https://doi.org/10.23873/2074-0506-2019-11-4-330-348

PHENOMENON OF DEMIKHOV.
At the Sklifosovsky Institute (1960-1986).
Research Coordination Council of the USSR Healthcare Ministry:
Missed opportunities. Part 2 (1963)

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Conflict of interests Authors declare no conflict of interest

Financing The study was performed without external funding

Glyantsev SP. Phenomenon of Demikhov. In the Sklifosovsky Institute (1960–1986). Research Coordination Council of the USSR Healthcare Ministry: Missed opportunities. Part 2 (1963). *Transplantologiya. The Russian Journal of Transplantation*. 2019;11(4):330–348. (In Russ.). https://doi.org/10.23873/2074-0506-2019-11-4-330-348

This paper has first put into scientific circulation the transcript of the Meeting of the Presidium of the USSR Healthcare Ministry Council for the Coordination of Scientific Research and Implementation of the Scientific Achievements that was held on October 8, 1963, and discussed the current state and development of scientific research in organ transplantation in the USSR. The presentations of the meeting participants who discussed the

reports of V.P. Demikhov and V.I. Burakovsky have been described and analyzed. The concept of organ homotransplantation put forward by V.P. Demikhov who did not take into account (in some speakers's opinion) the latest achievements in immunobiology was reasonably criticized. V.I. Burakovsky's proposals on establishing a Research Institute of Organ and Tissue Transplantation and the Problem Commission for Transplantology were considered rational, supported, and included in the Presidium Resolution.

Keywords: history of transplantology, USSR Healthcare Ministry, Research Coordination Council, Institute of Organ and Tissue Transplantation, Problem Commission for Transplantology, 1963

In the previous part of this article, we examined and analyzed the presentations of V.P. Demikhov and V.I. Burakovsky they made at the Meeting of the Presidium of the USSR Healthcare Ministry Council for the Coordination of Scientific Research and Implementation of the Scientific Achievements held on October 8, 1963, where the state and development of scientific research in organ transplantation in the USSR of that time were discussed. After their presentations, the speakers were asked questions, and then a discussion took place.

The Chairman of the Meeting was Professor I.G. Kochergin, the Deputy Minister of Healthcare of the USSR. The Meeting was attended by about 50 doctors and scientists from various Moscow institutions engaged in research in the field of immunology, biology, morphology, transplant immunity, experimental and clinical heart surgery, organ and tissue transplantation. This article briefly describes and analyzes the panel

discussion of V.P. Demikhov's and V.I. Burakovsky's presentations and the Resolution taken by the Council on the topics discussed.

The USSR Healthcare Ministry Council for the Coordination of Scientific Research and Implementation of the Scientific Achievements into Practice (Questions to speakers)

After V.P. Demikhov and V.I. Burakovsky had completed their presentations, I.G. Kochergin (Fig. 1) invited the audience to ask questions. Despite the fact that the Chairman suggested the panelists addressing questions to both speakers, indeed, the questions were addressed only to V.P. Demikhov

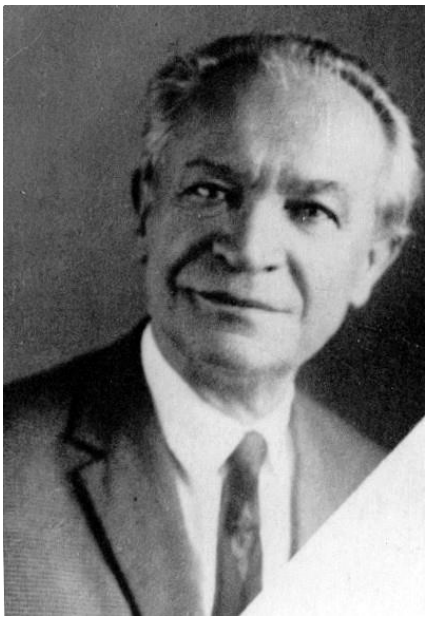


Fig. 1. Professor I.G. Kochergin, the Deputy Minister of the USSR Healthcare Ministry, a Corresponding Member of the USSR Academy of Medical Sciences

Professor M.I. Efimov (Ryazan[1]): "Has the speaker performed an experimental autotransplantation and what are the results? How would you rate the data of Medawar and Hasek[2], or do you take an original position on this issue?"

Professor S.A. Sarkisov, Full Member of the USSR Academy of Medical Sciences, Director of the Institute of Brain of the USSR Academy of Medical Sciences, (Fig. 2): "Along with remarkable surgical operations, there are no important immunological studies of these experiments. I would like to ask. I understood that you didn't find it necessary to do this, or [you didn't do it] because there were no appropriate conditions. Or do you think that this issue has already been solved by life? "

Mr. L.M. Lemenev, the Head of the Planning Department of the USSR Healthcare Ministry: "Why do you have no comprehensive research with biologists, physiologists, morphologists?"

Fig. 2. Professor S.A. Sarkisov, a Full Member of the USSR Academy of Medical Sciences

[1] Table 1 in a previous article erroneously stated that Professor M.I. Efimov was from Moscow.

[2] Medawar P.B. (1915–1987), Professor, the Director of the National Institute for Medical Research (London), Nobel Laureate in Medicine (jointly with F.M. Burnet, Australia) "for the discovery of artificial immunological tolerance" (1960). Hasek M. (1925–1984), Professor, the Director of the Institute of Experimental Biology and Genetics, Academy of Sciences of Czechoslovakia; he independently from P. Medawar, obtained the state of immunological tolerance in his experiments on parabiosis of birds in the period of their embryonic development.

R.L. Ginzburg: “Why do you disregard the immunological reactions to transplantation? You give importance to restoring the blood circulation. You have transplanted a lot of heads, hearts; so tell me, if there was at least one case of a prolonged graft survival. Has there been at least one case of a permanent graft survival? <...> The next question: Does the skin transplanted with the limb invariably adhere? The last question: You work at the Sklifosovsky Institute; there is rich human material there. Was there at least one case of an autoplastic transplantation? Of a finger at least?”

Professor I.G. Kochergin, the Chairman of the Meeting, **the Deputy Minister of Healthcare of the USSR:** “I will allow myself to ask the following question: For three years of work at the Sklifosovsky Institute, Demikhov has performed about 250 operations on 500 dogs for organ transplantation: of the head, heart, lungs, abdominal organs, sternum, homo extremities. But unfortunately, the Commission has no data on the results of these experiments? The models are good, and we know that Vladimir Petrovich is an excellent surgeon. Tell me, of these 250 operations, what the survival times were for a transplant of a head, skin, etc. Can you present such an analysis? You did not say anything about this in your report. There are 7 days, and if Grishka lived for 143 days, this is a completely different matter.”

Question from the audience: “Tell me, how many limb transplantations have you done?”

I.G. Kochergin: “Vladimir Petrovich, answer the questions that were asked” [1, p. 38–40][3].

The questions touched upon the most essential aspects of V.P. Demikhov's work: the attitude to autotransplantation, to conducting comprehensive research, to immunology. The main question was asked by I.G. Kochergin: “What are the survival times for the transplanted organs?

[3] The first figure in square brackets indicates the number of the source in the list of references; the second figure denotes the page number in the source.

But before V.P. Demikhov began answering the questions, we should pay attention to one detail. The USSR Healthcare Ministry Council for the Coordination of Scientific Research met to consider the issue "*On the current state and development of scientific research in organ transplantation*", and the invitees seemed to be interested in the issues related to the activities of one person. It was as if V.P. Demikhov was the only one responsible for the state and development of this problem in the country as a whole.

However, the questions were asked, asked specifically and to the point, and the attitude of I.G. Kochergin, the Meeting Chairman, to V.P. Demikhov was benevolent, judging the way he addressed him by his name and patronymic. And V.P. Demikhov began answering those questions.

> **V.P. Demikhov**: "The first question is whether autotransplantation has been performed? I didn't do this. I believe that this issue has been basically resolved, and dealing with resolved issues means wasting time. I observed the results of autotransplants in other scientists. <...>
>
> As for the data from [P.B.] Medawar and [M.] Hasek, I listened to both Medawar, and Hasek. Both of them in their studies [in homotransplantations] did not find antibody formation <...> At the British Exhibition[4] (Fig. 3), it was written that Medawar was awarded the Nobel Prize for the elimination of antibodies. I asked a Soviet immunologist whom I met at this exhibition: "How could it be understood that Medawar did not find antibodies in his experiments, but received the Nobel Prize (as it is written in the English booklet in Russian) for eliminating antibodies?" The immunologist answered me (saying between us) that we played him up. I told him to this that it would be better for you to play along with the Soviet and socialist countries.

