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PHENOMENON of DEMIKHOV

Achievements and prospects of heart transplantation in the USSR in the early 1970s

S.P. Glyantsev

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

135 Roublyevskoe Hwy., Moscow 121552 Russia;

N.A. Semashko National Research Institute of Public Health,

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

Corresponding author: Sergey P. Glyantsev, Prof., Dr. Sci. (Med.), Head of the Department of the History of Cardiovascular Surgery, A.N. Bakulev National Medical Research Center for Cardiovascular Surgery; Head of the Sector for the History of Medicine and Factography of the Department for the History of Medicine, N.A. Semashko National Research Institute of Public Health, spglyantsev@mail.ru

Abstract

The paper presents the analysis of two publications written by two pioneers of heart transplantation in the USSR, A.A. Vishnevsky with co-authors and G.M. Solovyov, which covered the state of the organ transplantation issue in 1971–1973 and gave predictions for its future development. It is shown that the authors of those publications saw and formulated the main trends in the development of the problem in one and the same way. Meanwhile, G.M. Solovyov, being the Director of the specialized Institute of Organ and Tissue Transplantation of the USSR Academy of Medical Sciences saw the issues of organ transplantation more in depth than A.A. Vishnevsky who headed the A.V. Vishnevsky Institute of Surgery of the USSR Academy of Medical

Sciences. In particular, this concerned immunological studies. Shortly after its establishment in 1969, the Institute of Organ and Tissue Transplantation arranged a powerful laboratory of immunogenetics on its base. The staff of that laboratory (L.V. Smirnova, Yu.M. Zaretskaya, L.P. Alekseev, V.I. Shkurko, A.M. Sochneva, I.V. Petrova, etc.) conducted world-class immunological studies, which results inspired certain optimism among surgeons. A more complicated situation was with the clinical issues of organ transplantation, with the solution of organizational, moral and ethical issues, where, in addition to doctors, the active participation of legislators, economists, and healthcare organizers was required. This paper presents comparative data on the state of political, economic, and organizational issues of organ transplantation in the Russian Federation between the 2010s and early 2020s. It is shown that the planned in the 2020s tendency of their positive solution and further development inspires certain optimism.

Keywords: history of transplantology, achievements and prospects in the USSR and in the RF, A.A. Vishnevsky, 1971; G.M. Solovyov, 1973; S.V. Gautier, S.M. Khomyakov, 2021

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MMA, Military Medical Academy

WHO, World Health Organization

VSD, vascular stapling device

ECM, electronic computing machine/computer

Introduction

In the previous article [1], V.P. Demikhov's experimental work in

1969–1970 was analyzed. It was shown that the main purpose of his activities at that period of time included persistent attempts to implement the methods he developed on animals into clinical practice. This, in particular, concerned: transplantation of an isolated heart and a cardiopulmonary complex; transplantation of the liver, lungs, and kidneys, transplantation of the intestine fragments, and transplantation of the sternum for the purpose of transplanting bone marrow, revitalizing cadaveric hearts for their subsequent transplantation; transfusions of homologous blood (from human to animals and from one animal species to another) in order to smooth down the rejection reaction during subsequent homotransplantations; creation of a mechanical heart to support the activity of an ill organ and much more.

It was also shown that the staff of the N.V. Sklifosovsky Institute for Emergency Medicine, who widely used homologous transplantation of cadaveric tissues in clinical practice, in particular, cadaveric blood, considered organ transplantation at the Institute to be premature. But the point here, in our opinion, is not at all the reluctance of this on the part of the administration of the Institute and its leading surgeons, but the fact that they, as the organizers of emergency medical care for Moscow residents, faced completely different tasks, which included clinical tissue transplantation (in particular, cadaveric blood) and did not include clinical organ transplantation.

The first successful kidney transplant in the country from a related donor on April 15, 1965, was performed by Professor B.V. Petrovsky (Fig. 1). Speaking in 1966 at a scientific conference in Ryazan devoted to reconstructive vascular surgery, he said the following about the future of Soviet transplantation:

«*We are present at the very beginning of the development of organ transplantation - a* ***trend that is destined for a great future*** (hereinafter, the bold is ours - A*uth.*). *We will be witnesses to this, and a major role in the success of this case belongs, first of all, to reconstructive vascular surgery, thanks to which it has generally become possible to carry out organ transplantation per se. Following a kidney transplant, no doubt, other vital organs will also be transplanted, such as the* ***liver, intestines, and, possibly, the heart***" [2, p. 52].

Fig. 1. Academician B.V. Petrovsky. 1970s

Time has shown that the outstanding surgeon of the twentieth century was absolutely right. On December 3, 1967, in Cape Town (South Africa), the world's first human heart transplant was performed by C. Barnard. The first similar operation in our country was performed on November 4, 1968 in Leningrad by A.A. Vishnevsky (Fig. 2) and I.S. Kolesnikov (Fig. 3) with a group of surgeons, immunologists, perfusiologists, anesthesiologists and resuscitators from A.V. Vishnevsky Institute of Surgery and the Hospital Surgery Clinic of the Military Medical Academy (MMA) named after S.M.Kirov. The second operation in this country was performed at the

Institute of Organ and Tissue Transplantation of the USSR Academy of Medical Sciences on June 10, 1971, by the Director of the Institute G.M. Solovyov (Fig. 4) with colleagues.

