DOI:10.23873/2074-0506-2018-10-1-57-67

PHENOMENON OF DEMIKHOV.
"Experimental Transplantation of Vital Organs" 1960.
Myocardial revascularization, experimental physiology of blood circulation

S.P. Glyantsev

A.N. Bakoulev National Medical Research Center for Cardiovascular Surgery, 135 Roublyevskoe Highway, Moscow 121552 Russia

Correspondence to: Sergey P. Glyantsev, Professor, Dr. Med. Sci., Head of the Medical History Department of Cardiovascular Surgery, A.N. Bakoulev National Medical Research Center for Cardiovascular Surgery, e-mail: spglyantsev@mail.ru

Received: 6 March 2017

Accepted for publication: 19 January 2018

The article (the last of five) presents the analysis of the final (6th and 7th) chapters from V.P.Demikhov's monograph "Experimental Transplantation of Vital Organs" (Medgiz State Press for Medical Literature in Moscow, 1960), where he described the experimental development of the mammarocoronary bypass (anastomosis) surgical technique and the experiments to study the physiology of blood circulation.

Keywords: V.P.Demikhov, "Experimental Transplantation of Vital Organs", 6th and 7th chapters, myocardial revascularization, physiology of blood circulation in the experiment

Glyantsev S.P. Phenomenon of Demikhov. "Experimental Transplantation of Vital Organs" (1960). Myocardial revascularization, experimental physiology of blood circulation. *Transplantologiya. The Russian Journal of Transplantation.* 2018;10(1):57–67. (In Russian). DOI:10.23873/2074-0506-2018-10-1-57-67

ASD – atrial septal defect

PT – pulmonary trunk

CHD – coronary heart disease
CS – coronary sinus
IVC – inferior vena cava
ITA – internal thoracic artery
RA – right atrium
RPA – right pulmonary artery
SVC – superior vena cava

Myocardial revascularization

The surgical reconstruction of coronary vessels and the direct myocardial revascularization technique of the mammarocoronary bypass developed by V.P. Demikhov were discussed in our article published earlier [1]. Here we, guided by the corresponding 6th chapter of his book, will show what preceded that idea, and substantiate well-known and little-known priorities of Demikhov.

When studying available literature on chronic coronary failure ("angina pectoris"), V.P. Demikhov found out, first, that in those years it was believed to be the result of: a) atherosclerosis, b) syphilis, or c) functional disorders (G.F. Lang, 1936); and second, that by the early 1950s, there had been several concepts and techniques for surgical improvement of coronary circulation (the operation of so-called indirect myocardial revascularization).

Proponents of surgical operations on the sympathetic nervous system proceeded from the belief that the coronary circulation failure was caused by an impaired function of the intrinsic cardiac nervous system. Those operations started with cervical sympathectomy according T. Jonnesco in 1916 (the first such operation in the USSR was performed by E.R. Gesse in Leningrad in 1924) and were under development throughout the first half of the twentieth century. For example, shortly before V.P. Demikhov set out to study the problem, in spring of 1948, Yu.Yu. Dzhanelidze had developed a method for treating the angina pectoris with a Novocaine block of the cardio-aortic plexus. That was followed by the so-called pericardial, myo-, omento- and organopexies that started with pericardiocardiopexy according to C. Beck from Cleveland (Beck I operation) in 1935. To improve the intergrowth between the pericardium and the epicardium, the latter was scarified; and the talcum powder or irritating fluids (e.g. phenol) were injected into the pericardial cavity; also, various methods were combined with each other.

An original technique of creating pericardial adhesion aimed at the intergrowth of additional vessels into the myocardium was developed by Professor B.V. Ognev, one of V.P. Demikhov's opponents, in 1952. To improve coronary bloodflow, he proposed to induce adhesive pericarditis by making small holes in the pericardium puncturing it to the epicardium[1]. However, all those operations, in V.P. Demikhov's opinion, *contradicted the nature*:

> "Logically approaching this issue," he wrote, "one might think that if the ischemic focus of the myocardium would have promoted the growth of vessels from the surrounding tissues, then in natural conditions, the epicardium always closely contacts the pericardium, and there could always have been such a spontaneous vascular ingrowth and the elimination of ischemic focus, but this does not happen. On the contrary, sometimes lime is deposited in the adhesion of the epicardium with the pericardium and a "carapaceous heart" is formed [2, p. 192].

