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Phenomenon of Demikhov.
At N.V. Sklifosovsky Institute (1960–1986). V.P. Demikhov and his experiments in the field of organ transplantation in 1969–1970

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Abstract

With the involvement of archival documents, the results of research performed by V.P. Demikhov and the employees of the Organ Transplantation Laboratory at the N.V. Sklifosovsky Research Institute for Emergency Medicine (further – Institute) in 1969–1970 have been analyzed. At that time, under V.P. Demikhov's guidance and his personal participation, the Laboratory carried out the following developments: (1) an anatomical method of heart and lung transplantation in experiment and on human cadavers; (2) a method of revitalizing the heart and the

whole human body using direct cardiac massage and a portable mechanical heart connected to auricles; (3) the method of liver transplantation in experiment and its anatomical rationale for clinical implementation in liver failure; (4) a method for assessing the function of a transplanted heart using electrocardiography; (5) the method of transplantation of the small intestine fragments; (6) a method of transplanting the pancreas, isolated or in combination with the duodenum and liver, to the renal vessels; (7) a method of replanting the cardiopulmonary complex on peripheral vessels for the treatment of terminal cardiopulmonary insufficiency, and a number of others. For experimental studies, the methods of an anatomical X-ray investigation of the main vessels and X-ray vasography of a transplanted heart were used. For heart transplantation, V.P. Demikhov's anatomical technique and biatrial Lower-Shumway technique were applied. To conduct a series of studies, V.P. Demikhov managed to attract large third-party organizations: the Krasnoyarsk Research Institute of Physics of the Siberian Branch of the USSR Academy of Sciences (creation of a mechanical heart), the Pyatigorsk Machine-Building Plant (creation of a portable thermostat to preserve revitalized organs), Central Research Institute of Tuberculosis of the Ministry of Health of the USSR (development of a method for implanting a cardiopulmonary complex to peripheral vessels), Research Institute of Poliomyelitis (operations on monkeys). We emphasize that all methods developed were recommended by the author for their implementation in clinic. A list of operations performed in the organ transplant laboratory in 1969–1970 is given. Most of the operations performed were transplantations (implanting) of the cardiopulmonary complex, isolated heart, and cadaveric heart revitalizations. It was noted that, in addition to the Research Topics included in the Working Plan of the Institute, V.P. Demikhov developed

many individual, search topics, including transplantation of halves of the body, head, liver, uterus, kidney, and sternum. All of them, after their completion, were planned for implementation in the clinic.

Keywords: history of transplantology, V.P. Demikhov, scientific and experimental activities, list of operations, 1969–1970

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CPC, cardiopulmonary complex
ECG, electrocardiogram
HLM, heart-lung machine
ICPC, isolated cardiopulmonary complex

Introduction

On January 31, 1968, the members of the Academic Council of the N.V. Sklifosovsky Research Institute for Emergency Medicine (further – Institute) unanimously re-elected Doctor of Biological Sciences V.P. Demikhov (Fig. 1) for a new 5-year term as the Head of the Organ Transplantation Laboratory. On March 27, 1968, V.P. Demikhov reported on his work at the Academic Council Meeting, for the first time in 8 years of his work at the Institute. In the debate after the report, the Council members emphasized that since V.P. Demikhov was a biologist, not a doctor, then the Institute Management needed to think about introducing the results of his research into clinical practice. Moreover, as Professor I.M. Grigorovsky said, "*the issue of organ transplantation is now being put forward as a priority task of medical science*." The resolution on the report was brief: "To take the presented report into consideration" [2].

Fig. 1. V.P. Demikhov. 1970s [1]

What did V.P. Demikhov do in 1968? As follows from the Reporting Documents from his Laboratory for 1968, he (1) performed transplantation of the cardiopulmonary complex (CPC) in experiment and developed an anatomical method for its transplantation on human corpses (Reporting Sheet No. 44; Investigators: V.P. Demikhov, L.L. Gugushvili); (2) he studied electrocardiograms (ECG) during heart homotransplantation (Reporting Sheet No. 45; Investigator: V.M. Goryainov); (3) he worked out methods for experimental liver transplantation (Reporting Sheet No. 46; Investigators: V.P. Demikhov, I.M. Grigorovsky, L.L. Gugushvili); and also (4) he continued improving his method of preserving revitalized organs for human transplantation (Reporting Sheet No. 47; Investigator: V.P. Demikhov) [3, p. 403].

Research conducted in the Organ Transplantation Laboratory of N.V. Sklifosovsky Institute in 1969

And now let us take a look at the Minutes of the Academic Council Meetings of the N.V. Sklifosovsky Institute for 1969. How do they reflect the work of V.P. Demikhov and his Laboratory?

At the Meeting on September 11, 1969, when discussing the Research Program results for 1969 and the Research Plan for 1970, after the presentations made by Doctor of Medical Sciences B.D. Komarov[1], the Director of the Institute (Fig. 2), Professors B.A. Petrov and I.M. Grigorovsky, as well as Yu.A. Muromsky, the representative of the Moscow City Executive Committee, V.P. Demikhov was the first to rise from his seat and asked "*at one of the next Academic Council Meetings to listen to the report on the work of the Laboratory he headed in order to have a clear idea of its work*" [4, p. 77–78]. In order to increase the efficiency of the Organ Transplantation Laboratory and the possibility of the earliest possible implementation of the results into clinical practice, B.D.Komarov suggested that the Council members should think about the advisability of transferring the Organ Transplantation Laboratory from the N.V. Sklifosovsky Institute to an institution relevant to the topic of its work.

