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PHENOMENON OF DEMIKHOV. In the Sklifosovsky Institute (1960-1986). Research Coordination Council of the USSR Healthcare Ministry: Missed opportunities. Part 1 (1963)

S.P. Glyantsev

A.N. Bakoulev National Medical Research Center for Cardiovascular Surgery,

135 Roublyevskoe Hwy., Moscow 121552 Russia;

N.A. Semashko National Research Institute of Public Health

12 Bldg. 1 Vorontsovo Pole St., Moscow 105064 Russia

Correspondence to: Sergey P. Glyantsev, Prof., Dr. Med. Sci., Head of the Department of the History of Cardiovascular Surgery at A.N. Bakoulev National Medical Research Center for Cardiovascular Surgery, Head of the Medical History Unit within the Medical History Department at N.A. Semashko National Research Institute of Public Health,

e-mail: spglyantsev@mail.ru

The article describes the key event for Soviet transplantology of the 1960, namely, the Meeting of the Presidium of the USSR Healthcare Ministry Council for the Coordination of Scientific Research and Implementation of the Scientific Achievements. The Meeting held on October 8, 1963, was initiated by V.P. Demikhov's letters addressed to Moscow City CPSU Committee and the USSR Healthcare Ministry. The attendees of the Meeting were 50 leading experts of the USSR in the field of surgery, immunology, and transplantology; the speakers at the Meeting were V.P. Demikhov as the principal speaker, and V.I. Burakovsky as the Chairman of the Committee that had studied V.P. Demikhov's proposals on the issue of organ transplantation and the prospects for scientific research in that area. V.P. Demikhov shared with the audience his ideas, which were well ahead of

their time; and the Commission noted the perspective and complexity of the organ transplantation problem, proposing a number of measures to improve the existed situation.

Keywords: history of transplantology, USSR Healthcare Ministry, Council for the Coordination of Scientific Research, V.P. Demikhov, V.I. Burakovsky, 1963.

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Heart-Lung Machine (HLM)

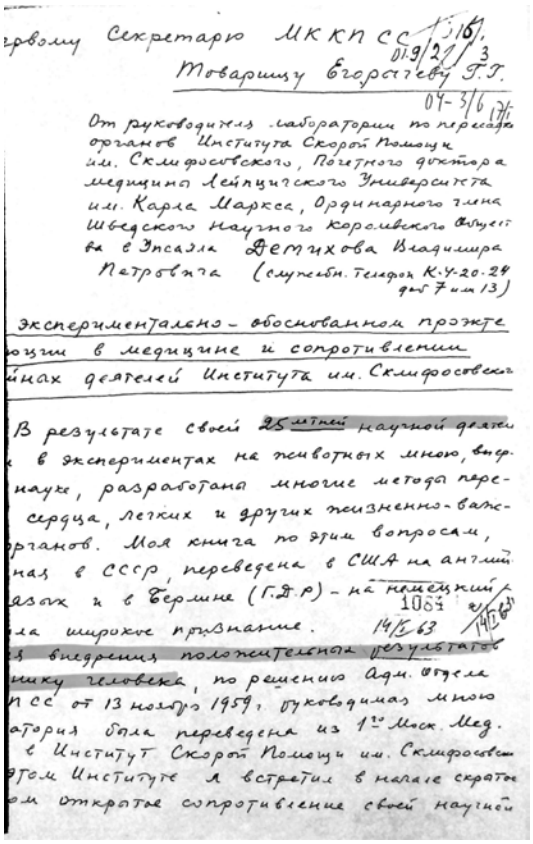
NIIEHAiI, transliterated abbreviation from Russian stands for the *Research Institute of Experimental Surgical Equipment and Instruments*

Letters to the "competent" authorities

It began in 1963 when V.P.Demikhov planned to perform the first in Russia heart, lung, or heart-and-lung transplantation in clinic. According to his original developed technique, It had to be a two-stage transplantation: first to the femoral vessels of a sick person, and then to the orthotopic position. However, apparently, by that time V.P.Demikhov began to realize that the idea that he had been cherishing for several years was far from being embodied in practice; because in January–February 1963, the following happened.

On January 14, 1963, V.P. Demikhov addressed a letter entitled “On the Experimentally-Grounded *Revolutionary* Project *in Medicine* (*italics by*

the author) and the resistance of the Sklifosovsky Institute Party leaders" to N.G. Egorychev[1], the First Secretary of the Moscow City CPSU Committee (Fig. 1). In the letter, the sender undersigned as "Demikhov Vladimir Petrovich, the Head of the Organ Transplantation Laboratory of the Sklifosovsky Institute for Emergency Medicine, Honorary Doctor of Medicine of Leipzig University named after Karl Marx, an Ordinary Member of the Royal Swedish Academy of Sciences in Uppsala, and "asked the influential Party Authorities and the City Party Committee to help him in implementing his organ transplantation technique in the clinic.



рвому Секретарю МККПСС
Товарищу Егорычеву Г.Г.

От руководителя лаборатории по пересадке органов Института Скорой Помощи им. Склифосовского, Почетного доктора медицины Лейпцигского Университета им. Карла Маркса, Ординарного члена Шведской научного королевского общества в Упсале Демихова Владимира Петровича (служебн. телефон К-У-20-24 доб 7 или 13)

экспериментально-обоснованном прожекте
ьзуя в медицине и сопротивлении
инах деятелей Института им. Склифосовского

В результате своей 25 летней научной деятельности
в экспериментах на животных мною, впер-
науки, разработана многие методы пере-
сердца, легких и других жизненно-важ-
рганов. Моя книга по этим вопросам,
ная в СССР, переведена в США на англий
язах и в Германе (Г.Д.Р) - на немецкий
ла широкое признание.
з внедрения положительного результата
ищу человека, по решению Адм. Отдела
ЦК от 13 ноября 1959, руководимая мною
аборатория была переведена из 1-го Моск. Мед.
в Институт Скорой Помощи им. Склифосовского
этом Институте я встретил в начале скрытое
ем открытое сопротивление своей научной

Fig. 1. A copy of V.P. Demikhov's letter of January 14, 1963, to N.G. Yegorychev, the First Secretary of the Moscow City Committee of the CPSU. From S.P. Glyantsev's personal archives

[1] In the letter - **G**.G. Egorychev.

Informing that his work received international recognition, and his book "Experimental Transplantation of Vital Organs" published in 1960, had been translated into English and German, V.P. Demikhov wrote the following:

> "At present, I have developed in detail the schemes of heart, lung and other organ transplants <u>on a human.</u> (underlined by Demikhov - *Author*) If these operations are implemented into clinic, then, according to many scientists, *a revolution will occur in medicine,* the *mortality from severe diseases will be dramatically reduced, and a human life expectancy will increase significantly* (*italics by the author*) <...>
>
> I will appeal on this issue to the Central Committee of the CPSU again[2], but I would like to inform you in detail in advance, and to receive possible assistance from your part. I ask you to allow me (in an accessible form for non-medical people) to make a presentation (with relevant illustrations) at a meeting of the Moscow City Committee of the CPSU on the plan for implementing scientific achievements in transplantation of vital organs and cross-circulation in medicine"[1].