Fig. 2. Professor A.A. Vishnevsky, Full member of the USSR Academy of Medical Sciences (left), and Ch. Barnard, South African surgeon (right) as delegates of the XXVII All-Union Congress of Surgeons, in the courtyard of the A.V. Vishnevsky Institute of Surgery. May, 1960

Fig. 3. Professor I.S. Kolesnikov, Full member of the USSR Academy of Medical Sciences. 1970s. From the archive of A. Kleban

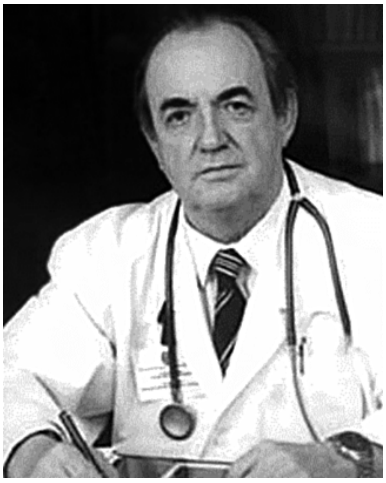

Fig. 4. Professor G.M. Solovyov, Corresponding Member of the USSR Academy of Medical Sciences. 1970s.

And although these operations were not successful, 2 years after they had been performed, both pioneers of the homeland heart transplantation shared their opinions on the achievements and prospects for organ transplantation, in particular heart transplantation, in the near future. Both articles were published 50 years ago and currently are hardly known to the readers studying the history of transplantology.

This article is devoted to the content-analysis and introduction of selected fragments of these publications by prominent Soviet surgeons to scientific circulation, as well as to the achievements of Soviet transplantation in the early 1970s, and prospects for its development in the coming years.

A.A. Vishnevsky, I.S. Kolesnikov, F.V. Balluzek, V.F. Portnoy "Achievements and prospects of organ and tissue transplantation". 1971

This article was published in 1971 in the July issue of the Military Medical Journal [3] (Fig. 5).

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Fig. 5. ***Military Medical Journal*** **where the article by A.A. Vishnevsky, I.S. Kolesnikova, F.V. Balluzek, and V.F. Portnoy "Achievements and prospects of organ and tissue transplantation" was published:** A) cover page; B) the title of the article. July, 1971

Note that the manuscript of the article was received by the editors of the journal in May, so its authors did not know about the operation, which G.M. Solovyov performed only a month after. It follows that the basis for writing the article was the data of world literature and the personal experience of the authors in the field of experimental and clinical heart transplantation. How did the pioneers of heart transplantology evaluate the achievements and prospects of clinical organ transplantation in the USSR? What did they propose for its development?

> "The development of this new and complex biomedical problem has entered a calm and businesslike phase. What can be said now, when the newspaper hype is behind us, and at the same time, when in the hands of specialists there are not assumptions, but strict scientific facts about real achievements in the field of organ transplantation in humans? - the authors asked. - To what extent have the most optimistic hopes, on the one hand, and active negativism, on the other, come true?"

> Under the optimistic hopes, A.A. Vishnevsky and co-authors implied that “the accumulated collective experience decisively refuted the view that transplantation is not yet ripe for clinical practice, since it supposedly does not have a sufficiently solid theoretical basis. This is essentially incorrect. <...> *Already now there is every reason to say that the process of formation of a new field of medical science, a new clinical specialty - transplantology, has been completed on the whole* (our italics - *Author*)".

It sounds tempting. But only for world transplantation, where 16 years have passed since the first successful kidney transplant, and 2 years have passed since a series of successful heart transplants. For the USSR, in our opinion, the statement was disputable. Indeed, in order for any new trend of medicine to become a medical specialty, it sometimes took decades. For example, cardiovascular surgery, which began in Russia at the end of the 19th century[1] , entered the register of medical specialties only in 1970 [4].

However, A.A. Vishnevsky et al. provided the following evidence for their opinion:

> (1) "the limitations of other modern treatments for many severe ailments"; (2) “establishing the fact of the existence of tissue groups close in their antigenic characteristics, within which the degree of immune conflict between the tissues of the recipient and the donor is minimal”; (3) "development of methods for suppressing the transplanted organ rejection reaction - immunosuppression [2]" [3, p. 21].

The first statement, according to the authors, did not require comments,

[1] The first cardiac wound suturing operations in the Russian Empire were performed in 1898 by V. Khorodynsky and V. Malishevsky, the employees of the Faculty Surgical Clinic of the University of Warsaw. The first successful cardiography in 1903 at the Basmannaya hospital in Moscow was performed by the leading surgeon of the hospital N.I. Shakhovskaya.