It is known that there were several research teams in our country that were involved in organ transplantation, and in particular the heart, at that time: 1) Laboratory for Organ Transplantation of the 2nd MOLGMI named after N.I. Pirogov (Head: Yu.M. Lopukhin), 2) Department of Faculty Surgery of the 2nd MOLGMI named after N.I. Pirogov (Head: V.S. Savelyev), 3) Research Institute of Clinical and Experimental Surgery of the USSR Ministry of Health (Head: G.M. Soloviev, later V.I. Shumakov), 4) A.V. Vishnevsky Institute of Surgery of the USSR Academy of Medical Sciences (Head: A.A. Vishnevsky and later

[1] Komarov B.D., Doctor of Medical Sciences, a follower of A.N. Bakulev. At the age of 40, he was appointed to the position of the Director of the N.V. Sklifosovsky Institute from the position of an Associate Professor of the Faculty Surgery Department named after S.I. Spasokukotsky at the Medical Faculty of the 2nd MOLGMI named after N.I. Pirogov; further he was awarded the title of Honored Scientist of the Russian Federation (2004), elected a Corresponding Member of the USSR Academy of Medical Sciences (1982), Russian Academy of Sciences (RAS) (2014), Academician of RAMTS (1994), Professor (1970); headed the N.V. Sklifosovsky Institute from 1968 to 1986; since 1986, has worked as a Chief Researcher of the Moscow Clinical Scientific Center named after. A.S. Loginov.

V.F. Portnoy) [2], 5) A.N. Bakulev Institute of Cardiovascular Surgery of the USSR Academy of Medical Sciences (Research Project Leaders: V.I. Burakovsky and G.E. Falkovsky). And V.P. Demikhov was well known in all these institutions.

Fig. 2. Professor B.D. Komarov, Director of the N.V. Sklifosovsky Institute for Emergency Medicine. 1970s [1]

G.A. Rezvetsova (a Chief Specialist in Emergency Medical Care of the USSR Ministry of Health - *ed.*) who took the floor after B.D. Komarov supported V.P. Demikhov's proposal to listen to his report on the Organ Transplantation Laboratory research at an Academic Council Meeting and dwelled in detail on the main provisions of the presentation made by Yu.A. Muromsky. There were no more speakers. The Council took the resolution: *"To finalize the Research Plan for 1970 in accordance with the requirements of the Academic Medical Council of the RSFSR Ministry of Health, to take into consideration and correct the comments on improving scientific documentation made by Yu.A. Muromsky*" [4, p. 77–78].

On November 12, 1969, another Meeting of the Academic Council of the N.V. Sklifosovsky Institute was held, where the Institute's

Research Plan for 1971–1975 was discussed. When the presentation, which did not say anything about the work of the Organ Transplantation Laboratory, was completed, V.P. Demikhov rose from his seat and asked: "*What to do?*". The speaker I.M. Grigorovsky evaded a direct answer, then B.A. Petrov, the Chairman of the Council, stood up and said: "<…> *Demikhov has not presented his plan yet; he must present it. Meanwhile, we should take into account that The Minister of Health B.V. Petrovsky did not allow the N.V. Sklifosovsky Institute to deal with the problem of organ transplantation, but only with their replanting"*. Then V.P. Demikhov asked for the floor and proposed to implant rather than transplant a liver or kidney from donors with blood of the same group as the recipient in clinic, if necessary. "*Experiments must be implemented in clinic, and the Research Plan of the Laboratory will be drawn up in accordance with the existing settings of higher authorities*," he concluded. Further presentations concerned the inclusion in the Plan of the issues of care for injuries, cadaveric blood transfusion. The Council took a resolution: "*To take the presented comments into consideration <...> consider the materials submitted by the Heads of the Clinics, Departments and Laboratories*" [4, p. 96–97].

1969 was over. As a result, many employees of the N.V. Sklifosovsky Institute were awarded prizes. In the Organ Transplantation Laboratory, the awards were granted to V.P. Demikhov, the Head of the Laboratory, for the publication of 6 articles in medical journals and making 2 presentations at scientific conferences; to L.L. Gugushvili (Fig. 3), a Senior Researcher, for 5 presentations made at scientific conferences; and V.S. Nepomnyashchaya, a Junior Researcher for an article in a journal and 5 presentations at scientific conferences [4, p. 120].

Fig. 3. L.L. Gugushvili, Senior Research Associate. 1960s [1]

The results of V.P. Demikhov and his collaborators' work in 1969 were included in the Reporting Sheets on the subject of "Trauma and traumatism" on the topic "Transplantation, preservation of organs and tissues."

Reporting Sheet No. 86.

Topic: **Experimental heart and lung transplantation; anatomical development of the method for heart and lung transplantation on human corpses**.

Start: Carried over from previous years.

End: 1969

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

Type of investigation: Experimental and anatomical, on human corpses.

Abstract: An experimental study was performed on 40 dogs, an anatomical study was performed on 20 human corpses; new schemes for heart and lungs transplant and implantation were developed.

Recommendations: It is possible to use the obtained data in clinic.

Note: articles in *the Experimental Biology and Medicine* journal (1969, No. 2) and in *the Italian Encyclopedia* (September 1969) [4, p. 115].

Reporting Sheet No. 87.

Topic: **ECG studies in heart homotransplantation**.

Project Leader: V.P. Demikhov.

Investigator: V.M. Goryainov.

Start: Carried over from previous years.

End: 1969

Abstract: 1500 ECGs were taken, ECG analysis makes it possible to make a prognosis for heart transplants both in experiment, and also in clinic.

Note: article *in the Experimental Biology and Medicine* journal (1969) [4, p. 117].

Reporting Sheet No. 88.

General title of the topic: **Revitalization of the heart and the whole human body by using a mechanical heart (according to V.P. Demikhov's method).**

Topic title: Revitalization of the heart in human corpses in the first tens of minutes after the onset of death, using a mechanical heart (according to V.P. Demikhov's method).

Investigators: V.P. Demikhov together with the Intensive Care Center (B.G. Zhilis).

Start: 1969

Abstract: The mechanical heart model was tested on 20 human corpses.

Recommendations: An original model of a portable mechanical heart has been created, which can be used in ambulance service.

Note: Research is ongoing [4, p. 118].

Reporting Sheet No. 89.

Topic: **Experimental liver transplantation and anatomical rationale [of the method] for the human clinic.**

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

Type of investigation: Experimental and anatomical, on human corpses.

Abstract: Anatomical studies performed on 35 animals and more than 100 human corpses.

Recommendations: In cases of liver failure, a short-term liver implantation or a complete liver replacement can be performed.