V.P. Demikhov did not exaggerate, speaking about the global recognition of his work. On February 8, 1963, the cinema DEFA-Studio (GDR) in its news programme showed an item about "Professor Wladimir Petrovich Demikhoff" and his dog Grishka, made in Moscow in the courtyard of the Sklifosovsky Institute in summer of 1962. *Professor Demikhoff* on the screen was auscultating Grishka's chest, speaking something to the camera and showing the electrocardiogram of two hearts; and in other frames, the dog was romping with a cat in the courtyard of the clinic. It is not difficult to guess that the German documentalists commented

[2] V.P. Demikhov attained the transfer of his Laboratory from the 1st MOLMI named after Sechenov to the Sklifosovsky Institute for Emergency Medicine after contacting the Administrative Department of the CPSU Central Committee.

on this plot as another scientific victory of Soviet medicine. But the experiment with Grishka, that, as some of his contemporaries believed, put an "atomic bomb under transplant immunity" [2], was not even mentioned in the Annual Report on the Sklifosovsky Institute Research for 1962. But in that document, there was such a section as “the Studies defining the scientific image of the Institute”. We should also note that German journalists bluntly called V.P. Demikhov a "Professor", being apparently unaware that the scientist who surprised the whole world was not even a Candidate of Science (Fig. 2).

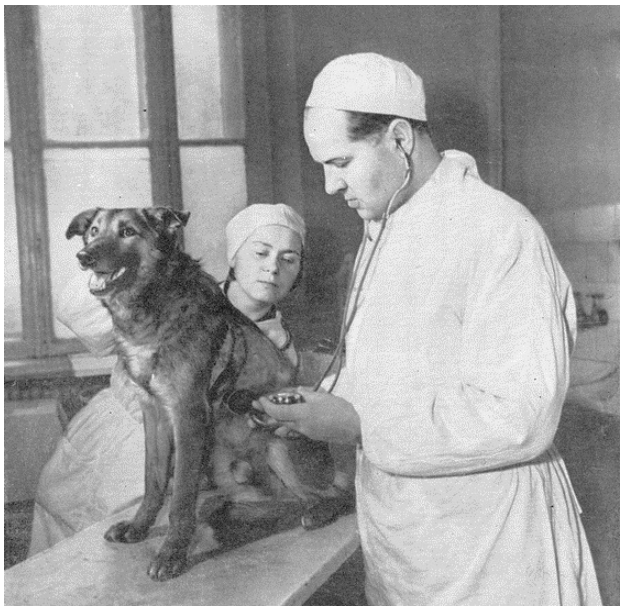
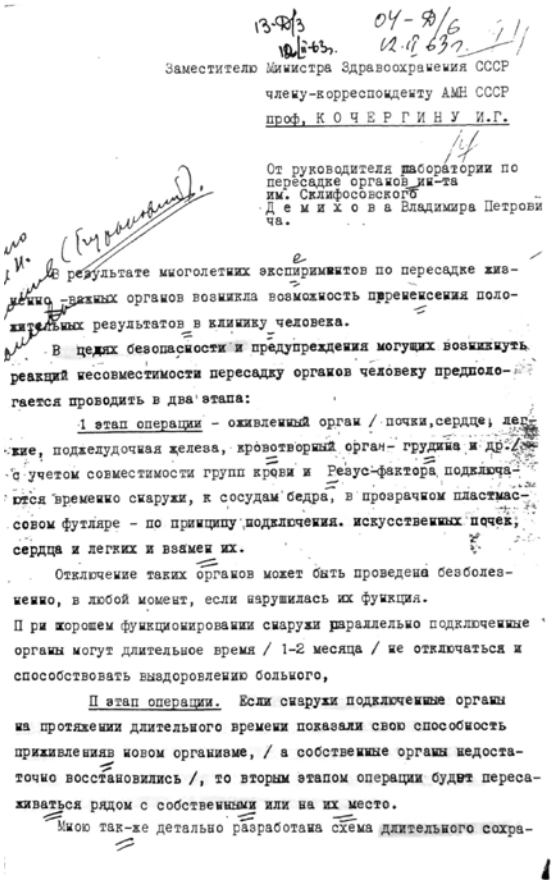


Fig. 2. V.P. Demikhov is auscultating the beating of two hearts in a dog with a second (additional) heart transplanted into its chest. 1963

A month passed. Having received no response from the City CPSU Committee, on February 10, 1963, V.P. Demikhov sent another letter addressing it to Professor I.G. Kochergin, the Deputy Minister of the USSR Healthcare Ministry, a Corresponding Member of the Academy of Medical Sciences, with a similar request “to assist in translating the results of organ

transplant experiments to human clinic” (Fig. 3). In addition to the detailed development of the two-stage vital organ transplantation technique: initially into the femoral vessels, and then into the chest, and the method of "long-term storage of organs alive", he described his "project of organizing special wards where the treatment of patients with irreversibly affected organs can be made using cross-circulation with a revived complex of organs". In other words, it was the project to create a "bank" of living organs. Noteworthy was the ending of this letter: “To discuss all these issues, it would be highly desirable to invite the following scientists ...”.



Заместителю Министра Здравоохранения СССР
члену-корреспонденту АМН СССР
проф. К О Ч Е Р Г И Н У И.Г.

От руководителя лаборатории по
пересадке органов ин-та
им. Склифосовского
Д е м и х о в а Владимира Петрови
ча.

В результате многолетних экспериментов по пересадке жизненно важных органов возникла возможность перенесения положительных результатов в клинику человека.

В целях безопасности и предупреждения могущих возникнуть реакций несовместимости пересадку органов человеку предполагается проводить в два этапа:

1 этап операции - оживленный орган / почки, сердце, легкие, поджелудочная железа, кровотворный орган - грудина и др./ с учетом совместимости групп крови и Резус-фактора подключатся временно снаружи, к сосудам бедра, в прозрачном пластмассовом футляре - по принципу подключения искусственных почек, сердца и легких и взамен их.

Отключение таких органов может быть проведено безболезненно, в любой момент, если нарушилась их функция.

При хорошем функционировании снаружи параллельно подключенные органы могут длительное время / 1-2 месяца / не отключаться и способствовать выздоровлению больного,

II этап операции. Если снаружи подключенные органы на протяжении длительного времени показали свою способность приживления в новом организме, / а собственные органы недостаточно восстановились /, то вторым этапом операции будет пересаживаться рядом с собственными или на их место.

Мною так-же детально разработана схема длительного сохра-

Fig. 3. A copy of V.P. Demikhov's letter of February 10, 1963, addressed to Professor I.G. Kochergin, the Deputy Minister of the USSR Healthcare Ministry, Corresponding Member of the USSR Academy of Medical Sciences. From S.P. Glyantsev's personal archives

In the list attached to the letter, the names of 25 doctors and scientists - from Candidates of Medical Sciences to Academicians, specialists in the field of morphology and physiology of the cardiovascular system, in cardiac surgery, transplantation of organs and tissues, transplantation immunity who, in V.P. Demikhov's opinion, could have been interested in the development of transplantation in the USSR and somehow support his ideas (Table 1) [3].

Forestalling the reader's acquaintance with this list, we emphasize that that was V.P. Demikhov's personal opinion, which did not reflect, in our view, the true state of affairs with heart surgery and immunology in the country.