He was satisfied neither with the operations of the reduced venous coronary bloodflow according to G. Fauteux (1935) nor with the arterialization of the cardiac venous system according to S. Beck (1946-1951), which he tried to perform, of course, experimentally, but without success.

---

[1] It is curious that the technique was afterwards extended to the ischemic myocardium, tunneling it with special instruments (V.M. Ishenin) or laser beams (Yu.Yu. Bredikis, etc.).

As the most physiological of all the methods proposed by that time, he singled out the following two: the implantation of the peripheral stump of the internal thoracic artery (ITA) in the myocardium according to A. Vineberg (experimental development since 1946; clinical introduction since 1950); and the excision of the sclerosis-affected part of coronary artery followed by the defect cover with a graft according to G. Murrey (experimental studies since 1947, clinical implementation since October 1951).

However, V.P. Demikhov himself did not reproduce those operations, because even theoretically they were vulnerable to criticism. The operation according to A. Vineberg, in his opinion, was ineffective, as it did not give immediate results; and the operation of coronary grafting according to Murrey was unpromising, as being technically extremely complicated[2].

We emphasize that, in contrast to his predecessors, V.P. Demikhov had a completely different solution being just as simple and original as anatomically and physiologically justified[3]. He decided to use the ITA stump for myocardial revascularization, but to suture it directly into the coronary artery below the site of its occlusion rather than into the myocardium bulk, as proposed by A. Vineberg (Fig. 1).

---

[2] The author himself also considered it as such in 1953.

[3] The operation of aortocoronary bypass grafting was first developed and reported by A. Carrel in 1910, but V.P. Demikhov did not seem to know anything about this.

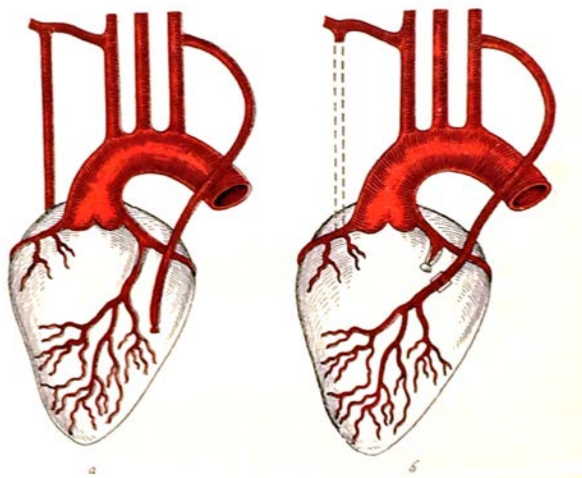

Fig.1. "Fig. 64. A. The scheme of Weinberg's surgery. The ITA end is sutured into the bulk of the myocardium bearing in mind the neovascularization with the newly formed vessels to be joined to the coronary vessels. B. The scheme of surgery up to V.P. Demikhov. The ITA end is sutured to the coronary artery below the site of its atherosclerotic narrowing" [Demikhov V.P. *Experimental Transplantation of Vital Organs*. Moscow: Medgiz Publ., 1960: the insert between pp. 192 and 193]

The anatomical prerequisites for the operation were the statements of some pathologists (N.N. Anichkov; A.I. Abrikosov, 1940; I.V. Davydovsky, 1956) about the atherosclerotic lesions predominantly occurring in the ostium of the anterior descending branch of the left coronary artery with its intact distal branches. The physiological basis for the intervention was the belief that

> "... restoring the patency of relatively large coronary arteries accessible for surgery can lead to an improved blood supply to yet unaffected myocardium " [2, p. 190].

The Payr's technique of vascular anastomosis was refined by Demikhov to the smallest detail. However, even for such a technically brilliantly trained surgeon as V.P. Demikhov, it took him 15 (!) months in order to master the technique of making vascular anastomosis for a record short time of 1.5 minutes, and, later on, for 55 seconds.