Note: article in *the Clinical Surgery* journal (1969, No. 6) [4, p. 119].

Reporting Sheet No. 90.

Topic: **Homoplastic transplantation of the small intestine in experiment.**

Investigators: L.S. Chakhunashvili, V.P. Demikhov.

Type of investigation: Experimental, laboratory, morphological.

Abstract: Intestine transplant operations were performed on 15 dogs.

Recommendations: Parts of the small intestine can be used in cases of extensive bowel resections [4, p. 120].

Reporting Sheet No. 91.

Topic: **Anatomical and experimental rationale of transplanting pancreas in combination with duodenum.**

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

Type of investigation: Experimental, laboratory, morphological.

Abstract: An experimental study was performed on 100 dogs, an anatomical study was performed on 26 human corpses.

Recommendations: At present, there has been risen a need for pancreas transplantation in patients with diabetes mellitus, the work makes a practical contribution to solving this problem.

Note: The article has been prepared for publication [4, p. 121].

Reporting Sheet No. 92.

Intermediate topic: **Physiological method of preserving revitalized organs for human transplantation.**

Topic for 1969: Creating physiological conditions (blood circulation, respiration, nutrition) to maintain the function and preserve revitalized organs for human transplantation.

Investigators: V.P. Demikhov together with the Intensive Care Center (B.G. Zhilis).

Type of investigation: physiological, morphological, experimental.

Abstract: The revitalization of human corpses was undertaken and a method for preserving organs was developed on 15 corpses.

Recommendations: The method makes it possible to preserve revitalized organs for human transplantation and gives an opportunity to examine their viability before transplantation; revitalized organs can also be transported to other clinics.

Note: Article in *the Experimental Surgery and Anesthesiology* journal (1969, No. 2) [2][4, p. 121].

When comparing the Research Reporting Sheets for 1969 with those for 1968 [3], one can clearly see how research was developing. So, on the topic "Experimental heart and lung transplantation and anatomical development of the method for heart and lung transplantation on human corpses", the experiments were performed on 40 dogs in 1968, and then in 1969 on 20 human corpses with a recommendation to use the obtained data in clinic. If in 1968 1000 ECGs were taken, then a year later their number increased to 1500[3]. In 1968, there was no topic "Revitalization of the heart and the whole human body by using a mechanical heart" at all. As for the topic "Experimental liver transplantation and anatomical rationale for the human clinic", its experimental part was worked out on animals in 1968, and on human corpses in 1969. There was no topic on homotransplantation of the small intestine in 1968 at all. In 1969, the topic of pancreas transplantation became new with recommendations to apply the method in the clinic in patients with diabetes mellitus. The topic “Physiological method of preserving revitalized organs for human transplantation” was an intermediate one and repeated the topic of 1968. In general, if in 1968 V.P. Demikhov and his colleagues developed four research topics, but in 1969 there were already seven such topics. Of these, there were some absolutely new ones.

[2]The illustration from this article was given in publication [3].
[3]Obviously, this is the total number of ECGs taken over several years.

We especially emphasize the fact that all Reporting Sheets contained the following recommendations on the possibility and even the need to apply the results of experiments in the clinic:

On the topic “Experimental heart and lung transplantation": it is *possible to use the obtained data in clinic*.

On the topic "ECG studies in heart homotransplantation": *ECG analysis allows making prognosis in heart transplants both in experiment, and also in clinic.*

On the topic "Revitalization of the heart and the whole human body by using a mechanical heart (according to V.P. Demikhov's method)": *the original model of a portable mechanical heart can be used in an ambulance service*.

On the topic “Experimental liver transplantation and anatomical rationale [of the method] for the human clinic”: *in cases of liver failure, a short-term liver implantation or a complete liver replacement can be performed.*

On the topic "Homoplastic transplantation of the small intestine in experiment": *parts of the small intestine can be used for extensive resections of the intestine*.

On the topic "Anatomical and experimental rationale of transplanting pancreas in combination with duodenum": *at present, there is a need for pancreas transplantation in patients with diabetes mellitus.*

On the topic "Physiological method of preserving revitalized organs for human transplantation": *the method makes it possible to preserve revitalized organs for human transplantation*.

Let us note topic No. 93 devoted to investigating the role of lymphocytes in homograft rejection reactions, which was studied at the Institute of Experimental Biology of the USSR Academy of Medical Sciences (Director: I.N. Maisky) together with the Laboratory of Blood

Transfusion and Tissue Preservation of the N.V. Sklifosovsky Institute (Head: G.A. Pafomov).

Reporting Sheet No. 93.

Topic: **On the mechanisms of the cytotoxic effect of immune lymphocytes in the homograft rejection reactions**.

Project Leaders: G.A. Pafomov (N.V. Sklifosovsky Institute), M.M. Kapichnikov (Institute of Experimental Biology of the USSR Academy of Medical Sciences).

Investigators: B.P. Shadrin, G.V. Bulava, N.N. Dakhina, Yu.P. Sukhov (Laboratory of Tissue Incompatibility of the Institute of Experimental Biology, USSR Academy of Medical Sciences).

Abstract: Methods have been developed for modeling the processes occurring in the recipient's body in response to *transplanted tissue* (our italics - *auth.*); the optimal methods were selected for immunizing the recipient with the donor material and methods for evaluating the results of the interaction of the recipient immunized lymphocytes on the donor cells in tissue culture;

Recommendations: The results of the experiment enable us starting a direct study of the mechanisms in which the donor lymphocytes[4] affect the homograft [4, p. 123].

One more topic No. 94 devoted to the preservation of cadaveric kidneys was developed by the staff of the Laboratory for Blood Transfusion and Tissue Preservation together with the Pathoanatomical Department of the N.V. Sklifosovsky Institute. In the experiments, the kidneys taken after the donor's death and connected to recipient's vessels began functioning after 1.5 hours. According to the developers, the obtained data could be used in clinical organ transplantation and as one of the methods to treat renal failure [4, p. 124]. Note that V.P. Demikhov developed this method back in the early 1960s; and in 1962, he

[4] As the document reads; in fact, it is about recipient's lymphocytes immunized with donor's material.

transplanted a kidney to a patient on the femoral vessels at the Botkin Hospital.