Table 1[3]. Surgeons and scientists who (in V.P. Demikhov's opinion) could be interested in transplantation developments in the USSR

No	Name, Academic degree/title	City	Affiliation, specialty, position
1.	Prof.[4] Androsov P.I.	Moscow	N.V. Sklifosovsky Research Institute for Emergency Medicine, Head of Department, Surgeon; worked in surgery of the esophagus
2.	Prof. Amosov N.M.	Kiev	State Institute for Medical Postgraduate Education, Head of Thoracic Surgery Department, Thoracic and Cardiac Surgeon
3.	Prof. Andreev S.V.	Moscow	Institute for Cardiovascular Surgery, the USSR Academy of Medical Sciences, Head. Laboratory of Pathophysiology and Pharmacology (Experimental Therapy) of the Cardiovascular System
4.	Prof. Kolesnikov S.A.	Moscow	Institute for Cardiovascular Surgery, the USSR Academy of Medical Sciences, Director, Cardiac Surgeon
5.	Prof. Yankovsky V.D.	Moscow[5]	In the 1930-1940s he worked at the Institute

[3] The table has been compiled by us; the names are given in the order in which V.P. Demikhov arranged them; the right column indicates the scientists' positions, the area of expertise early in 1963.

[4] Academic degrees and titles are listed as they were listed by V.P. Demikhov. By that time, some of the scientists mentioned in the list had been the Members of the USSR Academy of Medical Sciences (for example, V.V. Parin and B.V. Ognev) and the Laureates of prestigious scientific Awards (for example, N.M. Amosov and F.G. Uglov).

[5] This is indicated by V.P. Demikhov, but V.D. Yankovsky at that time had already lived in Ukraine.

			of Experimental Physiology and Therapy of the USSR Healthcare Board (headed by S.S. Bryukhonenko, the Director), where he developed artificial lungs and anticoagulant drugs
6.	Prof. Uglov F.G.	Leningrad	1st LMI named after Acad. I.P. Pavlov, Head of Hospital Surgery Department, Thoracic Surgeon
7	Prof. Filatov A.N.	Leningrad	1st LMI named after Acad. I.P. Pavlov, Head. of General Surgery, Department, General Surgeon; worked in vascular surgery and blood transfusion
8.	Prof. Efimov M.I.	Moscow	-[6]
9.	Prof. Zhukov-Verezhnikov N.N.	Moscow	Research Institute of Experimental Biology, the USSR Academy of Medical Sciences, Head of Immunobiology Department, Immunologist and Microbiologist
10.	Prof. Maisky I.N.	Moscow	Research Institute of Experimental Biology, the USSR Academy of Medical Sciences, Director, Immunologist
11.	Cand.Med.Sci. Kapichnikov, M.M.	Moscow	Research Institute of Experimental Biology, the USSR Academy of Medical Sciences, Art. Research Associate, Immunologist
12.	Prof. Lapchinsky A.G.	Moscow	Institute of Traumatology and Orthopedics named after N.N. Priorov, Head of Laboratory, Transplantologist
13.	Prof. Fedorov N.A.	Moscow	-
14.	Prof. Parin V.V.	Moscow	Research Institute of Normal and Pathological Physiology, USSR Academy of Medical Sciences, Director
15.	Prof. Studitsky A.N.	Moscow	Moscow State University named after M.V. Lomonosov, Head of Cytology and Histology Department at Faculty of Biology and Soil Science; Cytologist, Histologist
16.	Prof. Kraevsky N.A.	Moscow	Research Institute of Experimental and Clinical Oncology, the USSR Academy of Medical Sciences, Head of Pathological Anatomy Department, Pathologist, Hematologist
17.	Prof. Permyakov N.K.	Moscow	N.V.Sklifosovsky Research Institute for Emergency Medicine, Head of Pathological Anatomy Department, Pathologist
18.	Prof. Grigorieva T.A.	Moscow	2nd MOLGMI named after N.I.Pirogov, Head of Histology Department, Morphologist,

[6] The dash (-) means that the information on the place of work and the specialty of these scientists was unavailable.

			Histologist
19.	Assoc.Prof. Chervova I.A.	Moscow	2nd MOLGMI named after N.I. Pirogov, Associate Professor of Histology Department, Morphologist, Histologist; Heart Innervation Specialist
20.	Prof. Sinitsyn N.P.	Gorky	Gorky State Medical Institute, Head of Pharmacology. Department, Pharmacologist and Experimental Transplantologist
21.	Cand.Med.Sci. Zotikov E.A.	Moscow	Central Order of Lenin Institute for Blood Transfusion of the USSR Healthcare Ministry, Head of Immunohematology Laboratory, specialist in the field of transplantation immunity
22.	Ph.D. Panova M.I.	Moscow	-
23.	Ph.D. Fedotenkov A.G.	Moscow	-
24.	Prof. Gnylorybov T.E.	Minsk	Minsk State Medical Institute, Head of General Surgery Department, worked on skin grafting, blood vessel grafting, organ and tissue preservation
25.	Prof. Ognev B.V.	Moscow	Central Institute for Medical Postgraduate Education, Head of Operative Surgery and Topographic Anatomy Department; Experimental Transplantologist

We repeat that this was the opinion and preference of V.P. Demikhov. Therefore, the list does not contain the names of A.A. Vishnevsky, B.V. Petrovsky, V.V. Kovanov, B.A. Petrov; and the first in the list is P.I.Androsov, one of the surgeons who supported V.P.Demikhov and helped him to operate at the Sklifosovsky Institute.

The USSR Healthcare Ministry Council for Research Coordination and the Implementation of Scientific Achievements in Practice

V.P. Demichov's urgent request was heard. On February 25, 1963, I.G. Kochergin, the Deputy Minister of the USSR Healthcare (Fig. 4) signed the Order on establishing the Commission "to study the proposals of Comrade Demikhov V.P. on the issue of organ transplantation and the prospects for scientific research in this area". The Commission was headed by V.I.

Burakovsky, the Chief of the Department of Surgery for Congenital Heart Diseases of the Institute of Cardiovascular Surgery within the USSR Academy of Medical Sciences, and included M.M. Kapichnikov, Doctor of Biological Sciences, the Head of the Immunology Laboratory of the Institute of Experimental Biology within the USSR Academy of Medical Sciences, and N.G. Sushko, the employee of that Laboratory, I.D. Kirpatovsky, Doctor of Medical Sciences, the Head of Organ and Tissue Transplantation Laboratory of the USSR Academy of Medical Sciences at the Department of Operative Surgery and Topographic Anatomy of the 1st MOLMI named after I.M. Sechenov, and Yu.Ya. Gritsman from the Research Institute of Experimental Surgical Equipment and Instruments (NIIEHAiI). Note that Dr. I.D. Kirpatovsky was also a part-time employee of NIIEHAiI (Fig. 5).