[4] The British Trade and Industry Exhibition was held in Moscow in Sokolniki Park from May 19 to June 4, 1961.

Fig. 3. The cover of the booklet of the British Trade and Industry Exhibition held in Moscow, May 19-June 4, 1961

Hasek prepared the dogs for a heart transplant, and the Czechoslovak Academy invited me to come to them in the month of December. I agree to go there, they have committed to pay all the expenses, but our Ministry has refused [me] from the trip. The External Relations Department said that the trip was not planned. <...> It's about working with Hasek[5].

I am a biologist and pathologist. For 10 years, we together with the Institute of Experimental Biology [USSR AMS] have conducted research[6]. But for 10 years, the Institute can not convince me either with its facts, or with the data. Every time I invite them: "Come to the autopsy section and see what causes the organ to die." <...> They say to me: "We do not know the pathological anatomy and will not watch." What is happening [in the deceased organ]? I am always sending all the material for histological examination. And here I am dependent on Professor [T.A.] Grigoryeva[7]. It's not my fault.

[5] One can only guess what results V.P. Demikhov and M. Hasek could have obtained working together. Unfortunately, that did not happen.
[6] We are talking about the research together with I.N. Maisky and N.N. Zhukov-Verezhnikov.
[7] In 1960–1968, Professor T.A. Grigoryeva was the Head of the Histology Department of the 2nd Moscow State Medical University named after N.I. Pirogov; among other research, she studied the morphology of transplanted organs.

Mikhail Mikhailovich [Tarasov] and I wanted to invite a post-graduate student from [N.N.] Zhukov-Verezhnikov's Postgraduate School[8], but she was advised not to come to us. After each experiment, we send blood to the Institute of Experimental Biology [of the USSR Academy of Medical Sciences]. They say that they sometimes find incomplete antibodies. But here it is necessary to answer the question: whether these antibodies are the cause [of the graft death] or the consequence? It turns out that these antibodies are the consequence of the graft death.

[You ask,] why there is no comprehensive research. On the contrary, I strive to conduct such research. We conduct joint [morphological] studies with the Department of Histology of the 2nd Medical Institute (Headed by Prof. T.A. Grigoryeva. *Auth.*). I don't have such opportunities, but they have them. <...> I was ready to go to the Institute of Experimental Biology [of the USSR Academy of Medical Sciences to conduct immunobiological studies], but it so happened that at first Ivan Nikolaevich [Maisky] agreed [to work together], and then refused. <...>

I tried to conduct joint research with ten institutes, I submitted an application to Academician [N.N.] Blokhin[9] so that they give me the opportunity to address the debate at the Session [of the USSR Academy of Medical Sciences] and declare my desire to conduct research with these institutes of the USSR Academy of Medical Sciences. But I was not given such an opportunity. Then, without listening to me, the Presidium of the USSR Academy of Medical Sciences accused [me] of insufficient

[8] N.N. Zhukov-Verezhnikov (1908–1981), the Academician (Full Member) of the USSR Academy of Medical Sciences; in 1948–1950 he was the Director of the Institute of Experimental Biology, the USSR Academy of Medical Sciences, where he established the Laboratory of Experimental Immunobiology; in 1952–1954 he was the Deputy Minister of the USSR Healthcare Ministry; in 1955-1981 he headed the Immunobiology Department at the Institute of Experimental Biology, USSR Academy of Medical Sciences.

[9] N.N. Blokhin (1912–1993), Hero of Socialist Labor, Lenin Prize Laureate, Academician of the USSR Academy of Sciences and Academy of Medical Sciences; in 1960–1968 and in 1977-1978 he was the President of the USSR Academy of Medical Sciences.

competence in organ transplantation. The decision of the [Presidium] was signed by Psychiatrist [O.V.] Kerbikov[10]. <...>

In addition, I conducted head transplant studies with the Berlin Institute (GDR). There are three collaborative studies. But it's much more difficult to go to Germany. It would be easier for me [to conduct comprehensive research] in the Soviet Union. Now we are working together with the Institute of Tuberculosis [of the USSR Healthcare Ministry. Professor [N.M.] Gerasimenko is present here. We are pleased with each other. But they called Professor Gerasimenko and say: "Do not work together with Demikhov!" I don't know who is calling and who needs it.

In my experiments, there were cases of continuous survival. The most striking example is the dog Grishka with a transplanted extra heart and lungs, which lived for 141 days (Fig. 4). Associate Professor [I.A.] Chervova and Professor [T.A.] Grigoryeva are present here. They can confirm [the graft survival] histologically. There was very good graft integration. I have preserved the preparation slide.

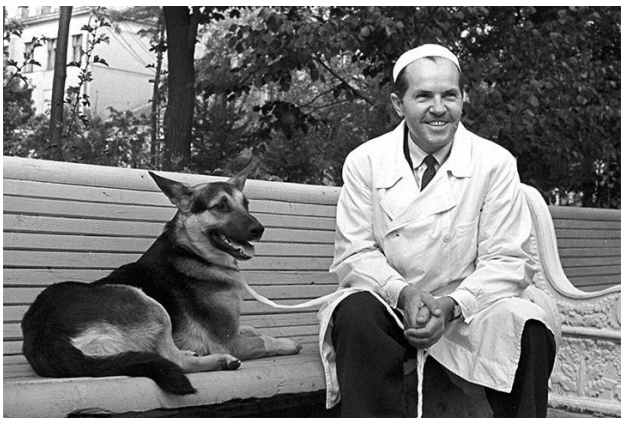


Fig. 4. V.P. Demikhov and Grishka dog. Photo by E. Tikhonov. July 1, 1962

[10] O.V. Kerbikov (1907–1965), Academician of the USSR Academy of Medical Sciences, Head of the Psychiatry Department at the 2nd MGMI n.a. N.I. Pirogov; he was a Member of the Presidium of the USSR Academy of Medical Sciences from 1962–1963, the Chief Scientific Secretary of the Presidium of the USSR Academy of Medical Sciences from 1963–1965.

As for the rejection process. Rejection occurs in skin transplantation. But does it occur due to the presence of antibodies or do the antibodies result from necrosis [of the transplanted skin]? Additional research is needed to find out.

The head transplanted from a mongrel to a shepherd dog lived for 29 days. And it integrated so well that it resulted in an adhesion-caused compression of the main vein, through which the blood returned from the head, and [the head died against] edema according to thrombophlebitis principle."

I.G. Kochergin: "We are speaking about the survival time of transplanted organs in your experimental material. The skin had taken and healed, but then the head died."

V.P. Demikhov: "Pathologists determined that the healing was with the primary intention, and the source of infection was in a single site only, and that was what caused the outcome.

The maximum survival period is 141 days. But this is a dog whose organs were quite viable. On day 141, the [transplanted extra] heart ceased to be auscultated. It was just November 8, a holiday. And we decided to invite everyone to attend this. I began to call the scientists of the Sklifosovsky Institute, but I did not find anyone. Here, the heparin infusion helped us, after which the rhythm of the [transplanted] heart was restored. Therefore, the picture there was very clear, both from the functional point of view, and from the point of pathology. Several dogs with a transplanted [second, extra] heart lived up to a month. The causes of their death were investigated and also completely clear to us.

A big drawback in our work is the blood coagulation issue. We have had thrombosis very often. In dogs, by comparison with humans, coagulability is increased...

Question from the audience: “Therefore, did one dog live for 141 days[11] and two live about a month?”

I.G. Kochergin: “As a Chairman, I’m interested in the following: I want to know what the survival times of the transplanted organs were. I just ask, how many survivals there were besides Grishka. What were the deadlines for the rest of the elements?"

V.P. Demikhov: “I did not expect that it would be necessary to report accurate data, so now I don’t have it with me. <...> I, of course, have all the protocols, but I can’t tell the exact numbers from memory now. About 2-3 dogs with a transplanted [extra] heart lived for up to a month. There were those who lived for three weeks, and there were cases when the dogs lived for 12 and 18 days. This is for transplanted hearts and lungs.

I also transplanted the sternum along with the skin and watched the adherence. In two cases, the sternum survived for 18 days. On the 18th day, cooling was observed, and the graft had to be cut off.

I transplanted the head, which survived for 29 days. In other experiments, the head survived for 7–10 days.