Research conducted in the Organ Transplantation Laboratory of the N.V. Sklifosovsky Institute in 1970

In 1970, Doctor of Biological Sciences V.P. Demikhov was introduced into the Academic Council of the N.V. Sklifosovsky Institute. At that time, the director of the Institute was Doctor of Medical Sciences B.D. Komarov, and his Deputy for Science was Doctor of Medical Sciences A.P. Kuzmichev.

At the Academic Council Meeting on June 17, 1970, after A.P.Kuzmichev's presentation about the Draft Research Plan for 1970 with a mention of research conducted by V.P. Demikhov, Professor I.I. Sokolov asked the speaker: "*Name the authors of the anatomical and experimental topics you have listed <...> And from which departments do they come from?*". I.I. Sokolov was supported by Professor N.K. Permyakov: "*It is not clear to me personally: 30 human heart transplant operations are planned for 1971. Who is the author of this work, and who will make such operations?* » [5, p. 2].

A.P. Kuzmichev answered the question of I.I. Sokolov, saying that all these works come from the Laboratory headed by V.P. Demikhov that the authors of the works are the Head of the Laboratory and his staff. The answer to N.K. Permyakov's question was as follows: "*It is planned to implant rather than transplant the heart. I think that V.P. Demikhov, the Head of the Organ Transplantation Laboratory, will explain to the Academic Council who will perform such operations in clinic and when.*" There were other questions answered by A.P. Kuzmichev, after which B.D. Komarov announced the debate [5, p. 3].

After a series of speeches about the lack of staff, personnel, residency positions, and other things, Professor B.A. Petrov took the floor and criticized the plans of V.P. Demikhov:

> "Dr. Demikhov presented the Research Plan, which raises great doubts and concerns. Indeed, read and be amazed! (Reads) "Improve resuscitation techniques using HLM in ambulances[5]." But how will the HLM (Fig. 4) work for several minutes while the car is driving? This topic, as well as the topic of implanting the cardiopulmonary complex, confuses me very much. Dr. Demikhov is a biologist. How can he, not having a medical education, perform such operations in clinic? As for the issues related to transfusion of blood from animals to humans, how can blood from monkeys and pigs be transfused to a dying person? It seems to me that such topics should be approached very carefully. Besides: 20 dogs, 6 pigs, 60 monkeys. Where do you get them, monkeys? How much is it?" [5, p. 6–7]

V.P. Demikhov answered these questions as follows:

> "The topic of organ transplantation is included in the topic of national significance. The issue of establishing the bank of organs is currently on the agenda. It is up to physiologists like myself who are to revitalize and preserve the organs. <...> The organ harvesting and revitalization can be carried out on the base of the N.V. Sklifosovsky Institute, and the organ transplantation should be performed at the Institute of Organ and Tissue Transplantation[6].
>
> Regarding the topics that are being discussed. I can report that for many years these topics have been developed by me together with the staff of my laboratory and will be developed in the future, *even if they are*

[5] HLM, heart-lung machine

[6] By this time, the Institute of Organ and Tissue Transplantation of the USSR Academy of Medical Sciences was founded on the basis of the City Clinical Hospital No. 52. It was headed by Professor G.M. Solovyov, the USSR State Prize Laureate, Corresponding Member of the USSR Academy of Medical Sciences.

not included in the Research Plan of the N.V. Sklifosovsky Institute. (our italics - *auth.*). In these cases, such research will be performed as unscheduled.

Regarding human operations. I can assist in such operations or provide advice and guidance. In the clinic of Professor B.A. Petrov, heteroliver is connected. Similarly, it is possible to connect the cardio-pulmonary complex. I am doing research of this kind …" [5, p. 8].

Fig. 4. Heart-lung machine designed by V.P. Demikhov and intended for a) revitalization of a cadaveric heart for the purpose of its transplantation; and b) resuscitation of those dying in ambulances. 1960s [1]

V.D. Demikhov was interrupted by B.D. Komarov:

"Many of the issues that Demikhov raises *become known for the Institute Directorate for the first time (*italics ours – *auth.*). In order to avoid disagreements about the conduct of certain investigations, one should first discuss them at the Academic Council, reach an agreement, and only then begin the developments" [5, p. 8–9].

The next speaker was L.B. Shapiro, the Head of the Ambulance Station, Honored Doctor of the RSFSR:

"... Regarding the search topics proposed by Demikhov. Apparently, Demikhov raised this question in his Laboratory. He has never raised this question for us. For example, using a new method of heart massage. I agree with Professor B.A. Petrov. It is necessary to discuss such issues with clinicians beforehand" [5, p. 9].

Critical speeches were continued by Professor N.K. Permyakov:

"I agree with the opinion expressed by A.P. Kuzmichev and the colleagues regarding V.P. Demikhov's plans. This plan seems somewhat fantastic, although Demikhov accomplished a lot. I would like to address the Administration with the fact that the implementation of Demikhov's Research Plan will require major organizational measures. Bank of Tissue; what does this mean for our Institute? This issue requires a very serious discussion, since such proposals are followed by significant financial costs" [5, p. 10].

V.P. Demikhov did not respond to these fair reproaches. He knew that many of the studies he was engaged in were unscheduled, and therefore, unfortunately, little or no unknown at the Institute (see Table 1).

Note that of all the speakers at that Meeting, only two people discussed other issues. Everyone else talked about the "fantastic" plans of V.P. Demikhov. Finally B.D. Komarov ended the debate:

"The plan [of the Institute's research] consists of two parts: the nationwide, the main one, and the initiative one. The main plan is mandatory, 60% of the budget is allocated to it. <...> As for the initiative plan, 40% of the budget is spent on it. <...> But when drawing up an initiative plan, it is necessary to take into account the prospects and the real costs that will be required. *In this light, a discussion of the research topics of the Organ Transplant Laboratory seems to be very useful* (our italics – *auth.*). It is

necessary that when drawing up the final version of the Plan, everything that was said was taken into account" [5, p. 11–12].