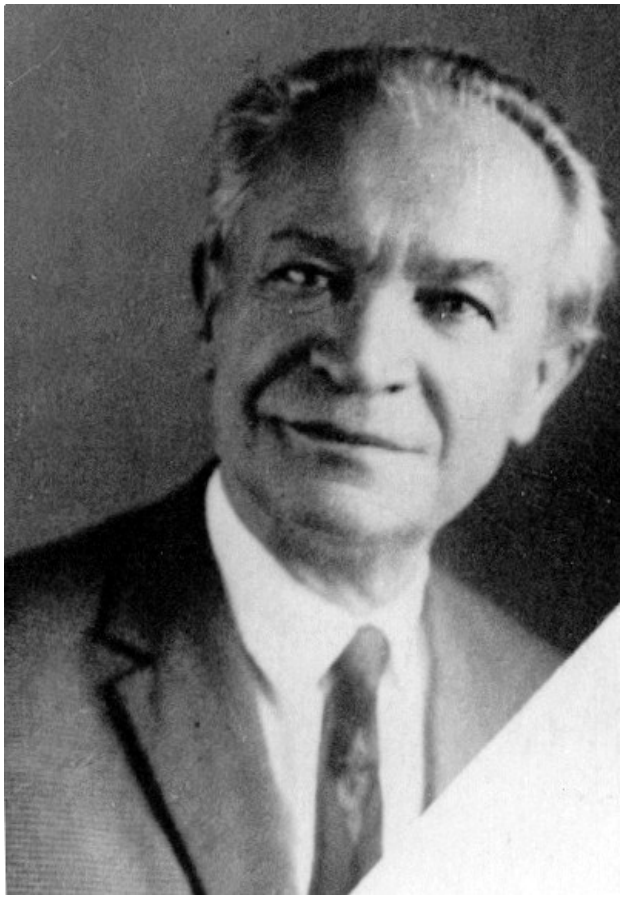
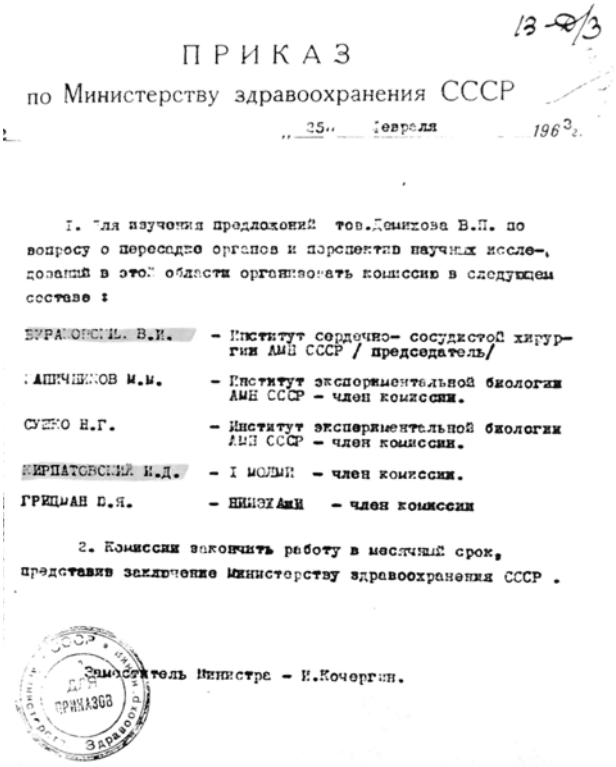


Fig. 4. I.G.Kochergin (1903–1980)



ПРИКАЗ

по Министерству здравоохранения СССР

„ 25 " февраля 1963 г.

13-82/3

1. Для изучения предложений тов.Демихова В.П. по вопросу о пересадке органов и перспектив научных исследований в этой области организовать комиссию в следующем составе :

БУРАКОВСКИЙ В.И. – Институт сердечно- сосудистой хирургии АМН СССР / председатель/

АПЧИШКОВ М.М. – Институт экспериментальной биологии АМН СССР – член комиссии.

СУЕНО Н.Г. – Институт экспериментальной биологии АМН СССР – член комиссии.

КИРПАТОВСКИЙ И.Д. – I МОЛМИ – член комиссии.

ГРИЦЮК Б.Я. – НИИЭХАИ – член комиссии

2. Комиссии закончить работу в месячный срок, представив заключение Министерству здравоохранения СССР .

Заместитель Министра – Е.Кочергин.

Fig. 5. The USSR Healthcare Ministry Order No. 82 dated of February 25, 1963. From S.P. Glyantsev's personal archives

We do not know why the Commission was headed by V.I. Burakovsky. After all, just 3 months before that, V.I. Burakovsky had defended his doctoral thesis on the treatment of a number of congenital heart defects under hypothermia and had no relation to heart transplants at that time. Most likely, the Commission had to be headed by Professor S.A. Kolesnikov, the Director of the Institute of Cardiovascular Surgery within the USSR Academy of Medical Sciences, as one of the country's leading specialists in heart surgery, but he recommended Dr. V.I. Burakovsky instead of himself. This can be indicated by the fact that the letter of V.P. Demikhov to the Healthcare Ministry contains someone's resolution, in which surnames

"*Kolesnikov (Burakovsky)"* were written, the second one being underlined by a double line (Fig. 3).

Established in February, the Commission worked for 7 months.

On October 8, 1963, a Meeting of the Presidium of the USSR Healthcare Ministry Council for Research Coordination and the Implementation of Scientific Achievements in Practice was held under the chairmanship of I.G. Kochergin to discuss the issue "On the status and development of research in organ transplantation".

We should emphasize that at that time, the research programmes in the field of cardiac surgery were carried out by the clinics headed by A.A. Vishnevsky, B.V. Petrovsky, A.N. Bakulev, and S.A. Kolesnikov in Moscow, by P.A. Kupriyanov, F.G. Uglov, and S.A. Hajiyev in Leningrad, by N.M. Amosov and L.N. Sidarenko in Kiev, by E.N. Meshalkin in Novosibirsk, and by B.A. Korolev in Gorky; and experimental studies on transplantation were carried out in the Organ and Tissue Transplantation Laboratory in the 1st MOLMI (I.D. Kirpatovsky), at the Central Institute of Traumatology and Orthopedics (A.G. Lapchinsky), at the Department of Operative Surgery and the Topographic Anatomy of Advanced Doctor's Training Institute (B.V. Ognev), and in a number of other institutions of the country, but only V.P.Demikhov was reporting on the status of that issue and the prospects of its development.

Nevertheless, all those who were interested in this issue in one way or another or directly involved gathered in the building of the Ministry of Health in Rakhmanovsky Lane. Among the members of the Presidium there were: I.G. Kochergin (Surgeon)[7], S.P. Mardashev (Biochemist), N.N. Zhukov-Verezhnikov (Immunologist) (hereinafter, the scientists and doctors

[7] Medical or scientific specialty of some participants of the Meeting is indicated in brackets.

listed in italics were those whom V.P. Demikhov asked to invite for the discussion of the issue of organ transplantation in his letter to the Moscow city CPSU Committee. - Author), V.I. Kabanov, L.M. Lemenev (Health Care Authority), N.I. Nisevich (Pediatrician), V.M. Smolyaninov (Pathologist), A.P. Smorchkov, B.G. Stoyanov (Dermatovenerologist), V.I. Pods (Surgeon), S.A. Sarkisov (Neuromorphologist).

There were many more invited people: Solntsev[8], T.S. Kuznetsov, V.A. Nazarov, N.M. Kiselev, *S.V. Andreev* (Physiologist), N.M. Gerasimenko (Surgeon), *T.A. Grigorieva* (Morphologist), *I.A. Chervova* (Morphologist), A.E. Gurvich (Critical Care Physician), *M.I. Efimov*, V.I. Govallo (Immunologist), A.M. Mamish, *I.N. Maysky* (Biologist, Immunologist), *A.G. Lapchinsky* (Transplantologist), I.V. Berezin, N.I. Ermakova-Berezina, L.V. Polezhaev, M.I. Perelman (Surgeon), R.L. Ginzburg, E.I. Smirnov (Healthcare Authority), L.G. Fishman, A.A. Safronov, B.A. Petrov (Surgeon), M.M. Tarasov (Healthcare Authority), Vyazova, Eingorn, Gaevskaya, A.M. Djavadyan (Surgeon), Gorbovitsky, Goldina, Kovalskaya, V.A. Bykova (Surgeon), Vladimirovskaya.