[2] Until the early 1970s, the term “immunosuppression” was adopted in the homeland literature.

since "*the mortality rates of patients with end-stage renal, cardiac, hepatic and pulmonary diseases speak for themselves*." As an example, they cited the life expectancy of patients with heart disease, which in 1968–1969 were selected by A.A. Vishnevsky and I.S. Kolesnikov as potential recipients. Of these, 8 patients with complex concomitant heart defects lived without surgery for an average of 9 months, 13 patients with coronary disease lives for 5.5 months, and 6 patients with severe forms of myocarditis lived for 3.8 months [3, p. 22]. According to the authors, a successful heart transplant could have significantly prolonged the life of these patients.

"*The issue of defining indications for kidney transplantation is somewhat more complicated,*" *the* authors write further, "*since this treatment method successfully competes with the method of chronic hemodialysis using an artificial kidney machine*." But even here, according to the authors, there are several reasons that make it possible to prefer transplantation of a biological kidney to an artificial one, in particular, the difficulties of organizing hemodialysis centers, the need for its frequent use, and the high cost of treatment. In addition, the possibilities of dialysis in the treatment of renal failure were limited at that time [3, p. 22]. The conclusion that follows sounds quite modern: "When assessing the clinical feasibility of organ transplantation <...> not so much the duration as ***the quality of life of patients*** *is of great importance* (bold ours - A*uth.*). *And if transplantation at least to some extent guarantees the patient's deliverance from the painful manifestations of deep disability, it deserves a special attitude*" [3, p. 22].

Regarding the second condition – the ways to reduce the severity of the immune conflict between the donor's and recipient's bodies, A.A. Vishnevsky and co-authors noted that since "the *set of tissue antigens is limited*", then "the *number of possible combinations of these antigens is*

also not so large and allows the selection of people who are quite close in terms of the "immunological passport". So, if among identical twins the frequency of such coincidences, according to the authors, was 1:1, then among relatives it was 1:4; and among unrelated groups of the population it can be from 1:70 to 1:100. Thus, "*if there is a sufficiently large number of "participants", the probability of selecting compatible pairs becomes quite real*." However, the authors believed that certain conditions are necessary for the implementation of such a selection. The first of them is the centralized registration of patients who need an organ transplant. Each patient should be carefully examined and, if there are indications for transplantation, sent to a transplant center, where his immunological status would be studied and the data entered into a special electronic computer card (ECM).

The further fate of such a patient will depend on how quickly an organ compatible in its antigenic characteristics with the recipient's body will be at doctors' disposal. Until then, the patient can be either outside the walls of the center, or on outpatient or inpatient treatment in a specialized department (cardiology, nephrology, hepatology, pulmonology, etc.).

The appearance of a donor triggers a number of actions, the main of which are the following:

> "donor typing <…> according to the system of histo-leukocyte antigens; transfer of this information to all interested transplant centers; selection of a potential recipient from among those registered; removal of the desired organ, its preservation and transportation to the appropriate transplant facility, where the patient awaiting transplant should arrive by this time <...> And since (based on the above statistical frequency of coincidences among random pairs), it is desirable to have at least 100–200 potential recipients on

the register, there arises an important organizational task of cooperation in the network of transplantation institutions, up to the creation of long-distance and international associations” [3, p. 23–24].

So there is a detailed and well-thought-out program for the development of transplantology in the USSR for the 1970s–1980s. At the same time, A.A. Vishnevsky and co-authors, well aware of the ideality of their proposals, nevertheless considered that a lot had already been developed and tested to create an "*organ transplantation service" in the country.*

“Thanks to the collaboration of a number of institutions (the Institute of Organ and Tissue Transplantation of the USSR Academy of Medical Sciences, the A.V. Vishnevsky Institute of Surgery of the USSR Academy of Medical Sciences, the Military Medical Academy named after S.M. Kirov and others[3], a joint card file of potential recipients has been created, whose immunological status data is stored in computer memory, a technique has been established for tissue typing, preservation of organs, and consequently, conditions have been created for their mutual (including long-distance) exchange” [3, p. 24].

It is easy to see that the authors put the overcoming of the biological incompatibility of the donor and recipient body at the forefront of creating such a service. But were these conditions enough to fundamentally solve the problem of heart transplantation in the country in the 1970s? Most likely not. And the "*card file of potential recipients*" would not have solved this

[3] According to our data, the Department of Cardiovascular Surgery of the F.G. Yanovsky Research Institute of Tuberculosis and Thoracic Surgery of the Ukrainian SSR Ministry of Health of the (Leader L.N Sidarenko, Scientific Advisor N.M. Amosov) was also engaged in preparation for clinical heart transplantation at that time).

problem. The article mentions that “the *method <...> of organ preservation has been established*”, but not a word was said about the need to create a *bank of donor organs*, of which V.P. Demikhov had been speaking and writing for many years. It is clear that his proposal to connect organs to a living organism - "physiological system" even today is a fantasy, but no one has offered any alternative yet.

In addition, for a successful operation, besides solving immunological problems, first, a careful selection of the recipient is required according to other parameters, in particular, the status of the vascular system of the lungs and other organs; and second, after transplantation, the patient needs a thorough care and effective treatment, which can be carried out only in institutions with a well-developed *resuscitation service* and a well-developed *system* for managing recipients in the postoperative period.