On September 23, 1970, a Dissertation Council was opened at the Institute for the defense of candidate theses in the specialties "Surgery", "Anesthesiology-Critical Care" and "Traumatology" [5, p. 117], and in October the N.V. Sklifosovsky Institute was given the status of the City Center for the Scientific Organization of Emergency Medical Service and the Coordination of Scientific Research for this Service in Moscow.

On this change of the status Professor B.D. Komarov made the presentation at the Meeting of the Academic Council of the Institute on October 22, 1970, on the topic “The role of the N.V. Sklifosovsky Institute as an organizational and methodological center for the management of emergency and urgent medical care”, and Professor I.I. Sokolov added: "*It is necessary that the Institute become the leader in the city in establishing a trauma service, as well*." It was also about the need to separate emergency medical care into an independent medical specialty. The speakers said that it was time to move from words to deeds [5, p. 25–126].

What was the Organ Transplantation Laboratory doing at that time?

Reporting Sheet No. 60 (spelling saved - *auth.*).

Topic: A**natomical development of the method for heart and lung transplantation on human corpses**.

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

Type of investigation: anatomical, on human corpses.

Abstract: The anatomy of large vessels of the chest cavity was studied on 40 corpses by X-ray anatomy. Transplantation and heart transplantation were performed on 20 corpses, according to various schemes, including the Shumway scheme (in 3 cases). After the operation, X-ray vasography of the transplanted heart was performed.

Transplantation of the cardiopulmonary complex according to Demikhov was performed on 10 corpses. Anatomical studies have shown the fundamental possibility of making a two-stage operation to transplant the heart, lungs and cardiopulmonary complex, depending on the indications. At the 1st stage, the cardiopulmonary complex in a special container can be connected to the femoral vessels. If such a complex functions completely, at the 2nd stage, the question of transplanting the heart, lungs and the entire complex to a natural place in the chest cavity can be raised.

Recommendations: The method of 2-stage heart and lung transplantation can be recommended for clinical practice.

Note: The results of the anatomical development of methods for transplantation of the heart, lungs and cardiopulmonary complex will be published in the form of an article [6, p. 75].

Reporting Sheet No. 61 (spelling preserved – *auth.*).

Topic: **ECG studies in heart homotransplantation**.

Project Leader: V.P. Demikhov.

Investigator: V.M. Goryainov.

Abstract: ECG monitoring of the transplanted heart condition performed in the Laboratory are continued, the material collected in previous years is being processed. After a successful operation, the ECG parameters of the transplanted heart are within the normal range; the heart rates of the native and transplanted hearts are different; the transplanted heart responds to changes in exercise load and intravenous fluid infusions. The appearance of pathological signs on the ECG often indicates deterioration in the transplanted heart function and should serve as an indication for additional examination of the graft by other methods. In some cases, with timely treatment, it is possible to prevent further development of weakening and prolong the life of the transplanted organ.

In 1970, 227 ECGs were recorded in dogs undergoing heart transplantation using various improved schemes. ECGs were also recorded in monkeys (Fig. 5) and dogs that had their own blood replaced with human blood.

Recommendations will be given upon the work completion.

Note: the materials were reported at the 5th All-Union Conference "Transplantation of Organs and Tissues" (Gorky, 1970) [6, p. 76].

Fig. 5. Transfusion of human blood to a monkey. 1970s

Reporting Sheet No. 62.

Topic: **Revitalization of the heart and the whole human body by using a mechanical heart (according to V.P. Demikhov's method).**

A new device was designed and tested experimentally and on corpses: a portable mechanical heart. An application for the method and device has been submitted to the Committee for Inventions and Discoveries.

Investigators: V.P. Demikhov together with the Intensive Care Center (B.G. Zhilis).

Abstract: Together with the Krasnoyarsk Institute of Physics of the Siberian Branch of the USSR Academy of Sciences, I designed and tested a portable device (fits in a pocket) − a mechanical heart − in an experiment on corpses; this device can be connected to a arrested heart under any circumstances, including in an ambulance, but provided the chest is opened for direct cardiac massage. We have also radically improved the method of direct heart massage, published and reported at the Republican Conference on Intensive Care on December 23–25, 1970. The device is connected to the heart according to a new scheme we have developed, through the auricles.

Recommendations: An original model of a portable mechanical heart has been created, which can be used in an ambulance service [6, p. 77].

Reporting Sheet No. 63.

Topic: **Homoplastic transplantation of the small intestine in experiment.**

Investigators: L.S. Chakhunashvili, V.P. Demikhov.

Type of investigation: experimental, laboratory, morphological.

Abstract: In 1970, 18 additional experiments on small intestine transplantation were made; various types of vessel connection and various lengths of intestine segments were tested. Physiological, histological and biochemical investigations were performed. In another series of experiments, the small intestine was transplanted along with the entire complex of abdominal organs.

The results show the principal possibility of replacing the small intestine in cases where its irreversible damage is observed over a large extent [6, p. 78].

Reporting Sheet No. 64.

Topic: **Anatomical and experimental rationale of transplanting pancreas in combination with duodenum.**

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

Abstract: The experimental and anatomical research on the method of pancreas implantation continued aiming at its further implementation in the clinic.

In experiments on dogs, the pancreas was transplanted according to various schemes − onto the vessels of the ileum area along with the duodenum, which end was sutured into the side of the small intestine or brought out. The pancreas was also experimentally transplanted in combination with the duodenum and liver. This complex was sutured to the vessels from the removed kidney. The possibility of connecting an additional pancreas with or without a duodenum to the iliac vessels "end-to-side" with suturing the end of the duodenum into the side of the small

intestine was shown on corpses. In case of irreversible lesion of the liver and pancreas (cancer), it is advisable to transplant the entire complex (liver, pancreas with duodenum or separately).

Recommendations: Pancreas implantation can be recommended for implementation into clinical practice [6, p. 79].

Reporting Sheet No. 65.

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

Abstract: since 1948, we have developed a physiological method for preserving revitalized organs for transplantation. In 1950, Author's Certificate of the USSR No. 85876 dated June 10, 1950, was obtained. Subsequently, the method description and its extended scheme were published in scientific and popular journals around the world.