The main speaker, V.P. Demikhov, and all members of the Commission that inspected the activities of his Laboratory: V.I. Burakovsky (Chairman), *M.M. Kapichnikov,* N.G. Sushko, I.D. Kirpatovsky, and Yu.Ya. Gritsman were present. There were totally 50 people.

V.P. Demikhov's speech

Starting with the fact that the main provisions of his speech were multiply copied and the copies were distributed in the audience ahead of time, V.P. Demikhov (Fig. 6) reported that "he would make several

[8] Some last names in the list are printed without initials.

additions". At the beginning he spoke about the immunological incompatibility phenomenon:

> "Now there is a big discussion on the issue of biological compatibility in transplantation of organs and tissues. Our data do not coincide with the immunological theory, and not only our data, but also the data of other scientists ... "[4, p.17].

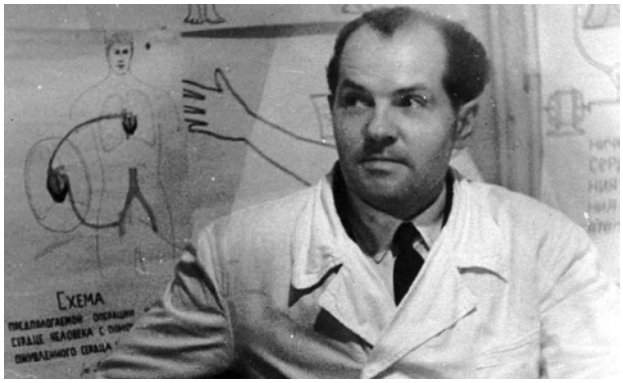


Fig. 6. V.P. Demikhov is ready for human heart transplantation. In the background: "The scheme of the proposed surgery on a human heart using a revived heart ...". 1963.

Further V.P. Demikhov gave examples of a long-term engraft of homologous tissues in animals and humans, specifically, bones and "half-joints", however, without having any other information about the survival periods of homoorgans besides his own observations. Speaking of the discrepancy between his data and the immunological theory, V.P. Demikhov was referring to the provisions adopted at that time, which limited the timing of the onset of the rejection reaction to 7–14 days. Indeed, the cases when the organs transplanted by V.P. Demikhov were functioning for several weeks, and Grishka's heart lasted for several months, clearly contradicted the

theory. Unfortunately, the concepts of a delayed and late rejection of transplanted homoorgans at that time had not been developed yet.

And V.P. Demikhov continued, citing the most interesting information about the trials of immunosuppressive drugs that had just appeared on the market:

> "There is a lot of information appeared that there are drugs eliminating biological incompatibility. The American company has sent the drug *6-mercaptopurine*. The wanted me to recommend their drug. When we began to test it, then the dogs that were injected with this drug had intoxication, and, by the way, the drug was administered by the American scientist Matlof from the Deterling Clinic[9]. Those dogs who did not receive the American drug felt well. <...> [Therefore] I could not believe in the curative effect of this agent. When the question arose to publish the results, the American surgeon said that there were very few cases. But those 4 cases clearly showed that this world-famous and advertised drug, 6-mercaptopurine, does not give a positive result for organ and tissue transplants, except for general intoxication... "[4, p.17−19].

Everything is remarkable in that passage: the world fame of V.P. Demikhov (it was not by chance that R. Deterling, who visited the USSR in May 1960, sent his staff member to the Soviet scientist), and his openness to the new, and the conviction of the priority of experimental knowledge over the theory (the death of 4 dogs meant for V.P. Demikhov much more than all the expensive advertising of a new drug). We also note that the new drug was administered by the American, so the tests were carried out fairly objectively.

[9] Professor Deterling Ralph A., Jr. (1917−1992) was the expert in the field of thoracic, cardiothoracic, and vascular surgery, the Head of the Surgery Department at the Medical Center of the Tafts University, Boston, Massachusetts, USA.

Further, V.P. Demikhov drew the attention of the Meeting participants to the conditions in which he had to work and to the possible application of the results of his experiments in clinic:

> "So far there are dog conditions for dogs, and this is not only with us [at the Sklifosovsky Institute], but also with other scientists, specifically, at Lapchinsky's who is present here. There is no clinic for keeping operated dogs. But, despite the great difficulties over the years, we managed to develop a number of schemes for the use in humans. <...>
>
> Most of the transplanted tissue in humans brings certain benefits, and now “tissue banks” have been created in many cities of the Soviet Union. Now we are talking about establishing "banks of organs", but this is a more difficult task requiring special conditions. <...> If you engraft a revitalized organ obtained from a human corpse, you can expect it functioning not for hours, but for weeks and months, and maybe years. The therapeutic effect will be many times greater compared with artificial organs. We also made an attempt to implant kidney. We performed such surgery together with the Urology Department of the Botkin Hospital ... The patient underwent surgery quite well ... Unfortunately, the implanted kidney did not excrete urine ... But despite this, the patient had a dramatic improvement, on the second day ... his native kidneys began to expel twice more urine ... We kept this kidney for 6 days, and during that time it was possible to transplant another kidney ... but it was technically difficult to do, and we had to remove this kidney. And a week later, the patient died ... "[4, p. 19−22].

Here was the second in the USSR (after the observation reported by Yu.V. Voronoi in 1931) case of implanting a kidney to the femoral vessels of a human with acute renal failure in order to prolong his life. But what kind of "technical difficulties" of the kidney reoperation did V.P. Demikhov speak about? After all, having vast experience, he could perform this surgery

quite easily. But in a personal talk with us about this observation, M.M. Razgulov, one of V.P. Demikhov's disciples said that V.P.Demikhov was not allowed to take another kidney from another corpse and implant it again (the first kidney did not excrete urine). However, V.P. Demikhov believed that the problem could be solved with the creation of a "*stock of tested revitalized organs*."

And then he described to the attentively listening attendees of the meeting a fantastic picture of the nearest (in his opinion) future:

> "Now the bone marrow is transplanted with a syringe. And if you transplant a whole hematopoietic organ - the sternum, then we can certainly say that these patients will feel much better. Once, I tried to perform a sternum transplantation surgery on a human (to the femoral vessels) in collaboration with the Moscow Institute of Blood Transfusion, but there I did not find sufficient mutual understanding because of the theory of biological incompatibility. Many researchers say that if you transplant bone marrow with a syringe, there will be no negative reaction. But [in our opinion] if [we implant] a whole sternum, we can certainly expect the manifestation of the "immunological paralysis" phenomenon, since this organ is very large.
>
> According to this scheme, you can transplant the heart and lungs. Transplantation can begin on the femoral vessels, in a case[10]. It is safe and allows you to pick up organs that will function well and survive. At the second stage, these organs can be transplanted to a natural place.
>
> If there had been appropriate conditions, then *we would have engrafted the heart and lungs on the femoral vessels, and then implanted to a natural place last year...* (hereinafter, author's italics). At that time, we agreed with the Institute of Cardiovascular Surgery upon conducting this operation together. We took to reviving the heart in the corpses delivered by

[10] The placement of organs in a plexiglass case with nutritional fluid is mentioned here.

ambulances. But we did not have (and now do not have) a thermostat that would maintain the temperature of the revived heart before the transplant.

The corpse is quickly cooled. In order for it not to cool, we need a temperature of $+37^{o}$. Unfortunately, for the past 15 years we have not been able to purchase a thermostat ... ”[4, p. 22 −23].

