detect immunological changes in tissues, he tried to overcome their incompatibility with biological methods; and in his research he went so far as to develop the technique of heart transplantation on human corpses. But even with such vast experience, he was far from implementing his results in clinic.

Our research has shown that in 1969, all the above-mentioned groups, including A.A. Vishnevsky and the participants of the first clinical heart transplantation group in the country, unconditionally recognized V.P. Demikhov's priority in the experimental study of this problem. However, none of the methods developed by him was used in the clinic at that time. It looked as if there was a certain gap between the biologist V.P. Demikhov and the experimental surgeons and clinicians, and none of them could cross it (Fig. 13).

Fig. 13. In the Institute of Surgery named after A.V. Vishnevsky of the USSR Academy of Medical Sciences (left to right): V.F. Portnoy, A.A. Vishnevsky, V.P. Demikhov. 1968 [From the collection of the Museum of A.N. Bakulev National Medical Research Center of Cardiovascular Surgery]

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The article was received on September 6, 2021;
Approved after reviewing September 14, 2021;
Accepted for publication September 29, 2021