A portable thermostat has been adapted to preserve the revitalized organs from corpses; and a thermostatic operating room is being purchased, which should come from the Pyatigorsk Machine-Building Plant in December 1970.

Recommendations: The implementation of the above method into practice requires establishing the bank of organs [6, p. 80].

Reporting Sheet No. 66 *(*spelling preserved – *auth.*).

Topic: **Implantation of an additional heart and lung housed in a case to peripheral vessels in the cardiopulmonary failure risk.**

Abstract:

Project Leaders: V.P. Demikhov, N.I. Gerasimenko[7].

Investigators: The staff of the Organ Transplantation Laboratory of the N.V. Sklifosovsky Institute, the staff of the Surgical Clinic of the Central Research Institute of Tuberculosis of the USSR Ministry of Health.

[7] Gerasimenko N.I., a Soviet Thoracic and Phthisiosurgeon, Professor, one of the founders of Phthisiosurgery in the USSR; in 1956–1961, he headed the Department of Pulmonary Surgery of the Institute of Thoracic Surgery of the USSR Academy of Medical Sciences; from 1961, he headed the Surgical Department at the Central Research Institute of Tuberculosis of the Ministry of Health of the USSR.

Abstract: In previous years, a method of 2-stage transplantation of the heart and lungs was developed in experiment at the laboratory. First (Stage 1), the heart and lungs (as a complex) from a similar donor are connected to the femoral or iliac vessels of an experimental animal. The graft is placed in a transparent plastic case (container)[8]. In this state, it is possible to confirm the function of a full-fledged connection [of the complex] to the body. If after 2–3 days or weeks of function, the graft is in good condition, then at the 2nd stage of the operation it can be transferred to a natural place either as a complex, or as separate organs (heart, one lung, both lungs, one of the lobes of the lung). <…>

When externally connected to peripheral vessels, the cardiopulmonary complex can alleviate the condition of a seriously ill patient suffering from a threatening form of cardiopulmonary insufficiency. In tuberculosis clinics, mortality from cardiopulmonary insufficiency is very high. Therefore, Professor N.I. Gerasimenko with his staff and the Organ Transplantation Laboratory began a joint experimental preparation for the implementation of positive results in clinic. Many experiments have been carried out by using the schemes that may be applicable to patients at a high risk of death from cardiopulmonary insufficiency. A container for transplantation was designed and manufactured.

Recommendations: The method of 2-stage heart and lung transplantation can be recommended for implementation in practice. The Organ Transplantation Laboratory for of the N.V. Sklifosovsky Institute is ready to take part in the joint implementation of the method with any clinic in Moscow and the Soviet Union.

Note: The first joint results were reported at the Republican and All-Union Symposia on extracorporeal connection of organs; published in the Proceedings of the 5th All-Union Conference "Transplantation of Organs and Tissues" (Gorky, 1970) [6, p. 81].

[8] This case (container) is named "the 2nd chest" in some 2-stage cardiopulmonary transplant operations.

Comparing the Reporting Sheets of 1969 and 1970, one can see the progressive movement forward of V.P. Demikhov and his staff. Thus, when implementing the topic “Anatomical development of the method for heart and lung transplantation on human corpses”, advanced techniques of X-ray anatomy of the main vessels and X-ray vasography of a transplanted heart were applied. The anatomical method of V.P. Demikhov and the Lower-Shumway biatrial technique were used for heart transplantation. A simple and easy-to-use method for assessing the transplanted heart function using ECG has been developed. A portable mechanical heart was designed and tested in the experiment and on corpses. Interesting were the investigations on the transplantation of fragments of the small intestine, pancreas, isolated or in combination with the duodenum and liver. A method of implanting CPC on peripheral vessels was developed for the treatment of end-stage cardiopulmonary failure.

Note that V.P. Demikhov managed to attract large third-party organizations to his research: the Krasnoyarsk Research Institute of Physics of the Siberian Branch of the USSR Academy of Sciences (creation of a mechanical heart), the Pyatigorsk Machine-Building Plant (creation of a portable thermostat to preserve vital organs), and the Central Research Institute of Tuberculosis of the USSR Ministry of Health (the development of a method for transplanting the cardiopulmonary complex to peripheral vessels).

Operations V.P. Demikhov performed in 1969–1970

We have stated above that not all the topics being developed by V.P. Demikhov and his Laboratory staff were mentioned in the Research Reporting Sheets. This is evidenced by the Record keeping Log stored in the collection of the Russian Museum of Medicine, which presents a list

of operations performed by V.P. Demikhov within the walls of the N.V. Sklifosovsky Institute from 1960 to 1984 [7] (Fig. 6).

Fig. 6. V.P. Demikhov (center) is operating. He is assisted by V.M. Goryainov (wearing a mask, on the left) and L.T. Minina (standing with her back). The operation is supervised by Professor N.G. Artsimovich (on the right). 1970s [1]

Table 1 shows the interventions performed in the Organ Transplantation Laboratory from January 1969 to December 1970, categorized by the type of operation.

Table 1. Operations performed in the Organ Transplantation Laboratory of the N.V. Sklifosovsky Institute in 1969–1970

No.	Operation name	Number	Dates
ISOLATED CARDIOLUNG COMPLEX TRANSPLANT			
1.	Transplantation (implanting) of CPC in a case (the 2nd chest) on the iliac vessels	3	17.06.1969–01.09.1970
2.	Transplantation (implanting) of CPC in a case on the vessels of the neck (the 2nd chest)	2	22.07.1969; 10.11.1970
3.	Transplantation (implanting) of CPC in a case (the 2nd chest) on the chest	2	08.09.1969; 12.03.1970
4.	Orthotopic transplantation (replacement) of CPC	7	25.09.1969–27.10.1970
5.	Isolation of an individual CPC; a student Rozhkova is mastering the technique	2	05.01.1970
6.	Transplantation (implanting) of CPC in a case(the 2nd chest) on the vessels of the inguinal region	2	04.08.1970; 08.09.1970
7.	Transplantation (implanting) of CPC in a case(the 2nd chest) on the femoral vessels	1	07.05.1969 (or 1970)
TOTAL:		**19**	**17.06.1969–10.11.1970**