V.P. Demikhov's words clearly showed how much he had done to bring the era of organ transplantation in our country closer to the goal of temporarily replacing the function of diseased organs in humans (kidney engrafting in the Botkin Hospital, failed sternum engraft at the Institute of Blood Transfusion, planning heart and lung transplantation at the Institute of Cardiovascular Surgery). It all came down to a simple, but "unsolvable" task - to purchase a thermostat for the corpses of potential donors in order to keep them warm until the organs were removed. If we take away 15 years from 1963, then it turns out that the idea of thermostatic control of corpses came to V.P. Demikhov's mind as early as in 1948, when he was just beginning his experiments on heart and lung transplants in dogs.

But to create a bank of organs, it was necessary to solve another problem, i.e. to learn how to support the vital activity of the revitalized human corpse organs before their transplantation. V.P. Demikhov developed a completely fantastic method for that:

"It is proved that with extensive brain impairments, the human body can live for a long time. <...> I had to support the life of the young man brought from a train station who had left the train and lost consciousness. His heart continued to work, but he was unconscious and had no breathing. The patient on mechanical ventilation was taken to the Sklifosovsky Institute. He had an extensive cerebral hemorrhage. True, breathing was not restored, and I had to

keep it artificially all the time. If we had had the appropriate conditions, then we could have kept that person's body alive for a long time. <...>

If the brain fails to revive, then you need to revive the whole body and maintain the life of such a body. But without a head, a human is no longer a human. The maintenance of the life of the body, of course, must be accompanied by an attempt to restore the brain function. If this could not be achieved, then this body will be kept alive in order to connect other organs to it and to keep them in a lively state for transplantation.

In order to practically accomplish this, we need special thermostats and thermostatic sterile rooms, the equipment for artificial respiration and blood circulation with the presence of qualified personnel. In such conditions, the body can live for a very long time. You can connect the heart, lungs, pancreas, all endocrine glands, liver and others. <...> In particular, we were able to revive the dog's heart, which had been kept for 24 hours at a temperature of +4° in the fridge ... "[4, p.24–26].

Such was V.P. Demikhov's vision of using a human body with a dead brain in 1963. Note that it was not yet about the harvesting of living organs, as is happening now. That time has not come yet. V.P. Demikhov suggested using such an organism for another purpose - maintaining the life of organs taken from a corpse and revived by perfusing their vascular bed with oxygenated blood. However, we should note that despite having a good technical representation of this, the author of the method did not at all take into account possible immunological reactions that must inevitably develop in such an interconnected body perfused with blood and organs without immunosuppression. In addition, V.P. Demikhov did not think about the composition of the liquid, in which living organs should be kept for a long time (as is well known, the problem of the optimal composition of the cardioplegic solution has not been solved yet). But these *purely biological*

problems could in principle be solvable. The main thing is different. He did not seem to care about the *ethical side of* his fantasies, which had no boundaries:

> "The connection of organs to a revived body should be done with the help of prosthetic blood vessels. Herewith, stillborn children can be connected to these prostheses. In maternity homes, such cases are frequent. And in these cases, when it is not possible to revive the brain, organs can be grown from the embryo; the body of a child whose brain has not recovered, will continue growing. And it will be possible to plan growing young organs. Due to the young body, the metabolism in the whole system will also be at the level of the young organism, and in this case rejuvenation will occur. There will be mutual rejuvenation of the organs, which will be connected to the systems as shown in the diagram (Fig.7).
>
> Then it will be possible to pass the prostheses from this system of living organs through into the next rooms. Now operations are made using mechanical heart and lungs which work for 3-4 hrs. And if the prostheses of blood vessels from the animated body are brought to the operating table, it will be possible to operate on the heart and connect seriously ill patients for cross-circulation not for 3–4 hours, but till recovery.<...>
>
> When implementing a system of revitalized organs, it will be possible to maintain the life of a human till transplantation even without internal organs, for example, in inoperable cancer of the abdominal or thoracic organs ...With the help of cross-circulation, it will be possible to remove all internal organs from them and maintain their life until new organs are collected and transplanted to them, of course, provided the brain or spinal cord has been unaffected.
>
> According to this scheme, connecting a human embryo will lead to the fact that, from the point of modern concepts, immunological tolerance will be practically achieved (according to Medhawar and Hasek)"[4, p. 26-28].

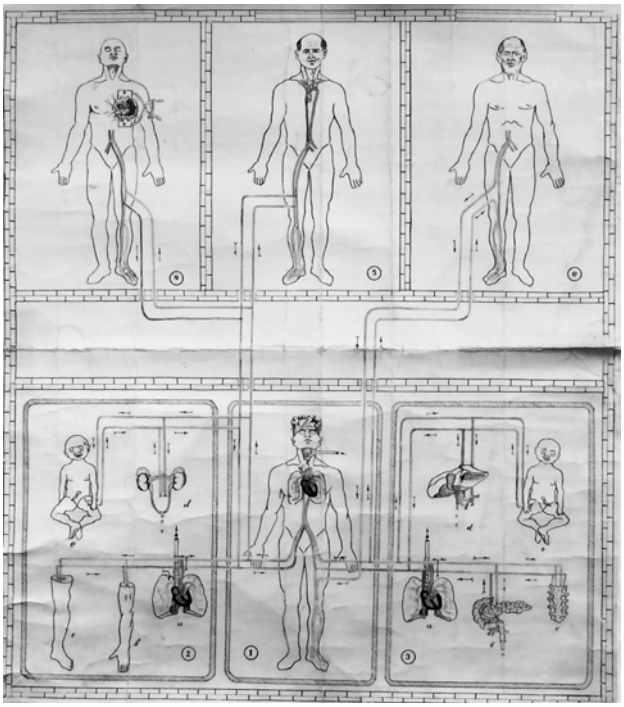


Fig. 7. The scheme of the human body connection to (1) isolated organs, organ complexes, the sternum, and brain-dead newborns (2, 3), human bodies undergoing heart surgery (4), those waiting for organ transplantation, and cancer patients (5), and old people wishing to rejuvenate (6). The scheme was drawn by V.P. Demikhov, 1963.

It is difficult to say with what feelings the audience listened to these arguments. Perhaps some twisted the finger at the temple. Anticipating the doubts of the audience, V.P. Demikhov commented on it like this:

> "It seems to many that all of this is Demikhov's fantasies. And in fact, all this is justified experimentally. Here is, in particular, a head transplant. The experiment showed that the head, along with fore-limbs without internal organs was quite viable. <...> We even had letters from patients who had complete paralysis and who asked us to implant their head on a healthy body ... "[4, p. 28].

But the fact of the matter is that not everything experimentally performed (we deliberately did not use the word "justified") on animals can be transferred to human clinic. And here, unfortunately, V.P. Demikhov reasoned as a biologist, rather than as a clinician, although he did his best to help sick people. But we should note, however, that V.P. Demikhov's idea of the technical feasibility (in his opinion) of transplanting a human head (or rather, body-to-head) was expressed by him on October 8, 1963, for the first and last time.

As you know, the Italian neurosurgeon S.Canavero who planned to perform this operation in December 2017, was so much criticized by fellow surgeons and the public (lawyers, psychologists, sociologists, economists, etc.) that he refused the idea, and Valery Spiridonov, the Russian programmer, who agreed to another's body implantation to his head, said that he had refused such a dubious future.