There were limb transplants, but the infection interfered along with thrombosis. We do not have a clinic. It is difficult to create certain sterility. We use antibiotics against infection, and they increase blood coagulation.

There were 4–5 experiments with limbs. And the operations were performed according to a new scheme. And although the limbs survived for 10 days, we noticed an interesting fact: there was swelling of the transplanted limbs, we dissected the adhesions around the vein, and the swelling was resolved. This edema was actually the result of a physiological process, that is, the result of an obstructed blood outflow from a transplanted organ” [1, p.40–48].

[11] The questioner did not understand: it was not Grishka’s dog who lived for 141 days, it was the second heart transplanted to it that worked for 141 days. After its stop, an autopsy was performed and a cardiopulmonary preparation was studied.

V.P. Demikhov's straightforward and sincere answers showed how difficult his search had been. Neither the staff (he wanted to invite a graduate student, but she was dissuaded), nor large-scale comprehensive research (V.P. Demikhov was not allowed to go to into the Czechoslovak Socialist Republic, I.N. Maisky refused to work with him, N.M. Gerasimenko was dissuaded; The Presidium of the USSR Academy of Medical Sciences refused him from collaborating with academic institutes), nor did he have adequate conditions for nursing the operated dogs (a sternum transplant had to be removed due to weather changes). The presence (or absence) of antibodies in the blood of the recipient, in V.P. Demikhov's opinion, did not prove the rejection reaction; and the survival of homografts for 3-4 weeks (and even more as the hearts in Grishka's chest survived for 141 days) contradicted the laws of immunobiology known to him at that time. And as for the edema of the transplanted homo-extremity, V.P. Demikhov did not explain it as the rejection reaction, but rather as an impaired blood outflow, since the edema disappeared after the venous blood return had been restored. Concluding the answers to the questions, V.P. Demikhov tried to return the discussion to the main topic on the state and development of research on organ transplantation.

> **V.P. Demikhov**: "What is the state [of the problem] abroad? My book, which is published here, has been translated in New York and in Berlin. It is the only organ transplant guide.
>
> Regarding limb autotransplantations at the Sklifosovsky Institute. <...> There have been many attempts[12]. However, there are only two successful transplants: one performed together with Professor [P.I.]Androsov, with a

[12] As an example, V.P. Demikhov cited a case of penile implantation in June 1963 by the surgeons at N.V. Sklifosovsky Institute, but "after 19 days he had to be cut off again. And there are many such cases. True, I did not participate in that surgery" [1, p. 50].

successful limb attachment; and the second case was in France. This suggests that the technique (of replantation. - *Auth*) has been mastered insufficiently[13]. <...>

I.G. Kochergin: "We are very interested in experimental material. But neither [V.P.] Demikhov's, nor Professor [V.I.] Burakovsky's presentations contained any of such material. And Vladimir Petrovich does not remember the necessary data. You know that the report of Comrade Demikhov is riddled with questions of biological reactions from beginning to end. And you, Vladimir Petrovich, had to give experimental material and dwell on it in detail in your presentation, and not enter into a dispute with an unknown enemy. But now the work has already been done, and now it remains for us to move on to discussing this issue" [1, p.48-50].

From the question and the conclusion of the Deputy Minister, it follows that he, instead of discussing the state of the problem as a whole, expected V.P. Demikhov presenting the data of his experiments. But it is no coincidence that V.P.Demikhov contemplated about biological reactions in homotransplantations in his report. It was him who looked at the problem of transplantation quite widely. It was clear to him that the main issue that needed to be solved nationwide was not a surgical issue, but a biological one.

The fact is that, as we have shown earlier [3], all V.P. Demikhov's research was aimed at finding the ways to overcome biological incompatibility in homotransplants, and one of those ways was parabiosis. Let us recall his remarks on the work carried out by him for 10 years

[13] We are talking about one of the country's first successful operations of replanting the right forearm in a young woman after traumatic amputation, which P.I. Androsov performed in 1951. The first successful replantation of a traumatically amputated forearm at the level of the middle third was performed using a vascular stapling device in 1950 by Z.Z. Boykova, N.P. Petrova, and M.G. Akhalaya in the Clinic of the Faculty Surgery Department named after S.I. Spasokukotsky at the Medical Faculty of the 2nd MGMI n.a. I.V. Stalin (the Director was Prof. A.N. Bakulev) [2].

together with the Institute of Experimental Biology of the USSR Academy of Medical Sciences, on his desire to hire a postgraduate student from immunologist N.N. Zhukov-Verezhnikov, about the experiments he conceived together with M. Hasek. Indeed, M. Hasek overcame the immunological tolerance by means of parabiosis in birds, but only in the period of their embryonic development. It remains only to guess what results the joint research of the Czechoslovak and Soviet scientists could have given.

The USSR Healthcare Ministry Council for the Coordination of Scientific Research and Implementation of the Scientific Achievements into Practice (Discussion)

But, speaking with I.G. Kochergin's words, “the work was done,” and it was time to move on to discuss what had been said and heard. The first to take the floor was Professor T.A. Grigoryeva, a histologist, who told the audience how the Department she headed came to the problem of studying organs after homotransplants, how she and her staff “*came into contact with V.P. Demikhov* ", and what they found in homohearts at autopsies.

> **Professor T.A. Grigoryeva**: “This Meeting, which is attended by representatives of many scientific disciplines, has every reason to comprehensively discuss the issue and outline the right ways to resolve it.
>
> We have been in contact with V.P. Demikhov for several years. We came to the need to establish this contact as a result of our own research in the field of neural trophism. To solve our own problems in relation to this problem, we resorted to the method of studying changes in organs and tissues after their separate innervation (sensory, motor, and autonomic). We have

found that each of the nerve conductors has its own specific meaning for the organ. <...> Having these data on hand, we started experiments on [auto] transplants (research by O.V. Volkova) <...> and established a direct relationship between the organ survival and preservation of its specific structure and its reinnervation. <...>

After that, we made contact with V.P. Demikhov. [At the beginning] together with him we examined a homotransplanted kidney. As we expected, there were all the changes in the transplanted kidney that we observed in a denervated organ (the thesis of I.P. Shlykov). Among the changes, those associated with sensitive denervation predominated. <...> There was an idea that in resolving the complex problem of graft survival, the problem of its reinnervation predominates, which can compete with the problem of tissue incompatibility. <...>

[Further] together with V.P. Demikhov, we studied 15 homotransplanted hearts (research of I.A. Chervova), including the one that lived and worked in the recipient for 142 days. The results of these studies are important not only for the problem of transplantation in its narrow sense. The transplant method allowed us to create a heart that lives in the absence of neural connections with the body. But this heart appeared to be not completely denervated. We found its native intramural nervous apparatus in it that was built on a reflex principle. This apparatus, providing a level of reflex functioning under conditions of intact vascularization, allows the transplant to remain viable. These data are of great importance for the morphology and physiology of the heart. They inspire hope that, when extracardial nerves (cut during transplantation) grow into a transplant, the transplanted heart can exist for a longer time.

Only brilliant surgical techniques developed by V.P. Demikhov allow this work to be performed. The studied homotransplants of the heart have shown that tissue reactions in it proceed less rapidly than, for example, in the kidney. This is most likely due to the presence in the heart of an intramural nervous apparatus that functions reflexively.

> This question is extremely important in the general spectrum of the problem and requires further research. I believe that the problem of organ and tissue transplantation, which now has neither a special coordinating institution, nor a Problem Commission and is therefore being resolved without the necessary planning and control, should find the both after today's Meeting. Establishing a Problem Commission (Task Force) for Transplantation is very important. But even more important is the creation of a special institution in which it will be possible to carry out comprehensive research on the problem. V.P. Demikhov should take an appropriate place in this institute. In the meantime, we need to take measures to improve his working conditions, which are far from prosperous, and provide him with the opportunity to continue his extremely important research." [1, p. 52–55].

T.A. Grigoryeva's speech is interesting in the following. First, in fact, in her research, she used experimental models developed by V.P. Demikhov, and those which he offered to many researchers for use in different years (most often, unsuccessfully). Fortunately, in this case, the scientific interests of V.P. Demikhov and T.A. Grigoryeva coincided. Second, having discovered during organ denervation the morphological changes similar to those that were present in the transplanted homoorgan, T.A. Grigoryeva came to the same conclusion that V.P. Demikhov had reached in due time: the restoration of the function in a transplanted organ contributes to its survival. In this case, we do not discuss the truth of this approach. We only state that V.P. Demikhov was not alone in his attempts to solve biological problems from the standpoint of physiology. Third, T.A. Grigoryeva was the first to support the idea of the need to create a specialized research institute and the Problem Commission for Transplantation in our country. Fourth, noting the merits of V.P. Demikhov in developing the problem, T.A. Grigoryeva pointed out the need to improve the conditions of his work.