ISOLATED HEART TRANSPLANT			
8.	Transplantation (implanting) of the heart on the iliac vessels	6	04.06.1969–01.12.1970
9.	Transplantation (implantation) of the heart on the vessels of the inguinal region	2	17.07.1969; 24.02.1970
10.	Transplantation of an additional heart into the chest cavity	3	31.07.1969–24.07.1970
11.	Transplantation (implanting) of the heart on the femoral vessels	1	15.09.1969
TOTAL:		**12**	**4.06.1969–01.12.1970**
REVITALIZATION OF THE HEART AND HEART-LUNG COMPLEX			
12.	Dog heart revitalization		
a)	By implanting an additional heart	1	01.08.1969
b)	By perfusion with human cadaveric blood using HLM 54 minutes after cardiac arrest	1	06.10.1969
c)	By connecting to the femoral vessels with silicone tubes (one of the hearts did not function for 23 minutes)	2	08.10.1969; 03.11.1969
d)	By connecting to the neck vessels with silicone tubes	2	14.10.1969; 20.10.1969
e)	By perfusion with dog blood using HLM	1	21.10.1969
13.	Revitalizing CPC of 4 monkey corpses at 3 hours after death by perfusion with human cadaveric blood using HLM	4	26.01.1970
14.	Revitalizing pig CPC by perfusion with human cadaveric blood	2	21.04.1969; 18.11.1969
TOTAL:		**14**	**01.08.1969–26.01.1970**
HEAD TRANSPLANT			
15.	Transplantation (implanting) of the head on the vessels of the neck	3	15.05.1969–22.12.1970
16.	Transplantation (implanting) of the head on the chest	1	10.09.1970
TOTAL:		**4**	**15.05.1969–22.12.1970**
ARTIFICIAL CIRCULATION			
17.	Testing a mechanical heart with the exclusion of the native heart from the blood circulation for 1 hour	1	16.01.1970
18.	Testing the HLM designed by Korolev	1	09.03.1970
TOTAL:		**2**	**16.01.1970; 09.03.1970**
CONNECTING THE BODY HALVES			
19.	Joining the body halves	10	25.08.1970–03.12.1970
20.	Transplantation of the posterior (lower) half of the body to the iliac vessels	1	12.11.1970
TOTAL:		**11**	**25.08.1970–03.12.1970**
OPERATIONS ON THE ABDOMINAL CAVITY			
21.	Passing a plastic coil (several meters long) throughout the gastrointestinal tract (from mouth to anus)	2	30.10.1970; 10.12.1970
22.	Inflating the stomach with air	2	14.04.1970; 16.10.1970
23.	Orthotopic liver transplantation without diaphragmatic incision in the recipient	1	20.10.1970
TOTAL:		**5**	**14.04.1970–10.12.1970**
OPERATIONS ON URINARY ORGANS			

24.	Transplantation of the uterus with appendages	1	16.04.1969
25.	Transplantation (implanting) of the uterus with appendages on the iliac vessels	1	15.05.1969
26.	Orthotopic uterus transplantation	1	09.12.1969
27.	Transplantation of the uterus into the abdominal cavity	1	11.12.1969
28.	Perfusion of a human cadaveric kidney by connecting to the vessels of a dog	1	10.02.1970
29.	Transplantation (implanting) of a human cadaveric kidney to a dog	1	30.03.1970
30.	End-to-side transplantation of the uterus of monkeys into the abdominal cavity (at the All-Russian Research Institute of Poliomyelitis, Vnukovo)	1	17.11.1970
31.	Transplantation of the uterus into the abdominal cavity according to the "end-to-side" type according to Oshariya's method (Tbilisi)	1	19.12.1970
TOTAL:		**8t**	**16.04.1969–19.12.1970**
EXCHANGE TRANSFUSION			
32.	Exchange transfusion of human cadaveric blood to a dog	7	15.09.1969–28.04.1970
33.	Exchange transfusion of human cadaveric blood to a monkey	2	02.02.1970; 02.02.1970
TOTAL:		**9**	**15.09.1969–28.04.1970**
OPERATIONS ON HEMATOPOIETIC ORGANS			
34.	Transplantation (implanting) of the sternum to the vessels of the neck	1	5.11.1969
TOTAL:		**1**	**5.11.1969**
OPERATIONS ON VESSELS			
35.	Cannulation of coronary vessels	1	31.10.1969
36.	Vascular suture training for Cuban surgeons	1	19.03.1970
TOTAL:		**2**	**31.10.1969; 19.03.1970**

According to the Record keeping Log, V.P. Demikhov, his staff and students performed 87 operations of 11 types in the period from April 21, 1969, to December 22, 1970 (Table 2).

Table 2. Total number of operations performed by V.P. Demikhov in 1969–1970

No.	Operation name	Number (% of total)
1.	Transplantation of an isolated CPC	19 (21.8%)
2.	Revitalization of the heart and CPC	14 (16.2%)
3.	Isolated heart transplant	12 (13.8%)
4.	Transplanting body halves	11 (12.6%)
5.	Exchange transfusion	9 (10.3%)
6.	Operations on the urinary organs	8 (9.2%)

7.	Operations on the abdominal organs	5 (5.7%)
8.	Head transplant	4 (4.6%)
9.	Operations on vessels	2 (2.3%)
10.	Cardiopulmonary bypass and mechanical heart	2 (2.3%)
11.	Operations on the hematopoietic organs	1 (1.2%)
TOTAL:		**87 (100%)**