As for overcoming immunological incompatibility, V.P. Demikhov insisted on his *concept of cross-blood circulation*, or "temporary parabiosis", which, in his opinion, would allow for the *complete adherence of the transplanted organs* .There is a case when bold ideas are far ahead of the technical possibilities of their implementation in practice. But V.P. Demikhov was not daunted:

> "When can all this be done and how realistic is it? If we had adequate conditions, then *we could even organize everything that year* (italics by the author). For this we need a thermostat, we need a room, and that this room is located next to the ambulance station. Our lab is located in such a place. <...> Mikhail Mikhailovich[11] once told me that he was ready to give a 4-storey

[11] M.M. Tarasov was the Director of the Sklifosovsky Institute.

building[12] where it will be possible to organize a bank of organs. If it is organized, it will give results. This requires special skilled staffs and round-the-clock duty, since it requires more care than that for ordinary patients. In addition, there must be an absolute sterility.

That Commission that was working[13] decided to subordinate our laboratory to the USSR Healthcare Ministry. This is very important, as we will have to quickly arrange the delivery of [corpses] of the dead [people] here.

In England, in the city of Leeds, they transplanted a kidney from a human corpse and created a special research center. True, they have a lot of excesses. They use the drug type 6-mercaptopurine ...

I ask the Healthcare Ministry for the help in organizing this whole business," finished V.P. Demikhov. [4, p. 28-30].

The end of V.P. Demikhov's speech well illustrated his position: it was only necessary to solve purely organizational issues, namely allocate and equip premises with appropriate equipment (for example, a thermostat), recruit qualified personnel, streamline the delivery of corpses, and the problem of organ transplantation will be solved and even without such "excesses" as immunosuppressive drugs that do not help, in V.P. Demikhov's opinion, but only with the help of the developed method of cross-circulation. We note another place in the report: as soon as a kidney transplant was performed in Leeds, a scientific center was immediately opened in the city to study the problem.

V.I. Burakovsky, speaking next, (Fig. 8) largely agreed with V.P. Demikhov, but offered to solve the problems of organ transplantation as a

[12] It is about the building where V.P. Demikhov's Laboratory was housed in the basement.
[13] This refers to the Committee headed by V.I. Burakovsky.

clinician, and the Commission headed by him approached the issue under discussion in a governmental scale.

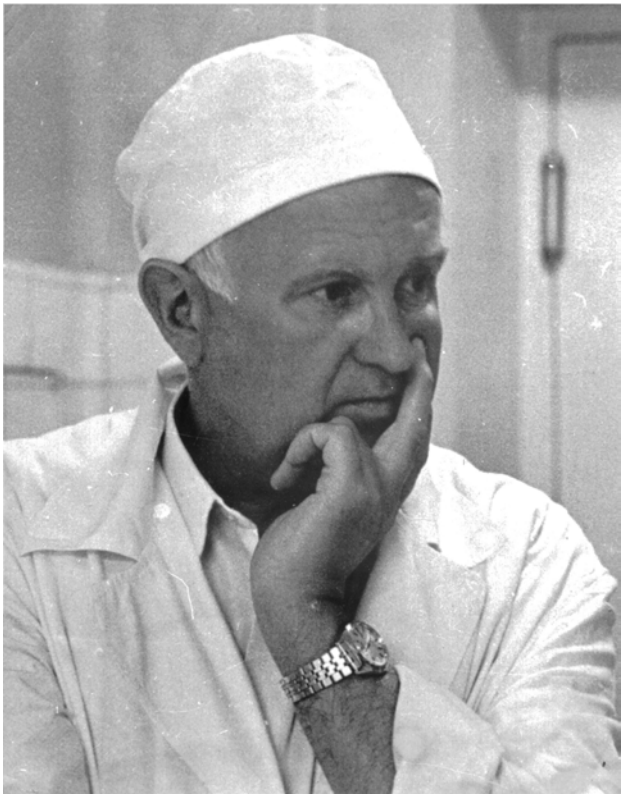


Fig. 8. V.I.Burakovsky. 1960s

V.I. Burakovsky's speech

Starting his speech with the Order of the USSR Healthcare Ministry on establishing the Commission, the tasks it was facing, and making a reservation that he himself had never dealt with organ transplantation, V.I. Burakovsky immediately stated that the issue of V.P. Demikhov's Laboratory is private and relatively small compared with the " huge in its importance problem" of organ and tissue transplantation in the country as a whole.

V.I. Burakovsky designated the main direction in which research should be conducted as "the study of the immunological tolerance mechanisms", since, in his opinion, "it was the successful impact on the reactivity of the recipient's body that allowed the American scientist to achieve a successful kidney transplant in heterozygous twins"[14]. "Unfortunately", V.I. Burakovsky added, "we have not yet created the necessary conditions even for the proper work of [immunological] laboratories ... And there are no necessary drugs".

V.I. Burakovsky stated the second direction as "the preservaion of organs and tissues." Agreeing with V.P. Demikhov, he said that for that purpose it was necessary to "create such a "bank" of organs where the vital activity of the latter would be supported by an artificially conducted blood circulation." V.I. Burakovsky did not support the idea of the previous speaker about using a body with a dead brain for that purpose, but suggested a more rational solution - to create proper "equipment and devices for artificial blood circulation" (ABC), and exercise preservation at a low temperature. "But all this," said V.I. Burakovsky "rests on the acquisition of expensive devices and much more." Indeed, in 1963, the USSR had already created both "native manufactured" ABC machines (for example, in the clinics of A.A. Vishnevsky, N.M. Amosov, and S.A. Kolesnikov), as well as mass-produced devices in Moscow (NIIEHAiI devices) and in Leningrad at the factory "Krasnogvardeets" (F.V. Ballusek devices). But their quality was low, patients died from hemolysis and air embolism even after relatively short operations [5], therefore, we did not have to rely on the use of native manufactured ABC for the purpose of *prolonged perfusion of living organs*.

[14] It is not clear what was spoken about, perhaps, about the second successful kidney transplantation from an unrelated donor performed by J.Murray in 1959.

The organ preservation in conditions of low temperature was associated with fewer problems. The technique of hypothermic perfusion was developed as early as in the 1930s under the guidance of S.S. Brukhonenko; and A.G. Lapchinsky successfully used the chamber for the preservation of cadaveric kidneys in cold conditions. But all those were specific cases. There were no commercially manufactured devices in the country [4, p. 32–33].

V.I. Burakovsky stated the third trend in the transplantation development in the USSR as the development of artificial blood circulation and hypothermia, but not for preservation, but for organ transplantation. Having told about his visit to V.P. Demikhov's Laboratory and his technique of beating heart transplantation, which V.I. Burakovsky called "virtuoso", he, nevertheless, was convinced that the future was for a heart transplant under conditions of artificial blood circulation and hypothermia, and not according to V.P. Demikhov's method. But in that case it would be necessary to arrange not only special clinical departments and operating rooms, but also the special artificial blood circulation laboratories equipped with the most sophisticated equipment and devices. In this regard, in V.I. Burakovsky's opinion, another problem arises: making operations under sterile conditions, which is impossible with high microflora resistance, without modern antibiotics, and careful bacteriological control.

Which way out did the Commission headed by V.I. Burakovsky see? And the way out was seen as follows.

> “There is a need to create a purposefully working institution - *a Research Institute for Transplantation of Organs and Tissues* (italics by the author)”, said V.I. Burakovsky, "First, the dissociation of the studies that are already underway is clearly seen. There are no conferences, no summarizing

materials, there is no coordination of what is being done ... a Problem Committee headed by competent people might also be created.

The second. [It is necessary] to create an official printing body: a newsletter on organ and tissue transplantation, in which the work of our scientists and foreign studies would be covered.