As for the selection of patients, as Professor F.V. Balluzek, a participant in the first heart transplant in the country, told us, that at first, those who selected recipients had no other criteria than severe heart damage. And when selecting donors with a life-incompatible craniocerebral injury, for example, their initial alcohol intoxication that was observed quite often in victims of domestic, industrial injuries or traffic accidents was not taken into account. These words, spoken in the early 2000s, are confirmed by an article published in 1971:

> “in real conditions with the current organization of ambulance service <…> as shown by the experience of a number of clinics of the Military Medical Academy named after S.M. Kirov, in fact, no more than 1-2% of all those who die on the territory of Leningrad, who would formally fit the definition of a potential donor, turn out to get in the transplantation center's “field of view”. But this is not enough. Numerous contraindications for taking an

> organ must also be considered, including: damage to the organ as a result of trauma, previous diseases [which are often not possible to establish], age-related abnormalities, *alcohol intoxication* (our italics - *Author*), infectious complications, etc. As a result, it turned out that organs from only one of five to ten corpses classified as donors are suitable for removal" [3, p. 24].

Without touching on the moral and ethical problems of organ transplantation, A.A. Vishnevsky and co-authors touched upon the issue of ascertaining the death of a donor. In their opinion, "*strict control by forensic medical examination, a scientifically based approach to determining death, the possibility of its sufficiently reliable prediction allow us to successfully solve this seemingly difficult problem*" [3, p. 24].

Recall, however, that back in 1969, "*strict control by a forensic medical examination*" meant a forensic physician statement of the fact of donor's death 30 minutes after his heart stopped, which did not bother the authors of the article at all. The fact is that in those years, V.F. Portnoy, an employee of A.V. Vishnevsky Institute of Surgery, a former student of A.A. Vishnevsky developed a method for resuscitation of a cadaveric heart some time after its arrest, with subsequent maintenance of its vital activity under conditions of coronary perfusion.

Which of the above was the conclusion about the prospects for the development of clinical transplantology in Russia? "*Under certain conditions, in accordance with the considered organizational principles, the patients in need of organ transplantation receive the necessary assistance*" [3, p. 25]. Let's pay attention to the word "receive". This, apparently, is about kidney transplants, which by 1971 were fully mastered in the USSR:

> "In 1967, the first kidney transplantation center in the country was

organized at the All-Union Research Institute of Clinical and Experimental Surgery (VNIIKiEKh) of the USSR Ministry of Health, where the students of B.V. Petrovsky launched a broad study and search for ways and methods to overcome tissue incompatibility. A research program was developed and three main areas were scientifically substantiated: selection of immunogenetically compatible pairs; suppression of the immunological resistance of the recipient's body; an impact on the graft in order to reduce the activity of incompatibility antigens" [2, p. 53].

In 1973 B.V. Petrovsky wrote: "Currently, about 500 kidney transplants have been performed in our country (235 transplants were performed in our clinic). Approximately 25-30% of this number were transplants from a living closely related donor, and 70-75% were from a corpse. The maximum life span of these patients is 8.5 years for a living donor kidney and 7 years for a cadaveric one. There are 12 kidney transplant centers in our country (Moscow, Kiev, Minsk, Riga, Kemerovo, Baku, Tashkent, etc.); three more are in the process of organization" [2, p. 54].

These data prove that in the late 1960s and early 1970s, organ transplantology in the USSR began to develop quite intensively, but only mainly in the field of kidney transplantation. By the way, all over the world, the number of clinics involved in kidney transplantation exceeded the number of institutions involved in heart, liver and lung transplants combined. In the article by A.A. Vishnevsky and co-authors, there is an interesting table with the data of the International Congress of Transplantologists on the status of this area of medicine in July 1970 (Table 1).

Table 1. Results of organ transplantation in the world (July 1970) [3, p. 25]

Organ transplanted	Number of institutions	Number of operations	Number of survivors	Follow-up period (maximum)
Heart	67	163	22	22 months
Liver	33	109	8	26 months
Lungs	18	24	–	10 months
Kidneys	238	Over 5000	Over 2000	18 years
Pancreas	8	18	4	9 months
TOTAL*	364	Over 5300	Over 2034	From 9 months to 18 years

*This column was added by us – *Auth.*

Let us pay attention to the fact that despite the significant predominance of *kidney transplants, heart transplantation* ranks first in the table and second in terms of the number of operations. The second thing to note is that by 1973 there were 12 transplantation centers in the USSR and 3 more were in the process of being organized, total 15. By this time, more than 360 such centers functioned all over the world, of which about 240 were engaged in kidney transplantation[4]. And third, transplantation *of all organs* mentioned in the table, including such a difficult organ for transplantation as the pancreas and the *cardiopulmonary complex not included in the table*, V.P. Demikhov has long worked out in detail in the experiment.