Most operations were performed on the transplantation of an isolated cardiopulmonary complex (ICPC) aimed at developing an anatomical method of heart and lung transplantation in humans. We found that in 1968 V.P. Demikhov performed 37 ICPC transplants, including 3 orthotopic transplants, 11 implantations on the chest, 7 implantations onto iliac vessels, and 16 implantations on some other peripheral vessels. However, in the same 1968, the world's first ICPC transplantation in a human was performed by D.A. Cooley from Houston [8]. And although this operation showed the feasibility of ICPC transplantation in humans, the single-stage technique used by D.A. Cooley turned out to be imperfect, in V.P. Demikhov's opinion: the patient lived only 14 hours. According to V.P. Demikhov's technique, ICPC transplantation in humans was planned in two stages: Stage 1 implied transplantation onto peripheral vessels (neck, chest, abdominal cavity, iliac, inguinal and femoral vessels). At that, the ICPC was placed in a transparent plastic case filled with a nutrient liquid for visual monitoring of the transplanted organs (V.P. Demikhov called this device the 2nd chest). And if no rejection reaction occurred within a week, the 2nd stage followed providing orthotopic transplantation of ICPC or individual organs: the heart, one lung, both lungs, one of the lobes of the lung. Perhaps as far as Soviet surgery missed the world priority in this type of transplantation, and also in the absence of any opportunities to translate the experiment to clinic, V.P. Demikhov made only 19 ICPC transplants in 1969−1970, including 7 orthotopic ones, 2 transplants onto the chest, and 3 onto the iliac vessels.

In the next article, we will show that in 1971−1972 V.P. Demikhov performed even fewer ICPC transplants: only 9, including 3 orthotopic ones, none onto the chest and 2 onto the iliac vessels. There were no opportunities, the interest was fading. Apparently, this interest was fading abroad as well. Following clinical failures, surgeons in the United States and other countries continued the experimental development of the operation, and the first successful ICPC transplantation in a patient with idiopathic pulmonary hypertension was performed by B. Reitz from Stanford University only in 1981, that was, 13 years after D.A. Cooley [8].

But V.P. Demikhov was not like that to retreat. In 1970, a new goal appeared in his experiments on ICPC transplantation: to implant an additional heart and lung enclosed in a case into peripheral vessels in a high risk of cardiopulmonary system failure (Reporting Sheet No. 66; [6, p. 81]). The second new problem was transplantation of an isolated heart using a 2-stage technique. But before using in clinic, it was necessary to develop this operation on human corpses. In parallel, the experiments were underway to revitalize the cadaveric heart and the whole body in various ways: by perfusion with using HLM and a mechanical heart; by connecting an additional heart, by connecting to peripheral vessels. Meanwhile, V.P. Demikhov made extensive use of human cadaveric blood, conducting experiments on exchange blood transfusions in dogs and monkeys. In addition to these experiments, he continued to study the possibility of transplanting halves of the torso, head, liver, uterus, kidney, and sternum.

We do not know why some of the operations mentioned in the Reporting Sheets were not included in the "List of experiments performed in the Organ Transplantation Laboratory of the N.V. Sklifosovsky Research Institute for Emergency Medicine for the period from 1960 to

1984" [7]. For example, transplantations of the small intestine fragments, of which, judging by the Reporting Sheets, 15 were performed in 1969 (Reporting Sheet No. 90; [4, p. 120]), and 18 in 1970 (Reporting Sheet No. 63; [6, p. 78]). Or operations of transplanting the pancreas in complex with the duodenum, of which 100 were performed in dogs in 1969, and 20 on human corpses (Reporting Sheet No. 91; [4, p. 121]), and various options were included in the Report of 1970 (Reporting Sheet No. 64; [6, p. 79]). Perhaps this happened so because L.S. Chakhunashvili was dealing with bowel transplantation, and L.L. Gugushvili with pancreas transplantation; and they did it in different institutions.

Another reason is also possible: the "List of Experiments" was created in 1984. By this time, some of the Laboratory's operational logs had been lost. For example, according to the List, in 1969 operations began on April 21 with the revitalization of pig's CPC by perfusion with human cadaveric blood. What research V.P. Demikhov was doing from January to mid-April is unclear. And there are many such "gaps" in Table. 1.

Conclusion

Thus, in 1969-1970, V.P. Demikhov and the staff of the Organ Transplantation Laboratory of the N.V. Sklifosovsky Institute improved a number of previous and developed several new methods of transplantation of isolated organs and their complexes: (1) anatomical method of heart and lung transplantation in experiment and on human corpses; (2) a method of revitalizing the heart and the whole human body using direct massage and a portable mechanical heart connected to the auricles; (3) the method of liver transplantation in the experiment and its anatomical rationale for implementation in clinic for liver failure; (4) the method for evaluating the transplanted heart function, using an

electrocardiogram; (5) the method of transplantation of small intestine fragments; (6) the method of transplanting the pancreas, either isolated, or in combination with the duodenum and liver, onto the renal vessels; (7) the method of implanting the cardiopulmonary complex onto peripheral vessels for the treatment of end-stage cardiopulmonary failure, and a number of others.

For experimental studies, methods of X-ray anatomical study of the main vessels and X-ray vasography of a transplanted heart were used. For heart transplantation, the anatomical method by V.P. Demikhov and the Lower-Shumway biatrial technique were used.

To conduct some research, V.P. Demikhov managed to attract large third-party organizations: the Krasnoyarsk Research Institute of Physics of the Siberian Branch of the USSR Academy of Sciences (creation of a mechanical heart), the Pyatigorsk Machine-Building Plant (creation of a portable thermostat to preserve vital organs), the Central Research Institute of Tuberculosis of the USSR Ministry of Health (development of the method for implanting the cardiopulmonary complex onto peripheral vessels), Research Institute of Poliomyelitis (operations on monkeys).

According to the " the "List of experiments performed in the Organ Transplantation Laboratory of the N.V. Sklifosovsky Research Institute for Emergency Medicine for the period from 1960 to 1984", in 1969–1970, 87 operations of 11 types were performed in the Organ Transplantation Laboratory. Most of the operations were transplants (implanting) of the cardiopulmonary complex, transplantation of an isolated heart, and revitalization of a cadaveric heart for further transplantation. It is clearly seen from the List of experiments that, in addition to the research topics included in the Research Plan of the Institute, V.P. Demikhov developed many individual, investigational topics, including transplantation of halves of the body, head, liver, uterus,

kidney, and sternum. We emphasize that all these methods were planned to be implemented into the clinic after the research.

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