The third. It is necessary to improve the supply of necessary equipment, medicines and drugs to those special laboratories that deal with these issues. We examined the Laboratory of Vladimir Petrovich. There are very original, interesting models there. Dogs with a transplanted heart and other organs live. But there is no deep study of these experiments. These experiments have not been studied from a physiology point of view. <...>

The fourth. Perhaps now we should undertake the expansion and integration of existing laboratories, for example, the one established by Professor V.V. Kovanov, a Corresponding member of the USSR Academy of Medical Sciences. In addition, we can create such a laboratory at A.V. Vishnevsky Institute of Surgery, at the Institute of Cardiovascular Surgery ... We have done a large number of [heart] operations. We will be happy to work on the transplantation of the lungs, heart. But for doing this, we need to expand our capabilities ..."[4, p. 33–36].

Denoting common issues, V.I. Burakovsky dwelt upon the activities of V.P. Demikhov's Laboratory. Pointing to a "significant 20-year work" and developed by V.P. Demikhov technically original techniques of transplanting the heart, lungs, head, sternum, and other organs, V.I. Burakovsky noted the lack of studying these models, insufficient provision of laboratory with research equipment. To improve the situation, the Commission found it appropriate to request the Healthcare Ministry to transfer the Laboratory from the jurisdiction of the Moscow City Healthcare

Department to the USSR Healthcare Ministry or the USSR Academy of Medical Sciences. Concluding his presentation, V.I. Burakovsky said:

> "I think that Vladimir Petrovich Demikhov made a lot of interesting and very important things. Our task is to take a critical look at his proposals, use what he can give for the development of the issue, prove that some of his views do not completely coincide with life, and I think he will be happy if we can prove it"[4 , p. 37] .

Worthwhile to note the tactfulness shown by the Commission headed by V.I. Burakovsky to V.P. Demikhov and his contribution to solving the problem. For the first time, at the level of the USSR Healthcare Ministry it was said:

> "V.P. Demikhov does not deny a possible occurrence of immunological shifts in the blood. He is well aware of the inferiority of his research and notes that "in order to finally clarify the role of the immunological processes of the non-adherence of the graft, further studies on animals with transplanted organs are needed" [6, p. 5] .

Noting the poor equipment of the Laboratory with electrophysiological equipment, the commission complained:

> “The only experiments in world science (on heart transplantation with survival up to 100 days) remain insufficiently studied in relation to the function of the transplanted organ, its metabolism; the issues of regulation, regeneration, changes at the level of cells and molecules have not been studied, which is largely due to a lack of funds, equipment, employees ”[6, p. 5].

The Commission also noted the fact that:

> "The scientific data obtained by V.P. Demikhov in the experiment *in organ transplantation put him forward among the most prominent experts of the world* (italics by the author), which was recognized by a number of foreign scientific institutions that assigned him the honorary title of Doctor of Medical Sciences and elected him as a Member. However, V.P. Demikhov still does not have an academic degree. The Commission believes that his experimental work, carried out over a period of 20 years, published articles and a monograph, as well as the development of original experimental operations, give him the right to be awarded an academic degree" [6, p. 5-6].

Stressing that "the main scientific proposal put forward by V.P. Demikhov and the use of “revitalized” corpse organs to replace the function of patient’s native organs ... *is now real* (italics by the author)", the Commission concluded:

> “The real success and relatively long-term functioning of the grafts can be achieved only when using the already studied methods of influencing the graft and the recipient in a specialized institution that has all the necessary conditions.
>
> V.P. Demikhov's Laboratory does not have such conditions, as well as does not have the ability to comprehensively study experimental animals. It should be pointed out that the Sklifosovsky Institute of Moscow City Health Department is not able to create proper working conditions for the Laboratory in the intended direction (insufficient funding, lack of specialized laboratories and specialists, low salaries of researchers). <...>
>
> Considering the great prospects and the exceptional complexity of the organ and tissue transplantation, in order to solve this problem more successfully, the Commission considers it appropriate:

"1. To create a specialized scientific research institute for transplantation of organs and tissues with clinical and experimental bases, equipped with everything necessary for conducting research at the modern level of medical science;

2. Given the fragmentation of research on this issue, organize a Problem Committee on the Transplantation of Organs and Tissues in the USSR Healthcare Ministry;

3. Withdraw the Laboratory of V.P. Demikhov from the system of Moscow City Healthcare Department, transferring it to the subordination of the USSR Healthcare Ministry or the USSR Academy of Medical Sciences with its expansion, increase in staff and allocations.

Dr. V.P. Demikhov has been made familiar with this conclusion.

Signatures: V.I. Burakovsky, M.M. Kapichnikov, N.G. Sushko, I.D. Kirpatovsky, J.Ya. Gritsman "[6, p. 6−8].

A few years later, a number of the Commission's proposals were brought to life. In particular, the Problem Committee and the Institute of Organ and Tissue Transplantation were established under the USSR Healthcare Ministry jurisdiction. But V.P. Demikhov's Laboratory remained at N.V. Sklifosovsky Institute with the same staff and the same funding. But this will be discussed in the following articles.

(To be continued)

References

1. Demikhov VP. *Ob eksperimental'no-obosnovannom proekte revolyutsii v meditsine i soprotivlenii partiynykh deyateley Instituta imeni Sklifosovskogo.* A letter to the First Secretary of the Moscow City Committee of the Communist Party of the Soviet Union N.G. Egorychev, January 14, 1963. Typescript (copy). Moscow, 1963; p. 2, 3. (In Russ.).

2. Glyantsev SP. Phenomenon of Demikhov. In the Sklifosovsky Institute (1960–1986). Scientific Revolution in Transplantation (1960–1964). Achievements of the USA and the USSR in the feld of transplantation and transplant immunity (1962). *Transplantologiya. The Russian Journal of Transplantation.* 2019;11(1):71–87. (In Russ.). https://doi.org/10.23873/2074-0506-2019-11-1-71-87

3. Demikhov VP. *Letter to the Deputy Minister of Health of the USSR, Corresponding Member of the Academy of Medical Sciences of the USSR, prof. Kochergin I.G., February 10, 1963.* Typescript (copy). Moscow, 1963; p. 2–3. (In Russ.).

4. State Archive of the Russian Federation, f. 8009, reg. 2, d. 2557. (In Russ.).

5. Bokeriya LA, Glyantsev SP, Loginov DT. K istorii nachala khirurgii otkrytogo serdtsa v Rossii (o prioritetakh vypolneniya pervykh operatsiy na otkrytom serdtse). *Byulleten' NTSSSKH im. A.N. Bakuleva RAMN «Serdechno-sosudistyye zabolevaniya».* 2006;7(6):71–84. (In Russ.).

6. Zaklyucheniye komissii, sozdannoy prikazom po ministerstvu zdravookhraneniya № 82 ot 25 fevralya 1963 g. dlya izucheniya predlozheniy V.P. Demikhova po voprosu o peresadke organov i perspektiv nauchnykh issledovaniy v etoy oblasti. Typescript (copy).Moscow, 1963. (In Russ.).

Information about the author

Sergey P. Glyantsev, Prof., Dr. Med. Sci., Head of the Department of History of Cardiovascular Surgery, A.N.Bakulev National Medical Research Center of Cardiovascular Surgery, Chief of the Medical History Unit within

the Medical History Department at N.A.Semashko National Research Institute of Public Health, https://orcid.org/0000-0003-2754-836X

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