The next speaker was A.G. Lapchinsky, the Head of the Organ Transplantation Laboratory at the Research Institute of Traumatology and Orthopedics named after N.N. Priorov, who immediately noted the smallness of the questions asked.

A.G. Lapchinsky, Candidate of Medical Sciences[14]: "I don't know about the others, but I have a feeling of dissatisfaction, because the issue on the agenda regarded to our situation with the problem of transplantation of tissues and organs, but the matter boils down to a discussion of V.P. Demikhov's work. And the main points for the Committee's Resolution on establishing an institute or a specialized institution for solving this problem were completely blurred in the presentations of the speaker and co-speaker. <...>

I believe that our task is to talk about the problem, and the problem of organ and tissue transplantation is the surgery of the future. And I especially support, because for many years I have said that such an institution must exist. In 1958, a number of leading surgeons [and scientists]: V.N. Shamov, A.A. Vishnevsky, N.I. Grashchenkov, P.A. Kupriyanov, I.G. Rufanov et al came forward with the proposal. They wrote a letter in which they said that it was necessary to organize an institute for transplanting organs and tissues. I once submitted a letter to the Minister M.D. Kovrigina, in which I wrote that (he quotes the letter) "... if the existing situation is not changed and the center coordinating the transplantation work in the USSR is not created, then we risk lagging behind the world foreign science." <...>

At a Nephrology Congress in Prague, American scientists reported that they had transplanted kidneys to 50 people and not only to identical twins, but also from unrelated people and corpses; there were 50 patients in England, 27 patients in France. And in our country, no one is doing this right now. <...>

[14] In 1970, A.G. Lapchinsky defended his doctoral thesis on the topic: "Autotransplantation and limb homotransplantation in the experiment".

Meanwhile, we started kidney transplants earlier than abroad. For the first time, a kidney from a corpse was transplanted to a patient in 1934 by Yu.Yu. Voronoi who had made 5 such operations by 1950.

Amburge who now holds a leading position in kidney transplant studies abroad[15] reported a year ago that the kidneys can be transplanted only from living donors, since their function is irreversibly impaired when blood circulation in an isolated kidney is interrupted for more than 45 minutes. Meanwhile, in our experiments on dogs, we have shown that, using our originally developed technique for the preservation of isolated kidneys by cooling with a cardiopulmonary bypass in our proposed device (Fig. 5), we can store isolated kidneys safe up to 28 hours. After replantation, such kidneys survived and restore their function so well that one kidney preserved by using this technique, and transplanted onto the dog's neck at 28 hours after separation from the body, was able to fully perform a urinary function. ... Ambürger and Weiss spent the whole day in our Laboratory studying our technique, because, having mastered it, they hoped to use kidneys from fresh corpses instead of living donors for transplants. And now they have managed to do that.

[15] Hamburger J. (1909–1992), a French nephrologist and immunologist, the founder of Nephrology; Member of the French Academy of Sciences, the Head of Nephrology Clinic of the Paris University at the Necker Hospital; in different years, he headed the French and International Society of Nephrologists, the International Society for Transplantation; he performed the first kidney transplantation in France in 1952, the first successful transplantation between twins in 1954, the first homo kidney transplantation in 1959, and a successful transplantation using immunosuppressants in 1962.

Fig. 5. Employees of NIIEHAiI (from left to right): Engineer G.P. Tarasov, Hematologist G.V. Medvedev, Deputy Director on Research S.S. Bryukhonenko, and the Head of Organ and Tissue Transplantation Laboratory A.G. Lapchinsky near the apparatus for organ and tissue preservation under hypothermia and artificial circulation conditions. December 22, 1953. From S.A. Perestoronin's archives

To cope with incompatibility, sublethal doses of irradiation and chemical agents are used. This requires special expensive equipment that we do not have. And it doesn't bother anyone, nobody deals with it.

We need a coordinating center in the form of an Institute or a large laboratory <...>, in which, along with experimental work, clinical treatment of patients would be performed using transplantation of whole organs and tissues. At this institution, there should be a central tissue bank for the collection of [organs and] tissues from corpses for transplantation and the development of techniques for [their] storage. This new institution should be responsible for the development and implementation of transplantation techniques in clinical practice. It should maintain contacts with foreign scientists in this specialty, using the achievements of native and foreign researchers. Without this, we are clearly starting to lag behind, especially in the field of clinical application of transplantation methodology.

In February 1964, the New York Academy of Sciences convenes the first International Conference on homoplastic transplantations and sent us an

invitation to attend it. However, the USSR Healthcare Ministry that planned to participate in this conference, now wants to refuse sending our scientists who have developed the transplant problem for us to New York. This is wrong, and it happens because there is no necessary center for transplants in the USSR, not even Problem Commission for Transplantation at the USSR Academy of Medical Sciences. It is urgent to create such a center." [1, p. 56-58].

A.G. Lapchinsky's speech shows how far forward the Soviet scientists moved in the early 1960s with regard to the organ preservation for transplantation, how much information they possessed about world advances in the field of transplantation, and how well their developments were known abroad. We draw attention to the fact that A.G. Lapchinsky spoke of the need to begin the clinical use of organ transplantation in the USSR; in his opinion, our country was lagging behind in this field.

The next speaker was Professor I.N. Maisky, the Director of the Institute of Experimental Biology of the USSR Academy of Medical Sciences, the leading research institution in immunology, with whom V.P. Demikhov had worked for 10 years.

Professor I.N. Maisky: "Following the Minister's Order issued in 1957, the Institute of Experimental Biology took a number of measures to expand work on the study of tissue biological incompatibility. In particular, the first [All-Union] Conference [on Transplantology] was held at the Institute; about 150 people attended the Conference where 70–80 presentations were made. Later on, in conjunction with [V.P.] Filatov Institute, the second All-Union Conference was held in Odessa and was attended by 500 people; there 200 presentations were made. A conference will be convened in Yerevan on December 19, 1963, where about 200 presentation will also be made.

All this testifies the fact that in the Soviet Union there are a lot of people who are interested in this problem. Now, in the USSR, we have more than 100 points at departments and institutes where they study this problem. The Conference in Odessa showed that specialists from various fields: surgeons, pathophysiologists, biologists, and biophysicists joined the process <...>.

However, in order to more successfully develop this problem, it is necessary to take a number of measures. The first important step to be taken should be the creation of the Comprehensive Problem Commission, where we could exchange our views on various issues, where it will be possible to move this problem forward together. Therefore, regardless of whether a special institute or laboratory is established, a Problem Commission should be created. I believe that this should be done immediately.

No one doubts regarding the fact that this problem is biological. Not only immunologists, but also the biologists of other areas: morphologists, biochemists, physiologists; and surgeons should also participate in solving the problem. I have already said here that there are more than 100 points in different institutes and departments that are interested in this problem. But all these points are very weak. Here is V.P. Demikhov who is working at it with a small group of people. A.G. Lapchinsky <...> But serious work cannot be carried on further in this way. It is necessary to take into account the fact that much has already been done in this matter abroad, for example, in England, the USA, and other countries.

In studying this problem, we must first unite with Czechoslovakia, where this work is well-arranged (I mean M.Hasek, to whom V.P.Demikhov was not allowed to go. *Auth*). Therefore, in order for us to keep up, we need to know and take into account all the data that is available abroad.

And the last issue. It has now been shown that nucleic acids can change hereditary families of cells. This is a great achievement in science. Therefore, biochemistry must get involved in the study of biological incompatibility. The new approach will provide an opportunity to really attend this problem

and do more than abroad. Therefore, it is necessary to create a Problem Commission, to involve all specialists who can contribute to the solution of this important Task."

Professor I.G. Kochergin: "Unfortunately, you circumvented the question: where and when such a center can be created<...> At such a large meeting, of course, it is difficult to resolve this issue. We will create a Commission of scientists, representatives of the Ministry, and we will make consultations. The issue requires serious thought and speculation in consultation with our scientists" [1, p. 59–61].