There is nothing about this in the analyzed article. But it is said that

> "The very fact that people with a transplanted heart live for more than two years without experiencing signs of heart failure suggests that a new method of treatment deserves attention, opens up new perspectives. <...> All this once again confirms the main conclusion that modern transplantation has not only earned *the right to exist in a number of clinical specialties* (our italics -

[4] The Director of the Institute of Cardiovascular Surgery of the USSR Academy of Medical Sciences, S.A. Kolesnikov, who visited the USA in 1961, stated that about 300 clinics were engaged in heart and vascular surgery in the USA. In the USSR at that time, cardiovascular surgery was developed by only a few institutions

Author), but also requires the most resolute support, the most urgent elimination of difficulties on the way of its transition to new, more advanced organizational forms" [3, p. 26].

It is difficult to disagree even today with the words about "*resolute support*", about " *immediate elimination of difficulties*" and about "*transition to new, more perfect organizational forms*", said in May 1971. But still, there was no specialty “Transplantologist” in the Nomenclature of Medical Specialties approved by the USSR Minister of Health Order No.280 of May 4, 1970, with numerous additions made before 1994, which was canceled by the Russian Federation Minister of Health Order No. 317 issued in October 18, 2002, [4].

G.M. Solovyov. Achievements and prospects of the organ transplantation problem. 1973

A month after the article by A.A. Vishnevsky and co-authors was published, in June 1971, the second in the country heart transplantation, also unsuccessful, was performed by Professor G.M. Solovyov, the Director of the Institute of Organ and Tissue Transplantation of the USSR Academy of Medical Sciences, Corresponding Member of the USSR Academy of Medical Sciences, and 2 years later he published a similar paper [5] (Fig. 6). What changed in the country in solving the problem of heart transplantation during that time?

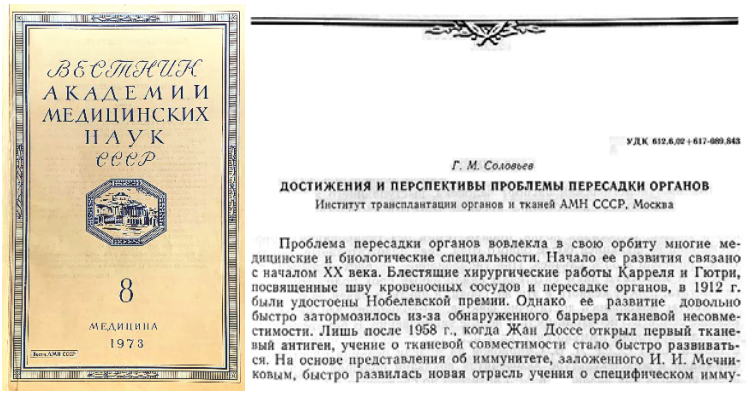

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Fig. 6. *Bulletin of the USSR Academy of Medical Sciences* where the article by G.M. Solovyov "Achievements and prospects of the organ transplantation problem": A) cover page; B) the title of the article. August, 1973

Note that if A.A. Vishnevsky and co-authors published their proposals for solving this problem in the specialized Military Medical Journal, for which A.A. Vishnevsky, was a member of the Editorial Board. The article by G.M. Solovyov was published in the Bulletin of the USSR Academy of Medical Sciences, the country's most prestigious medical journal. It is also characteristic that both papers *had no list of references*, which indicates their originality.

In his article, Professor G.M. Solovyov, the winner of the State Prize of the USSR (for the development and implementation of kidney transplant operations in clinic), a Corresponding Member of the USSR Academy of Medical Sciences, continued the discussion of the organ transplantation problem, which main provisions were put forward in 1971 by A.A. Vishnevsky and co-authors.

The article begins with a brief historical excursion, and then the author cited data on organ transplants in the world as of November 1, 1972. For

ease of perception, we summarize them in Table 2, the similar to that one cited by A.A. Vishnevsky and co-authors in his article. Note that 1 year and 4 months have passed between the data given in the two tables.

Table 2. The results of organ transplantation in the world as of November 1, 1972, compared with the data for July 1971 [5, p. 3]

Organ transplanted	Number of institutions in 1972	Number of operations in 1971/1972	Number of recipients in 1972	Follow-up period (max.) in 1971/1972
Heart	Not available	163/199	196	22 months/4 years
Liver		109/172	168	26 months/3 ½ years
Lungs		24/32	32	10 months/10 months
Kidneys		Over 5000/11214	10346	18 years old/14 years old
Pancreas		18/30	30	9 months / 1 year
TOTAL*		Over 5500/over 11500	10743	From 9 months to 18 years

* This column was added by us - *Auth.*

It is clearly seen how rapidly the world transplantology developed in the early 1970s. In just 1.5 years, the number of organ transplants has doubled (from 5,500 to 11,500), mainly due to kidney transplants. Little by little, but transplantations of the heart, liver, lungs, and pancreas continued. Since the operations were performed in 10,743 patients, it means that almost 800 of them were reoperated.