But the result surpassed all expectations. The dog operated on by Demikhov on August 1[4], 1953, survived for more than 7 years with the ligated anterior interventricular branch of the left coronary artery and a mammarocoronary anastomosis performed by the Payr's method. The next experimental dog survived for 2.5 years. And another one did also for over 2 years, and after that it was used for another experiment. In the two former cases, a functionally adequate anastomosis demonstrated complete anatomical patency, as displayed in the post-mortem coronary angiogram presented in Fig. 67 in V.P. Demikhov's book. (Fig. 2).

[4] The date "September 1" was stated by error on page 194 of V.P. Demikhov's book.

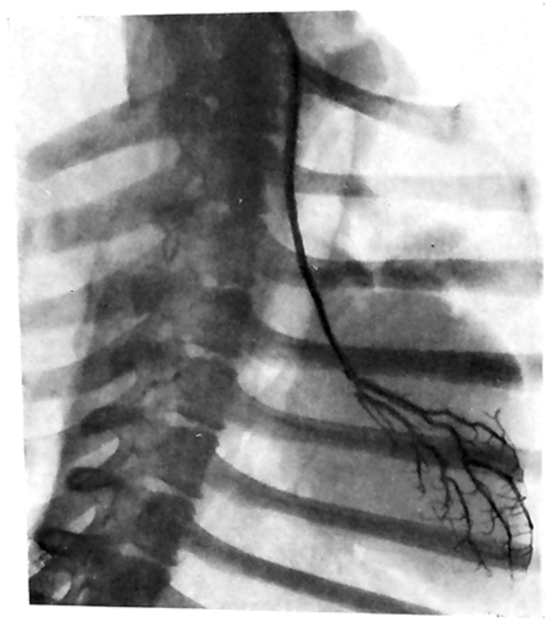

Fig. 2. "Fig. 67. The internal thoracic artery sewn into the coronary artery, the both are filled with the contrast agent" [Demikhov V.P. *Experimental Transplantation of Vital Organs*. Moscow: Medgiz Publ., 1960: the insert between pp. 196 and 197]

Given the fact that, according to V.P. Demikhov, that study was conducted 1.5 years after the operation on the dog named Large performed in September 1953, its date was February 1955. It is known, however, that the first intravital selective coronary angiogram was obtained by F.M. Sones from Cleveland (USA) only in October 1958 by accidentally inserting the tip of the catheter for cardiography in the ostium of the coronary artery, and the first in the USSR coronary angiogram in a human was obtained by L.S. Zingerman and Yu.S. Petrosyan in 1961 [3, p. 88]. Then, what technique did V.P. Demikhov use to perform coronaroangiography? Perhaps by inserting the ureteral catheter into the mammary artery during autopsy. Unfortunately, that was not mentioned in his book; non-mentioned was either the fact that no one previously reproduced this technique. So, it turns out that he was the first to develop that diagnostic technique though applied post-mortem.

Having reviewed Chapter 6, we come to a conclusion that V.P. Demikhov performed the operations of mammarocoronary anastomosis during the years of 1952-1956, making totally 15 such procedures. Meanwhile, 3 dogs survived for more than 2 years, and one did for over 3, and another one lived for more than 7 years. Kymography showed that the blood pressures in the ITA and coronary artery were similar; and by studying the volumetric blood flow, Demikhov proved a 5-fold (!) advantage of his methodology over A. Vineberg's operations. Again, it remains unclear as to what methods he used to measure blood pressure and volumetric blood flow in arteries with a diameter of 1.5 mm.

In summer 1955, together with P.I.Androsov, he began developing an operation on a human corpse and on an anthropoid ape, which, in our opinion, could be one of the reasons for his dismissal from the Institute of Surgery [4]. Had anyone placed such an anastomosis on a monkey before him? Carefully reading the chapter, we came across several more Demikhov's priorities. Operating in 1955 on human corpses, he saw internal thoracic and coronary arteries incommensurable in diameter and suggested to use an autovascular or nylon insert as extensions (adapters), and also an inverted "Y-shaped" shunt. He started the development of these prostheses together with N.B. Dobrova, a post-graduate student of V.V. Kovanov [2, p. 198]; and he made a mechanical seam of coronary arteries using V.F. Gudov's device in 1955 together with P.I. Androsov.