Having cited a speech by Professor I.N. Maisky almost completely, we are far from intending to criticize the Director of a large academic institute for his position in developing the methods to overcome transplant immunity. After all, I.N. Maisky was just an "experimental biologist", and the issues of implementing the results of the experiment into the clinic did not, by and large, concern him.

However, surprising is the lack of initiative in the leader of the research team called upon to solve all the issues that I.N. Maisky was speaking about. In order to organize scientific conferences, he needed an Order to be issued from the USSR Healthcare Ministry, and in order to express the idea of creating a Problem Commission, he needed a meeting of the Council for the Coordination of Scientific Research of the USSR Healthcare Ministry. And what about I.N. Maisky? In his speech, he did not mention any scientific achievement of his institute in the field of immunology; he did not express a single fresh idea, just repeating what others had said before him.

Why did not he, like his colleague, the experimental biologist V.P. Demikhov (or together with him), initiate all those activities at the level of the USSR Academy of Medical Sciences, the Authority his Institute

belonged and reported to? Why did not he combine the "100 low-power points" in one powerful fist? Why did not he sound the alarm about the country's lagging behind the world science in immunology? Why did not he study immunological tolerance in parallel with P.Medawar and F.M.Burnet? They were his contemporaries. Well, how can't one help recalling the famous lines of A.S. Pushkin: "*Who is not bored to play the hypocrite, / Repeat the same in different ways, / trying pretentious to assure in that / What everyone has been sure for quite long ...".*

Let's pay attention to the final word of I.G. Kochergin in whose head the idea of creating a second commission was already born to consider the proposal of the first commission, chaired by V.I. Burakovsky.

The next to ask for taking the floor was V.I. Govallo[16], the Senior Research Associate of the Organ and Tissue Transplantation Laboratory headed by Professor V.V. Kovanov where V.P. Demikhov worked from 1955 to 1960.

> **V.I. Govallo**: "V.P. Demikhov's presentation and the materials distributed by him, like all other ones, his unreasonably frequent speeches create a dual impression.
>
> On the one hand, there is a 20-year dedication to the idea and purposeful activity. On the other hand, the complete neglect of the biological side of the problem and ignorance in the knowledge of literature devoted to the problem, at least over the past 25 years. The ideas about the current state of tissue incompatibility do not correspond to the state of the matter that existed back in the time of [I.I.] Mechnikov, but also make difficult the serious attitude of a respected audience.

[16] Govallo V.I. (1932–2010), Immunologist; in 1965 he defended his doctoral thesis on immunological studies of patients after tissue transplantation; further he was a Professor, one of the founders of immunotherapy of malignant neoplasms in the USSR (Fig. 6).

Along with the development of all biological disciplines, all our ideas about the mechanisms of the development of protective immunological reactions have fundamentally changed, and progress in the field of immunology was more significant than the evolution of experimental surgery. It is now well-known that the immunological response does not always follow the standard pattern of antibacterial protection, where serum antibodies are the main factor. It is well-known that in clinical conditions, such as tuberculosis and brucellosis, allergies, and autoimmune lesions, there is a special type of protective reactivity associated with the activity of the lymphoid cells of the body. This is the so-called delayed hypersensitivity. The transplant immunity is among the phenomena of this delayed hypersensitivity. It has been reliably shown that when transplanting alien cells in millipore chambers, when only serum proteins and not cells have access to the transplant, the homograft survives indefinitely long. The passive transfer of the transplant immunity from recipients to the normal animal may be exercised only by the suspension of lymphoid cells but not serum. Thus, it is obvious that to continue building the evidence against the immunological theory of incompatibility on the absence of antibodies in the blood of operated animals means to show the basic ignorance of the essence of the matter.

Fig. 6. Professor V.I. Govallo

I turn to the analysis of the provisions put forward by V.P. Demikhov.

First. The speaker claims that an immunological reaction occurs 7 days after transplantation and is thus a reaction to an already dead graft. However, using modern histochemical and electron microscopic methods, it was shown that the appearance of hyperbasophilic cells, being the inducers of the immunological reaction, and the changes in regional lymph nodes, corresponding to the stages of active immunogenesis, occur 3-4 days after the primary and 1-2 days after second homotransplantation. Thus, the immunological reaction develops in terms of the initial adherence of the homograft and predetermines its further fate.

Second. In immunobiology, as [V.P.] Demikhov claimed, there is a proposition that the immunological reaction supposedly develops only in response to the introduction of proteins of another kind. This is fundamentally wrong, because the whole theoretical basis of immunology is based on an unshakable position that the immunological reaction serves to preserve and maintain the constancy of the protein environment of the body. <...> [Therefore], under certain conditions, an immune response to native proteins is also possible, which leads to the development of autoimmune damage. <...>

Third. Homotransplant death after 30 days, as [V.P.] Demikhov says, does not fit into the framework of immunological concepts. This is far from the case. It is well known that with an increase in the dose of antigenic irritation (the extent of the transplanted tissue. *Auth.*), there is an extension in the survival time of the homologous skin. The experiments have shown that long-term taking of alien donor skin can be obtained by transplanting its massive flaps (“immunity paralysis.” *Auth.*), by multiple homoplastic skin grafting in short intervals, by treating the recipient with extracts of donor tissues, as well as by preliminary parabiosis of the donor and the recipient. Thus, a long homograft survival is not only fit into the framework of immunological concepts, but also predetermined by immunological regularities.

Fourth. [V.P.] Demikhov argues that substances that define the main blood groups should characterize tissue compatibility. He claims that "*organ transplantation based on blood groups should not cause incompatibility reactions*." This is a blunder! It has now been shown that those antigens that determine blood compatibility (erythrocyte antigens) are not at all identical to tissue compatibility antigens. <...>

Fifth. At the beginning of his presentation [V.P.] Demikhov talked about the "new" drug, 6-mercaptopurine. But this is far from a new drug. It has been used for more than 5 years and is not a panacea in the fight against incompatibility; 6-mercaptopurine is known as an antagonist of adenine and hypoxanthine, the substances involved in the synthesis of nucleic acids. That is why it suppresses proliferative processes in the lymphoid organs of a recipient. Hence the partial effect of suppressing the immunological response to the homograft. However this drug is very toxic. It is necessary to dose it extremely carefully. This should have been considered before using, and even more so before discrediting 6-mercaptopurine.

Sixth. One of the most significant provisions put forward in [V.P.] Demikhov's presentation, is the lack of proper conditions required for complex organ transplant operations. No words, this is an important condition. But non-adherence of allokidney or donor heart is not primarily associated with postoperative care and infection. After all, if [V.P.] Demikhov had transplanted the autologous kidney in the same conditions, the result would have been opposite. Consequently, for all other circumstances, the cornerstone of homotransplantation problem is solving the problem of tissue incompatibility. That is why today we have to subdivide: autotransplantation is a purely surgical problem, and homotransplantation is a purely biological one.

There is no need to continue listing all the lapses of the report you have listened to. Returning to its assessment, I would like to note that [V.P.] Demikhov's hard work and interest could be of considerable benefit if his technical skills were guided by the correct biological understanding.

> The issue of the evolution of the organ and tissue transplantation field, a further development of tissue incompatibility problem is naturally associated with the expansion of the front of research, with the research integration. The prototype of the team studying this important and interesting task is the Organ and Tissue Transplantation Laboratory headed by V.V. Kovanov within the USSR Academy of Medical Sciences. It is represented by not only surgeons, but also by immunologists, pathophysiologists, histologists, biochemists, etc.). This is still an initial success, but the success that should be developed in every way. This is warranted by the practical significance of the problem." [1, p. 62–68].