By November 1, 1972, more than 300 kidney transplants, 2 unsuccessful heart transplants, and not a single transplant of other organs had been performed in the USSR. In other words, in the 1930s–1950s, due to the priorities of S.S. Bryukhonenko and Yu.Yu. Voronoi, selfless labor of N.P. Sinitsyn and V.P. Demikhov, as well as other experimenters who developed advanced methods of organ preservation (A.G. Lapchinsky), Soviet surgeons were ahead of their foreign colleagues or were on a par with

them, but after operations of J. Murray (kidney transplant, 1962), J. Hardy (lung transplant, 1963), T. Starzl (liver transplant, 1967) and C. Barnard (heart transplant, 1967), our country began to lag behind in the number of clinical organ transplants.

Despite this, the article by G.M. Solovyov was optimistic. Just like A.A. Vishnevsky, he tried to outline the program for the development of organ transplantation in the USSR for the coming years, in which immunological research played an important role.

> "The main issues or the main problems of transplantation today, in the opinion of G.M. Solovyov, are the following: the selection of a donor and recipient for tissue antigens, controlled immunodepression[5], the search for methods for obtaining artificial tolerance in humans; organ preservation and determination of the viability of transplant organs; development of surgical aspects of transplantation and, finally, the solution of organizational, moral and ethical problems associated with obtaining donor organs and their transplantation" [5, p. 3].

Further all listed questions (or problems) are discussed in the article.

> 1. "**Tissue typing, selection of donor and recipient.** At present, - begins the presentation of this topic G.M. Solovyov, - in various laboratories of the world, 35 leukocyte antigens were isolated, united by the HL-A system (Human Leukocyte A system), 11 of them are included in the international classification, 14 are confirmed in several immunological laboratories around the world. The rest are undergoing interlaboratory identification. <...> Modern immunology makes it possible to determine the so-called. immunological passport of a person acting as a donor or recipient in an organ

[5] Currently, the synonym more often used is immunosuppression.

transplant. <...> [Besides this], typing of the donor and recipient greatly facilitates the implementation of immunosuppression after surgery and improves its results" [5, p. 4].

2. "**Controlled immunosuppression.** Among the immunosuppression means in the modern clinic, mainly 3 main groups of immunosuppressors are used. The first group includes the so-called. cytostatics <...> to the second includes glucocorticoids <...>, the third group includes biological immunosuppressors, immune antilymphocyte sera <...> And using different points of application of these immunosuppressor types, changing their dosage, immunosuppression can be varied depending on the specific immunological situation.

The modern clinic allows us to assert that today the combination of tissue typing with the selection of a recipient and a donor and controlled immunosuppression is already a real and vital way to overcome the barrier of incompatibility" [5, p. 5].

In this regard, the importance of methods for diagnosing the rejection crisis and the extent of participation of cellular and humoral immunity factors in it increases. <…>

Modern science has changed the idea that the rejection crisis is a purely immunological drama for the patient. This pathological process takes place in the microcirculation of the transplanted organ and is always accompanied by circulatory disorders. It was found [in the experiment] that with <...> the introduction of heparin, the number of antibody-forming cells in the lymph nodes decreases <...> These data allowed us to use heparin as an immunosuppressant in patients with a transplanted kidney when they develop infectious complications in cases where the use of imuran and prednisolone would be deadly for the patient" [5, p. 6].

3. "**Obtaining artificial tolerance in humans.** This problem has not yet been solved in clinic. However, it can be said that long-term (over a number of years) use of immunosuppressants and the presence of a foreign organ in the recipient's body qualitatively and quantitatively change the

immune response to the transplanted organ, and the resulting state can, with some reservations, be considered artificial tolerance " [5, p. 6].

Over time, this position was confirmed by many clinical observations and allowed, in a number of cases, after a certain number of years, to reduce the doses of immunosuppressants or completely abandon them. But in this context, we are interested in something else.

“It seems to us,” wrote G.M. Solovyov, "that numerous experimental works will be important for the clinic, in which researchers achieve immunological tolerance[6] with various types of antigenic loads on the recipient's body. One of the likely mechanisms may be the depletion of cellular and humoral immunity factors” [5, p. 6].

The names of the researchers are not named, but we know how V.P. Demikhov passed the similar way, transplanting large tissue arrays and trying to achieve a condition that he called "immunological paralysis."

4. “**Organ preservation and determination of organ viability**. <…> The works of M.V. Bilenko from the Laboratory of Organ and Tissue Transplantation of the USSR Academy of Medical Sciences (headed by V.V. Kovanov) showed the significance of ischemic consequences in an organ during its preservation. Currently, there are more and more works showing that the degree of viability of the transplant organ affects the outcome of the operation no less than the immunological conflict. <...> Among the methods of short-term preservation, many researchers (V.I. Shumakov, Belzer) prefer hypothermic perfusion of an organ <...> [at the same time] such process of organ preservation can be a test for assessing its viability. <...> the increase in the organ weight and decrease in the volume

of perfusion at a constant pressure of the perfusate <...> seems to be the simplest and with an increase in the weight of the kidney by 25%, consider it unsuitable for transplantation. <…> Today, the only method of long-term preservation is deep freezing of an organ at a temperature of –25 ° C and below with the use of cryophylactics <…> We are well aware that large-scale organ transplants after solving immunological problems will take place only if a long-term storage of typed and preserved organs is possible" [5, p. 7].