Did V.P. Demikhov see the prospects of using his developments in clinic? We believe he did! After all, at that time, atherosclerosis and coronary artery thrombosis had already been considered as directly associated with myocardial infarction (A.L. Myasnikov, 1954), so V.P. Demikhov was well aware that his operation could serve to prevent this fatal disease:

> "Based on the data of our experiments, we believe that direct anastomosing *a supplementary artery* (our italics – S.G.) with a coronary artery below the affected site can presently be an effective surgical method for improving coronary circulation in the atherosclerosis ... <...> [the latter] being one of the causes of myocardial infarction.
>
> On the principle side, the feasibility of plastic surgery on coronary vessels can be considered as proved. To carry out such an operation on human coronary vessels, a careful preliminary training and exercising in this technique in operations on animals is required" [2, p. 190, 198, 199].

Pay attention to the phrase "*a supplementary artery*". In our opinion, this means *any artery* that could be used for systemic-coronary bypass. As for the selection of patients for the mammarocoronary anastomosis operation, V.P. Demikhov laid out his principles in 1957, when together with A.E. Plutenko and G.I. Tsurenko developed a method of intravital diagnosis of coronary atherosclerosis.

What was done in the world at that time to address a similar issue? That's the point, that American and European surgeons in those years lagged far behind our hero as in understanding the need for ensuring a direct blood supply to the myocardium, and, even more so, in the technique of implementing this concept.

When there had been two dogs with Demikhov's mammarocoronary anastomoses running for a year in the yard of N.V. Sklifosovsky Institute in the USSR, an American scientist C. Beck developed the operation of *pericardiocardiopexy* using pericardial fat and a partial ligation of the coronary sinus (Beck II operation); and in Italy, the *ITA ligation* surgery developed by D. Fieschi as early as in 1939 was put into practice. The same placebo operation was performed in the United States in 1955, in Leningrad (by V.I. Kolesov in the 1st LMI named after I.P. Pavlov), and in Moscow (by A.N. Bakulev, Kh.N. Muratova in the Institute of Thoracic Surgery of the Academy of Medical Sciences of the USSR) in 1958. In 1954–1958, B.V.Ognev conducted a series of experiments to stimulate the formation of intercoronary anastomoses by ligation of the coronary arteries. And only in 1960, R. Goetz in the USA, having previously developed a similar operation on dogs, performed the first mammarocoronary anastomosis in clinic using the same technique as V.P. Demikhov, connecting the ITA and the coronary artery with a cannulae by E. Payr's technique. And in 1964, V.I. Kolesov from Leningrad was the first in the world who successfully performed such anastomosis by means of 4 interrupted sutures.

Did V.P. Demikhov's developments play a role in making those operations? Most likely, as shown by L.A. Bokeria and co-authors [3] in 2002, R.Goetz did not know anything about that. Surgery was just "pregnant" with this topic, and the birth was inevitable. However, according to our data, V.I. Kolesov was both well familiarized with the technique of creating an anastomosis according to V.P. Demikhov, and also used it at first, but later refused it as a dangerous one because of the development of pressure sores on the tube and fatal bleeding. One can read about the vicissitudes of mammarocoronary anastomosis implementation in clinical practice in the special literature [3, p. 104-108, 5]: about how V.I. Kolesov was not given the floor for presentations, and about how his works were not published, and about the fact that only in the mid-1970s that operation took its place among other ways of systemic-coronary bypass grafting. That was, almost 20 years after it had been *completely* developed by V.P. Demikhov.

Let's enumerate his priorities in the field of myocardial revascularization in coronary heart disease (CHD):

1. Development of the technique for *systemic-coronary* anastomosis on a *beating* heart.

2. Development of the *concept* and *technique of the mammarocoronary anastomosis* operation by using ITA.

3. Proving the feasibility of making this operation on humans.

4. The invention of autologous vascular and synthetic inserts (supplements).

5. The invention of the inverted Y-shaped extension to the ITA stump (a sequential shunt).

6. Using a special device for creating a vascular anastomosis.

By the way, V.I. Kolesov had never made references to his predecessor and his method anywhere. However, that did not prevent us in our report at the Conference dedicated to the 100th anniversary of the birth of V.I. Kolesov held in St. Petersburg in September 2004 from proposing that the mammarocoronary anastomosis operation on a beating heart should be termed Demikhov-Kolesov operation:

> "This is our duty to the deceased great scientist and our national duty. National one because all peoples strive to commemorate the inventions and works of their scientists, being proud of them. This feeling has not been developed by the Russians so far",

said D.D. Pletnev on the perpetuation of memory of S.P. Botkin in one of his eponyms. These words can rightfully be conferred to V.P. Demikhov [6].