We shall comment on what has been said. First, everything V.I. Govallo was talking about (and he spoke absolutely correctly) related to homotransplantation of tissues (skin, blood, etc.) and was not fully known for whole organs V.P. Demikhov was dealing with (let's take I.I. Mechnikov's "immunity paralysis" phenomenon, which was not fully understood in organ transplantation of those years). Second that we have repeatedly emphasized: all V.P. Demihov's activity was devoted to the search for ways to overcome the biological incompatibility in organ homotransplantations. And it was not his fault that his capabilities were limited and he did not have the ability to study other immunity factors different from serum antibodies [4]. But I.N. Maisky, who had collaborated with V.P. Demikhov for 10 years, undertook nothing to improve the situation. Most likely, for 5 years working next to V.P. Demikhov, V.I. Govallo had the possibility of studying tissue reactions during homotransplantation, as well as the possibility of *"directing V.P. Demikhov's technical skills for correct biological understanding"* but never offered him to look for lymphocytic infiltration at the site of the transplanted organ

contact with the recipient's tissues, instead of looking for antibodies in the blood. Third, let's not forget that some of V.P. Demikhov's views were shared by his contemporaries. Earlier, we mentioned that in 1959, when asked by a correspondent about why, in his opinion, the dog's head transplanted onto the vessels of the neck had lived for more than 20 days, V.V. Kovanov, V.P. Demikhov's Chief, replied that perhaps there were some unknown biological mechanisms that allowed isolated parts of the body to survive for such a long time, and that "the *hypothesis of incompatibility has to be revised*" [4]. A previously speaking T.A. Grigoryeva who was difficult to be blamed of bias, put forward the concept of reinnervation and restoration of organ function as one of the conditions for its survival.

However, in general, V.I. Govallo was right: if V.P. Demikhov's experiments in the field of organ transplantation had a global priority in the 1940s, nevertheless, by the beginning of the 1960s his heterotopic two-stage heart transplantation, kidney transplantation on the femoral vessels, etc., as well as his views on parabiosis as a method of overcoming biological incompatibility, had been already outdated. But we ask a question: who impeded V.I. Govallo from conducting experiments with organ transplants in the Laboratory, which, in his words, was a "*prototype of the team dedicated to the study*" of this problem? That's the whole point, that after V.P. Demikhov had left the Laboratory headed by V.V. Kovanov, and presented by V.I. Govallo, they stopped working with organ transplantation.

The circle is closed: on the one hand, V.P. Demikhov was criticized for the fact that he, with his views, was on the roadside of world immunobiology, but on the other hand, no one was eager to investigate the organ transplantation issues with him or to study the recipient's body lymphoid system response to transplantation.

We note that criticizing V.P. Demikhov's views reasonably and conclusively V.I. Govallo ignored the first two proposals of V.I. Burakovsky's Commission (on the establishing the Research Institute for Transplantation and the Problem Commission), replacing them with an advertisement of his laboratory, and put to doubt the last proposal (on improving the working conditions for V.P. Demikhov): the point was, allegedly, rather in biology than in working conditions.

The next speaker was Professor of Physiology S.V. Andreev from the Institute of Cardiovascular Surgery of the USSR Academy of Medical Sciences. Expressing satisfaction with the level of the Meeting, indicating the importance of the issue, S.V. Andreev considered it necessary to recall that it was V.P. Demikhov who had been the initiator of the Meeting, and whose data on the long-term organ survival "*highlighted the problem of incompatibility*". Next S.V. Andreev supported T.A. Grigoryeva and reported on "the *work of Soviet biochemists in recent years [that] showed that the synthesis of tissue protein in denervated tissues was inhibited because nucleic acids were destroyed during denervation of the cell*". Further confirming that "the *problem of incompatibility was, first of all, of immunological significance*," S.V. Andreev proposed that V.P. Demikhov should "*reconsider his position*", and agreed that "*it was necessary to create both the Commission and <...> the Institution <...> for a deep and comprehensive study of the whole problem with the participation of scientists of all disciplines, [which] should become the center of Soviet and world science*" [1, p.69–70].

Without having said anything new, S.V.Andreev, however, was the only one named V.P. Demikhov by name and patronymic and the first one

pointed to him as to the initiator of the discussion of this urgent and complex problem at the level of the Ministry of Health.

Yu.Ya. Gritsman, the Research Assistant of the Research Institute of Experimental Surgical Equipment and Instruments drew the attention of the Council members to the very important, in his opinion, aspect of the issue under consideration: the clinical one.

Yu.Ya. Gritsman: "Having 15 years of experience in the field of transplantation in experiment and in clinic, I came to the conclusion that every human surgery provides much more understanding of the issue than dozens of experiments. Performing the kidney homoplasty in the clinic, replanting the limb to the patient, we, in our team, clearly saw the difference between the clinic and the experiment; how much differently the body of a sick person reacts compared to the body of a healthy animal. <...> The problem of blood transfusion would never have been realized if it had been developed only in an experiment. <...> Therefore, the issues of incompatibility must be resolved in clinic where there are already sufficient indicators of homoplastic operations: skin grafts, bone fragments, half-joints, cartilage, cornea, limb replantation, kidney homoplasty. <...>

Therefore, in the future transplantation research center, where both the experiment and the clinic will be presented, the leading department should be clinical. This department cannot be opened on the basis of existing hospitals and clinics for the following reasons:

1) Special conditions of sterility are required not only for the operations themselves, but also the postoperative period; 2) Special equipment is needed for irradiation, for the preservation of tissues and organs, observation of patients; 3) Doctors should have special training in the field of transplantation and should not be distracted by any other work, since nursing such patients requires great attention; 4) The staff should comprise a large number of theoreticians (immunologists, biochemists, physiologists, radiologists,

microbiologists, etc.) who would deal with the investigational part of the work and verify the clinical experience in the experiment [1, p. 71–72].

Professor M.I. Efimov invited the audience to return to V.D. Demikhov's presentation and noted that its content does not match the title. "*The presentation does not cover the state of the matter in the Soviet Union and that with regard to the experience of foreign authors,"* M.I. Efimov began. Further, stressing V.P. Demikhov's achievements in the development of techniques for the transplantation of vital organs, M.I. Efimov criticized the position of the speaker regarding transplant immunity; V.P. Demikhov, they say, he admits only those facts that are convenient for him, and "avoids *those that say that biological incompatibility is a firmly established position."*

Professor M.I. Efimov: "Vladimir Petrovich, you say that the problem of autoplasty has been resolved. But once the problem has been resolved, then all the technical issues [of transplantation] have been resolved. So, the matter is rather in the biological incompatibility than in the technique. <...> It is necessary to solve the problem of incompatibility, and then go for an organ transplant" [1, p. 73–74].

M.I. Efimov's remarks were fair: after all, if autografts survive, then it is not a matter of transplantation technique, but something else. And the problem of homotransplantations cannot be resolved only by a technique. However, the author of the article has no doubt that V.P. Demikhov understood that well. As he understood his limitations in the ways to move forward the problem of organ immunity.

The floor was taken by Professor B.A. Petrov, the Chief Surgeon of N.V. Sklifosovsky Research Institute, the Corresponding Member of the USSR Academy of Medical Sciences.

Professor B.A. Petrov: "... I'll dare being brief. Even before V.P. Demikhov's Laboratory was implanted in the Sklifosovsky Institute, it was clear for its staff that the problem of organ transplantation was not all technical, but to a large extent biological. <...> Now, after three years, when V.P. Demikhov persistently performed the same experiments on a heart and lung transplant from one dog to another, and in some cases a head transplant from one dog to another (having spent 460 dogs over the past time), there is no doubt about the correctness of our beliefs: <...> organ transplantation from one animal to another with its prolonged survival and functioning is impossible without complying with the laws of biological compatibility. Unfortunately, V.P. Demikhov sees in his experiments, as in the whole problem, the exclusively technical aspects <...> he does not want to reckon with protein incompatibility, does not study this aspect of the issue, makes no attempts to influence it, does not hear any arguments and, despite constant failures, repeats the same experiments from month to month, from year to year. That is why I agree with those speakers who say that it is necessary, if I may say so, to ***release V.P. Demikhov from himself*** (*emphasized by the author*).

He should be subordinated to the team, he should be integrated in a special institute or in a special laboratory where he will see the scientific side of the problem, where he will learn to understand what organ transplantation and survival mean in a living organism, where he will see in which way the success of the graft survival can be influenced.

There is no doubt that V.P. Demikhov is a skilled dog operator. But he is a solitary handicraft man, being left to his own ideas, does not obey anyone, does not listen to anyone, and, having closed his ears, stubbornly insists that organ transplantation is a purely technical problem. It is necessary

to put V.P. Demikhov in other conditions. We must teach him to work in the direction that science requires" [1, p. 77–78].