V.P. Demikhov worked and in this direction, as well. In 1947, he came up with a method to remove the cardiopulmonary complex with coronary and pulmonary circulation to preserve the viability of the heart before transplantation; and in 1963 he proposed to preserve the viability of organs by means of their normothermic perfusion using a special "physiological system", a body of a human with life-incompatible head injuries. A.V. Vishnevsky who had also the experience of a long support of human heart function, together with V.F. Tailor proposed for this purpose a special device. It turns out that no new ways of keeping the heart in a working state were offered by G.M. Solovyov who focused on the cryopreservation of cadaveric kidneys.

5. "**Surgical aspects of the organ transplantation problem**. Unfortunately, in the literature ... there is an opinion that the surgical problem is not so complicated and for the most part has already been solved, - G.M. Solovyov begins this section of the article, ending this sentence with the words: "To us, this opinion seems to be a delusion. The operation of organ transplantation is and remains a complex reconstructive intervention, including the connection of vessels of different calibers and a number of other complex

[6] As stated in the text of the article.

elements associated with the functional peculiarities of the transplanted organs. <...> The speed, accuracy and thoroughness of the surgical intervention will always matter in transplant surgery.

As an example, one can point to the possibility of using vascular stapling devices for heart transplantation and the use of rapidly polymerizable adhesive for sealing both vascular anastomoses and atrial sutures" [5, p. 7].

Recall that back in 1959, that is, 12 years before the article by G.M. Solovyov had been published, at the International Conference in Munich V.P. Demikhov demonstrated a vascular stapling device (VSD), which caused a sensation among Western surgeons, and the Western media dubbed it the "Soviet suture machine." Subsequently, V.P. Demikhov widely used VSD to achieve the "*speed of surgical intervention*" in the transplantation of the heart and other organs, thereby reducing the surgery duration and achieving the "*accuracy and thoroughness*" of anastomoses.

It follows that "the *possibility of using vascular stapling devices for heart transplantation*" in the USSR was proven long ago and put into practice, but in experimental practice. Words by G.M. Solovyov also testify that he did not have his own experience of using the VSD.

It is possible that for the first time in Russian literature G.M. Solovyov touched upon the following very important aspects of the organ transplantation problem.

6. "**Organizational moral and ethical problems of organ transplantation**. We are witnessing, - he wrote, - the creation of interstate associations in Western Europe and the USA, which identify and type patients in need of organ transplantation. The necessity of such associations arose because, on the one hand, to use any viable organ for transplantation with the best match for tissue antigens, it is necessary to have at least 150 recipients

prepared for the operation. On the other hand, a whole system is needed to identify possible donors from whom an organ can be taken in the event of death or the onset of brain death.

The creation of such organizations requires the joint work of specialists: surgeons, immunologists, perfusionists, anesthesiologists and resuscitators, equipped with transport, a communication system, electronic computers for the rapid selection of compatible donor-recipient pairs, and, finally, the equipment for the organ preservation and storage[7]. To overcome possible errors of a forensic order, the participation of forensic experts is mandatory in this work. <…>

A new branch of medicine - transplantation - requires certain changes in the consciousness of society, since the life-saving organ-replacing operation of one person is always accompanied by the death of another person. If this death is inevitable or has already occurred, the taking of organs for transplantation, in the name of the life of another person, should not be considered in the public mind as something unusual and traumatic for those around and close to the deceased. <…>

We hope that the improvement in the results of organ transplantation and progress in still unresolved scientific issues will contribute to the solution of moral and ethical problems" [5, p. 7].

In general terms, the organizational aspects of organ transplantation problem, which G.M. Solovyov wrote about, coincided with those mentioned in 1971 by A.A. Vishnevsky and co-authors. But the issues of morality and ethics were raised for the first time by G.M. Solovyov. True, they did not concern the transplantation of the heart, which since ancient times had been considered a bodily (pump), mental (emotions) and spiritual (connection with God) organ. But at that time it was not customary to deal

[7] Over time, it became clear that there was no point in preserving and storing the heart before transplantation. Obviously, these words were meant for kidney transplantation.

with the problems of the soul and spirit.

> "Organ transplantation," G.M. Solovyov wrote at the end of his article, is an extremely interesting, relevant and rapidly developing branch of medicine, which in most of its sections is still a scientific problem. However, there is no doubt that, with the successful development of the objectives it faces, it will soon become a public health issue. <…>
>
> We believe, – G.M. Solovyov assured, that the forecast of American scientists that the main problems of organ transplantation will be solved in the next decade (in 1982) is justified. The task of Soviet scientists is to make a worthy contribution to the development of this problem and to organize the implementation of the organ transplantation method in Soviet health care" [5, p. 8].

Unfortunately, these words did not turn out to be life-altering. Were the main problems of organ transplantation solved in the USSR by 1982? We believe they were not[8] .