Experimental physiology of blood circulation

But let's not forget that, by education and his main specialty V.P. Demikhov was neither physician nor surgeon, but a biologist and physiologist; and his experiments, along with the development of organ transplantation techniques (models) and the search for conditions for transplant engraftment pursued another goal: to study normal and experimentally changed circulation patterns. After all, in his experiments, he deliberately brought the cardiovascular system of an experimental animal to an extreme state (for example, removed the heart), and then, using his methods, tried to restore a disturbed balance (connected a mechanical heart, transplanted an allogenous heart, or connected a heartless body to another one in which the heart functioned). It is not unexpectedly that the last, 7th chapter, of his book was devoted to "some questions of the circulation physiology in relation with organ transplants."

The mechanism of blood circulating in the human body had occupied the minds of scientists since long ago. So, since the time of Galen (II century) for 15 centuries, it was believed that the expansion and contraction of the heart chambers, ensuring the suction of blood (from the caval veins by right auricle) and air (from the pulmonary veins by the left auricle), and pumping the blood (into the lungs by the right ventricle) and the air (into aorta by the left ventricle), occur due to rhythmic expansions and contractions of the thorax during breathing.

Having described the circular blood movement, or blood circulation, in 1628, W. Harvey established that both those functions were provided by relaxations and contractions of the heart that drives blood through the lungs from the right to left cardiac chambers (the pulmonary circulation) and from the left to right chambers through the whole body (the systemic circulation). This had been a general belief until the beginning of the twentieth century, when Professor M.V. Yanovsky from St. Petersburg, a former student of S.P. Botkin came up with the concept of the so-called peripheral heart.

V.I. Borodulin, the historian of cardiology, wrote in 2011, "This concept originated from S.P.Botkin's statements on the similar nature of innervations between the vessels and the heart, and on the disharmonic functional behavior of various cardiovascular system departments as possible causes of compensatory disorders in heart diseases. The concept was clinically based on a great number of observations, <...> which ran beyond the traditional concepts implying that solely the heart provides the blood movement, and the vessels only distribute the blood. Panofsky's theory of the peripheral heart stating that the *peristaltic contractions of small arteries* (italics by SAG.) constitute the most important factor of blood circulation in normal heart and in heart pathology, provoked heated debates and was the subject of discussion at the VIII-X Congresses of internists of the USSR (1925-1928). Later his theory was temporarily consigned to oblivion, but since the mid-20th century, there was a renewed interest in this problem among physiologists and cardiologists" [7]. However, the interest was mainly critical, since among some clinicians, especially M.V. Yanovsky's followers, the theory was still prevalent.

The examples of the critical interest in this doctrine included the V.P. Demikhov's experiments which gave the results that clearly contradicted to the ideas postulated by M.V. Yanovsky in 1901-1927. P. Demikhov reported all that at the Session of the USSR Academy of Medical Sciences in Ryazan in 1951, at the Meeting of the Physiology Department of Moscow State University named after M.V. Lomonosov in 1952, and at the Academic Council Meeting of the Internal Medicine Institute of the USSR Academy of Medical Sciences on January 15, 1953, the Institute being headed at that time by A.L. Myasnikov, the Academician of the USSR Academy of Medical Sciences, a leading Soviet internist and cardiologist. V.P.

Demikhov presented the evidence of no "peripheral heart" phenomenon basing on the following experiments, facts, and observations:

First, the results of kymographic recording of blood pressure in peripheral veins clearly showed that the pulse waves are transmitted to the venous walls *from large arteries* through capillaries, rather than *from small arteries* or capillaries. When the pulmonary artery was clamped, the pulmonary vein wall oscillations ceased and resumed only after the clamp was removed. In other words, there was no reason to speak of any self-contained peristaltic contractions of the walls of small arteries and capillaries, as well as of transferring these contractions to veins.