That emotional and harsh speech of V.P. Demikhov's direct Executive was in many ways consistent with the truth. However, we cannot agree with the statement that V.P. Demikhov "*did not take into account protein incompatibility, did not study this aspect of the issue, did not make attempts to influence it*." It is enough to look into his book [5] and see numerous photographs of histological preparations removed after autopsy of homo-organs, as well as the chapter on immunology, to understand that this is not so. We repeat once again: V.P. Demikhov resolved the technical aspect of the issue as early as working at A.V. Vishnevsky Institute. All the following years, the principal thing he was engaged in was the search for ways to overcome that what B.A. Petrov called "*protein incompatibility*". But not by means of pharmacological agents (let us recall how he "rejected" 6-mercaptopurine) or radiation (which he did not have), but by biological methods available to him: parabiosis, the selection of the same-blood-group donor-recipient pairs, transplantation of an additional heart, transplantation of the heart and lung into the femoral vessels, etc. And it was not his fault that none of the immunologists could offer him anything more up-to-date.

The discussion was concluded by A.E. Gurvich, "*a specialist in antibodies*" as he introduced himself, who proposed to have a look at V.P. Demikhov's achievements on the positive side.

A.E. Gurvich: "It is difficult for me to agree with Vladimir Petrovich on a number of points. However, I agree with him in very many things. Unfortunately, the debate went the wrong way, and this path was largely predetermined by an unsuccessful presentation of Vladimir Petrovich, which

did not reflect everything that was done by him during his work. Let's see what happened 15 years ago when Vladimir Petrovich started organ transplants. As for heart transplantation in mammals, only one case was described, and in that case, the heart was transplanted to the neck; there were two experiments on limb transplantation, one of which belonged to [A.G.] Lapchinsky. There was nothing else.

What has been done by Vladimir Petrovich at the recent time? Dozens of options for various operations have been developed. Was it conceivable to think earlier that one could cut out a dog's heart and lungs and insert alien organs into it? <...> But that operation was developed by Vladimir Petrovich. It would be absolutely wrong to dismiss all these achievements.

It was said here that the Meeting was devoted to the transplantation issue in general, but we must clearly and distinctly say that the Commission inspected only V.P.Demikhov's Laboratory, therefore, we should talk only about it. It must be clearly understood that neither the creation of the institute nor the laboratories would solve the problem. Everything is decided by people. Recently [V.V.] Kovanov's Laboratory was established, although the people of whom they made up the Laboratory had not made a single organ transplant experiment before the Laboratory establishment... " [1, p. 79].

So, in one sentence A.E. Gurvich depreciated the conclusions of earlier speaking V.I. Govallo, noting that the Laboratory staff he represented did not have an experience with organ transplants. This was V.P. Demikhov's strong and weak points. The strong point was that no one in the country, but him, was engaged in vital organ transplantations into an orthotropic position, and the weak point was that, since no one had had such models, no one was involved in their immunology either. A.E. Gurvich continued:

A.E. Gurvich: "... No one had any doubts that this Laboratory (meaning the Organ and Tissue Transplantation Laboratory of the USSR

Academy of Medical Sciences. *Auth.*) needs staff, imported equipment. Perhaps this is correct. <...> Why does the Ministry not support the person who has worked in organ transplantation for 20 years and has gained recognition in world science? No one spoke about the significance of [V.P.] Demikhov's work, and all said only that he had good hands. But I think that this is not only a matter of hands, but also of independent thinking.

Now about the immunological part. Here, a Senior Research Associate [V.I.] Govallo spoke. He is young and speaks very convincingly. But all this is more complicated than it might seem on the basis of his speech. Earlier, a great importance was really attached to antibodies circulating in the blood. Vladimir Petrovich argued that they were not the core of the matter, [since he did not find them]. Now the majority of researchers have come to the same point of view. The decisive role was given to tissue immunity. However, this is an obscured issue. <...> The outstanding immunologist Burnet (meaning F. Burnet the Nobel Prize Laureate. - *Auth.*) said in 1962: "There are no real possibilities seen to use the practical doctrine of tolerance" and "there is no hope for organ transplantation."

Therefore, it would be wrong to think that when using what is known in immunology today, we cannot transplant organs. And here the struggle of opinions is necessary. Vladimir Petrovich has been working in this area for a long time, has his own point of view, and he needs to be supported, despite the fact that his views differ from those of most researchers" [1, p. 80].

I.G. Kochergin wanted to stop the debate noting: "*Instead of taking part in a creative discussion, he* (obviously, A.E.Gurvich. *Auth.*) s*aid:" I was right, and everyone was wrong"*, but Professor N.N. Zhukov-Verezhnikov, the Head of the Immunobiology Laboratory at the Institute of Experimental Biology of the USSR Academy of Medical Sciences, a Full Member of the USSR Academy of Medical Sciences asked for the floor, (Fig. 7).

Fig. 7. Professor N.N. Zhukov-Verezhnikov, a Full Member of the USSR Academy of Medical Sciences

Professor N.N. Zhukov-Verezhnikov: “Comrades, <...> we need to define some kind of trend, and it seems to me that there can be two of these trends, and that they cannot be opposed to each other.

The first trend is overcoming tissue incompatibility <...> There are enough models with which this incompatibility can be studied. One model is mice, laboratory animals. Other models have been very little spoken about. These are surviving organs and tissues for testing mutagenic substances during attempts to change (homogenize) the antigenic structure. But for this, truly “miracles of surgery” are needed. Maybe the results will be negative. But we have to go this way.

Already on this alone, the second trend has been concluded; purely surgical experimental-physiological investigations in the spirit of [A.G.] Lapchinsky, [V.P.] Demikhov, and others.

I would not really like the opposition of biology and physiology to be preserved today. We should not need to rush from physiology to immunology" [1, p. 81].

With his speech, N.N. Zhukov-Verezhnikov clearly wanted to reconcile the physiological views (of V.P. Demikhov, T.A. Grigoryeva, M.I. Efimov, A.E. Gurvich) and the immunobiological views (of V.I. Govallo, I.N. Maysky, S.V. Andreev, B.A. Petrov), speaking out at the end for establishing the Research Institute for Transplantation and the Problem Commission, "*so that someone could submit summaries and plans to the table of Ivan Grigoryevich [Kochergin]*"), and as if passing the floor to the Chairman for conclusions.

"I believe," began **Professor I.G. Kochergin, the Chairman of the Meeting, the Deputy Minister of the USSR Healthcare Ministry, a Corresponding Member of the USSR Academy of Medical Sciences,"** that the exchange of views was very useful. And although I have to review the literature by the nature of my activity, I must say that there have been a lot of new facts for me today. <...>

Apparently, all of us agree that it is necessary to create a scientific center without deciding now whether it will be a department, laboratory or institute. That, on the basis of this center, a [Problem] Commission should be organized, which will be able to coordinate all the large, creative, search work. I agree with the proposal to create such a coordinating centre. But how and where it will be, we can decide in a working order, after discussing the matter at the Board Meeting of the Ministry and in consultation with the Academy of Medical Sciences. But this issue must be resolved.

Second remark. In response to comrade Gurvich. I believe that all the speeches in no way tried to belittle or, moreover, discredit the enormous experimental work carried out by Dr. Demikhov and his staff.

The merit of Comrade Demikhov as an experimenter is great, even if we have mentioned an aspect of the surgical technique creation only. And this is a great contribution to solving the problem. In addition, he studied both histology and morphology. In any case, we must not oppose immunology to surgery, etc. The matter is that this is hardly necessary to prove at the present time.

Therefore, I highly appreciate the work of Vladimir Petrovich Demikhov. But I cannot but say that he had a whim in his head that there is only a technique, only difficulties with physiology. But there is immunobiology. (Further referring to V.P. Demikhov. *Auth*.) You have been criticized; you will fight back until you prove that the deadlines need to be extended.

Thus, without reducing the role and merit of [V.P.] Demikhov, who amazes very few sophisticated people, and they raise his work to a degree of sensation. ~~This is what spoils our calm atmosphere.~~ (this sentence is crossed out in the transcript. *Auth*.) I believe that even Boris Alexandrovich [Petrov] spoke very restrained.

I agree with the conclusions made by the speakers. We need to decide who should coordinate this problem. Of these 10 (100? *Auth*.) Laboratories, there should be the Centralized one. Why doesn't Nikolai Nikolaevich [Zhukov-Verezhnikov] take over the coordination? Moreover, it is necessary to combine the immunological issues with the surgical ones. The Commission should include [V.V.] Kovanov, [B.A.] Petrov, [V.P.] Demikhov, [V.I.] Burakovsky, [A.G.] Lapchinsky, [M.I.] Efimov (the list is read).