Conclusion

Thus, the analysis of two publications devoted to the state of the organ transplantation problem in 1971-1973 and the forecast of its development in the near future, written by two pioneers of heart transplantation in the USSR - A.A. Vishnevsky and co-authors and G.M. Solovyov, showed that the authors of the articles saw and formulated the main trends of the problem development in a similar way. Meantime, G.M. Solovyov, being the Director of the specialized Institute of Organ and Tissue Transplantation of the USSR Academy of Medical Sciences saw the issues of organ transplantation more

[8] The first successful clinical heart transplant in the USSR was performed in 1987 by V.I. Shumakov.

in depth than A.A. Vishnevsky who headed the A.V. Vishnevsky Institute of Surgery of the USSR Academy of Medical Sciences.

In particular, this concerned immunological studies. Shortly after its establishment in 1969, the Institute of Organ and Tissue Transplantation of the USSR Academy of Medical Sciences arranged a powerful laboratory of immunogenetics on its base. The staff of that laboratory (L.V. Smirnova, Yu.M. Zaretskaya, L.P. Alekseev, V.I. Shkurko, A.M. Sochneva, I.V. Petrova, and others) conducted world-class immunological studies, which results inspired certain optimism among surgeons. A more complicated situation was with the clinical issues of organ transplantation and with the solution of organizational, moral and ethical issues, where, in addition to doctors, the active participation of legislators, economists, healthcare organizers, and also, in our opinion, philosophers, psychologists and theologians was required.

By the mid-2010s, the problems of organ transplantation in Russia remained practically the same as 40 years ago. At the same time, if the political, economic and organizational issues of organ transplantation turned out to be completely solvable (at least within Moscow and St. Petersburg), then philosophical, psychological and religious issues are still far from being resolved. To confirm this position, we present an excerpt from a scientific study by M.G. Minina, which was completed in 2016 with the defense of a doctoral Thesis in the specialty "Transplantology and artificial organs":

> “According to UNOS (United Network for Organ Sharing, USA), in 2013 there were **131,994** recipients on the uniform National Waiting List for transplantation of all organs, while the number of cadaveric donors over the same period of time did not exceed **7,578** donors ().

In 2013, more than **21,000** donor organs were transplanted in the United States, representing 16% of the national need for transplants. A similar situation is observed in European countries. The Eurotransplant international organization indicated in its 2012 report **2,046** deceased donors whose organs were used for transplantation to recipients, while 15,027 recipients were on the Eurotransplant uniform Waiting List, and only **7,358** donor organs were transplanted ().

According to the joint project of the National Transplant Organization of Spain (Organizatión National de Transplantes, ONT) and the World Health Organization (WHO), in 2013 less than 10% of the world's global need for donor organs was met (Matesanz R., 2009).

In the Russian Federation in 2013, **5339** patients were on the waiting list for heart, liver and kidney transplantation; the number of organ transplants performed over the same period was **1091** operations from **420** cadaveric donors (Gaultier S.V., 2014)" [6, p. 3].

We summarized the data in Table. 3.

Table 3. Status of organ transplantation in the USA, European countries, and Russia in 2013-2014

Country	Number of recipients on the waiting list	Number of transplanted organs	Number of cadaveric donors
USA	131 994	21 000	7 578
Countries of Europe	15 027	7 358	2046
Russia	5 339	1091	420

It is easy to calculate that in Russia in 2014, the number of patients on the waiting list was 2.8 times less than in Europe, and 25 times less than in

the United States. Accordingly, the number of transplanted organs was 7 times less than in Europe, and 19 times less than in the USA. The number of donors was 4.9 and 18 times less, respectively.

However, by 2021 the situation in the country had changed for the better compared to the situation 6 years ago (Table 4).

Table 4. Status of organ transplantation in Europe and Russia in 2021

Country	Number of recipients on the waiting list	Number of transplanted organs	Number of cadaveric donors
Countries of Europe[9]	13460 for all organs	6398	Not available
Russia	6313 for kidneys 2272 for liver 736 for heart	2318	652

According to S.V. Gauthier and S.M. Khomyakov, in the period from 2012 to 2021 in the Russian Federation, there was an increase in the number of recipients on the waiting lists for kidney transplantation by 2 times (up to 6313 people, or 10.5% of the number of patients receiving replacement therapy), by 4.7 times (up to 2272) for liver transplantation, and by 1.8 times (up to 736) for heart transplantation. In total, 2318 organ transplants were performed in Russia in 2021, or almost twice more than in 2014, which amounted to 15.9 operations per 1 million population, of which 271 organs were transplanted to children [7].

This trend allows us to look to the future with optimism and hope that the conclusion of S.V. Gauthier, the Chief Transplantologist of Russia, he

made at the II All-Russian Conference "Organ Donation − the Key Problem of Transplantology" in 2009: "*Transplantology as a type of high-tech medical care for the Russian population remains in one of the last places in terms of development rates* " [6, p. 3] may soon become history.

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Information about the author

Sergey P. Glyantsev, Prof., Dr. Sci. (Med.), Head of the Department of the History of Cardiovascular Surgery, A.N. Bakulev National Medical Research Center for Cardiovascular Surgery; Head of the Sector for the History of Medicine and Factography of the Department for the History of Medicine, N.A. Semashko National Research Institute of Public Health, https://orcid.org/0000-0003-2754-836X, spglyantsev@mail.ru

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