An Order may then be issued to give effect to this Commission. You need to consult very seriously here. It is necessary to give the Commission a period of two months to agree upon all issues, so that there is no next Order, which would turn out to be largely impossible to implement. <...> Besides

[V.P.] Demikhov and [V.I.] Burakovsky, I would like to mark out Professor [T.A.] Grigoryeva, she approached very objectively, she managed to study in contact with Demikhov ... (hereinafter, the ellipsis follows in the transcript. *Auth.*)

There is another talented experimenter. This is [A.G.] Lapchinsky. He has interesting data outlined in studies of the immunobiological trends.

I thank all the participants for the advice coming from the heart."

Voice from the audience: “What you say is without perspective. Something needs to be done to help [V.P.] Demikhov regarding the expansion of the premises, etc."

I.G. Kochergin: “I did not want to talk about these schemes, I will leave it aside. We will not talk about help now. We give a two-month period to make decisions. And along the way, we will solve these issues.”

A voice from the audience: "There is no room, no employees, no money."

I.G. Kochergin: “Now we cannot solve these issues. Maybe we will create a center in this location.”

A.E. Gurvich: “It seems to me that the Meeting was convened in connection with the inspection of [V.P.] Demikhov's Laboratory, and something needs to be said about the work of this Laboratory.”

I.G. Kochergin: “The agenda says: On the state of the issue. We did not record: on the work being done in [V.P.] Demikhov's Laboratory. We have taken it as an example. We could just have turned to the Laboratory of [V.V.] Kovanov or [A.G.] Lapchinsky, as well. But we took the Laboratory of [V.P.] Demikhov. That was our choice. Let me once again thank all those present and declare our Meeting closed” [1, p.83–87].

The USSR Healthcare Ministry Council for the Coordination of Scientific Research and Implementation of the Scientific Achievements into Practice (Resolution)

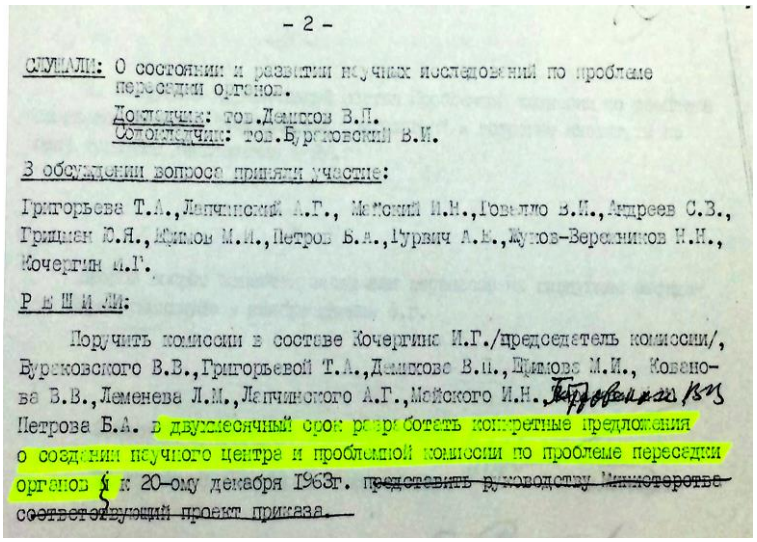
Thus ended that truly historic Council, which outlined the approaches to a definite change in the affairs with the problem of organ transplantation in the Soviet Union. But it is unlikely that the decision made would have been be different if the Meeting participants had considered the situation in the Laboratory of V.V. Kovanov or A.G. Lapchinsky. V.P. Demikhov was chosen just because he wrote letters to the Moscow City Committee of the CPSU and to the Healthcare Ministry. And the initiative is always punishable.

The Resolution of the Presidium of the USSR Healthcare Ministry Council for the Coordination of Scientific Research and Implementation of the Scientific Achievements into Practice was as follows:

> "To entrust the Commission that shall include I.G. Kochergin (the Chairman of the Commission), V.I. Burakovsky, T.A. Grigoryeva, V.P. Demikhov, M.I. Efimov, V.V. Kovanov, L.M. Lemenev, A.G. Lapchinsky, I.N. Maisky, M.I. Perelman, B.A. Petrov, within two months, develop precise proposals on the establishment of a Research Center and a Problem Commission on the issue of organ transplantation, and by December 20, 1963, to submit the corresponding Draft Order to the Ministry Management" [1, 2].

In the final version of the Meeting Minutes signed by I.G. Kochergin, "Petrovsky B.V." was written on top of the printed "Perelman M.I." with someone else's hand (obviously, of I.G. Kochergin), and the words "submit

the Draft Order to the Ministry Management" are crossed out (Fig. 8). It is clearly seen that only the first two points of the proposals of V.I. Burakovsky's Commission were written in the Resolution and the third one on improving V.P. Demikhov's working conditions was absent.



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СЛУШАЛИ: О состоянии и развитии научных исследований по проблеме пересадки органов.

Докладчик: тов.Демихов В.П.
Содокладчик: тов.Бураковский В.И.

В обсуждении вопроса приняли участие:

Григорьева Т.А., Лапчинский А.Г., Майский И.И., Говорило В.И., Андреев С.В., Гришин Ю.Я., Шимов М.И., Петров Б.А., Гурвич А.К., Жуков-Вережников И.И., Кочергин И.Г.

Р Е Ш И Л И:

Поручить комиссии в составе Кочергин И.Г./председатель комиссии/, Бураковского В.В., Григорьевой Т.А., Демихова В.П., Шимова М.И., Ковенова В.В., Леменева Л.М., Лапчинского А.Г., Майского И.И., Петрова Б.А. в двухмесячный срок разработать конкретные предложения о создании научного центра и проблемной комиссии по проблеме пересадки органов и к 20-ому декабря 1963г. ~~представить руководству Министерства соответствующий проект приказа.~~

Fig. 8. Abstract from the Minutes of the Meeting of the Presidium of the USSR Healthcare Ministry Council for the Coordination of Scientific Research and Implementation of the Scientific Achievements dated of October 8, 1963, p. 2 [State Archive of the Russian Federation, f. 8009, reg. 2, d. 2557, l. 2]

Unfortunately, we did not find any documents on the work of this second Commission in the Russian Federation State Archives.

Conclusion

Thus, the review of the document that we first introduced into scientific circulation, the transcripts of the Meeting of the Presidium of the USSR Healthcare Ministry Council for the Coordination of Scientific Research and

Implementation of the Scientific Achievements into Practice held on October 8, 1963, and devoted to the state and development of scientific research in the field of organ transplantation, showed that in 1963, a turning point was outlined (not yet occurred, but was only outlined) in the attitude of the country's Healthcare Authorities to the problem of organ transplantation. For the first time (on V.P. Demikhov's initiative), a Commission was created under the Chairmanship of V.I. Burakovsky that considered the issue of organ and tissue transplantation and proposed real measures for its further development; for the first time that issue was considered at the level of the USSR Healthcare Ministry.

For the first time, it was proposed to establish a specialized Research Institute for Organ and Tissue Transplantation in the country that would meet the requirements of up-to-date medical science, and to arrange a Problem Commission for Transplantology. For the first time, the country's future outstanding cardiac surgeon V.I. Burakovsky who defended his doctoral thesis only 3 months before spoke and was heard at a top level meeting. It was the Commission he headed that first proposed the establishment of both the Research Institute for Transplantation and the Problem Commission.

And just then, in October 1963, Academician B.V. Petrovsky, the pioneer of clinical organ transplantation in the USSR, was first involved in resolving the organ transplantation problem, when he was included in the USSR Healthcare Ministry Commission to consider the proposals of V.I. Burakovsky's Commission on the establishment of the Research Institute for Transplantation and the Problem Commission. The outcome of those events is known. In 1965, B.V.Petrovsky and his staff performed the country's first successful clinical orthotopic kidney transplantation (before that, the kidneys

had been transplanted to patients' femoral vessels); and in 1969, on his initiative, the Scientific Research Institute of Transplantation and Artificial Organs of the USSR Healthcare Ministry was organized, the first Director being G.M. Soloviev.

And only the last of the V.I. Burakovsky's Commission proposals were not completed, those were the proposal on the transfer of V.P. Demikhov's Laboratory from the jurisdiction of the Moscow City Healthcare Authority to the system of the USSR Healthcare Ministry or the USSR Academy of Medical Sciences, on its expansion, increase in staff and investments, and T.A. Grigoryeva's proposal on appointing V.P. Demikhov in the future Research Institute for Transplantation to the position that would be corresponding to his merits.

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Received: September 30, 2019

Accepted for publication: October 2, 2019