Second, the "peripheral heart" theory saying that the force of even one heart contractions is not sufficient to push blood through the vascular system, especially at the capillary level, contradicted to the results of V.P. Demikhov's experiments with "cross circulation", when one heart ensured blood circulation in two bodies simultaneously.

Third, V.P. Demikhov gave several convincing theoretical arguments on no possible acceptance of the "peripheral heart" theory; and his arguments could be compared with proving the blood circular movement by W.Harvey who was known to have substantiated some of his opinions also just theoretically, using mathematics. In Demikhov's reasoning, presented in his book on pages 202-206, we can see not only a connoisseur of literature and a thinker, but also an excellent polemicist, able to see the logical contradictions in the evidence of another person and provide reasoned arguments.

The next issue studied by V.P. Demikhov in his experiments simultaneously with the issue of the "arterial peripheral heart" and organ transplantations was related to blood circulation in capillaries where the peripheral heart, but the capillary one, had also been discovered by that time.

The mechanism of its functioning was explained in different ways: by capillary peristalsis, oncotic reasons, the contractility of pericytes. However, V.P. Demikhov again, from a purely theoretical standpoint, left no stone unturned from this theory either, being a convinced cardio-centrist.

He also tried to clarify the mechanism of blood flow in the veins. At that time, there were several points of view on the issue. Some scientists believed that the venous blood flow is driven by the so-called suction force of the heart diastole. For example, Academician K.M. Bykov, a prominent Soviet physiologist (1954) argued that the pressure in the veins of the thoracic cavity was lower than the atmospheric pressure. Other authors stated that the suctioning force is driven by the lung respiratory movements (that was known since the time of Galen), as well as by the diaphragm and even the skeletal musculature. The third main role was assigned to the "venous peripheral heart".

Most of these mainly speculative theories were based on an extremely weak experimental base and subjective theoretical calculations. V.P. Demikhov was armed with a huge experimental experience, numerous organ transplant models, and power of observation. While measuring the pressure in the carotid artery during thoracotomy and within long-term heart transplant operations, he did not detect its changes, concluding that the suction force of the chest and diaphragm does not play any role in the circulation at all.

He also was original in solving the issue of the diastolic suction of the heart:

" Our first experiment on the heart replacement with a mechanical device showed that when there was insufficient blood flow to the atria, an attempt of blood suction by the device resulted in the collapse of elastic walls of the hollow veins and to the termination of the suction action." [2, p. 213].

Moreover, to elucidate the mechanism of venous blood flow, V.P. Demikhov conducted specific experiments, which showed that neither thorax movements, nor diastole, or negative pressure in the hollow veins play any role in the movement of blood along the peripheral veins, which depends on the left ventricle contractility only. In other words, the blood comes in the right heart only under the pressure of arterial blood rather than from a suction or anything else.

How much all that was important for heart surgery was shown by the development of the cava-pulmonary anastomosis operation, the essence of which is to turn off the right heart from the circulation when the a natural outflow of blood from it is difficulty (in isolated stenosis and pulmonary artery atresia, pulmonary artery stenosis in Fallot's tetralogy, etc.). Initially, the pioneers of that method (C. Carlon, W. Glenn, F. Robicsek et al.) doubted that in case of passing the bloodflow from the superior vena cava directly into the pulmonary artery bypassing the right ventricle, the left heart would be able to provide a complete blood circulation both in the body and in the lungs [8, 9]. However, the experience showed that there was nothing to be worried about. Later on, right- and left-sided, bilateral (full, total) and bidirectional caval-pulmonary anastomosis operations were developed (Fig. 3), as well as the techniques of hemodynamic correction of heart defects in the modified bypass of the right heart, when the left ventricle alone being the systemic one [10]. However, neither in the USSR, nor in other countries V.P. Demikhov' experiments were considered the grounds for the development of those techniques, and had only a physiological significance. In any case, nothing is known about mentioning his name in relation to proving the ability of the left ventricle to assume the function of a systemic one.

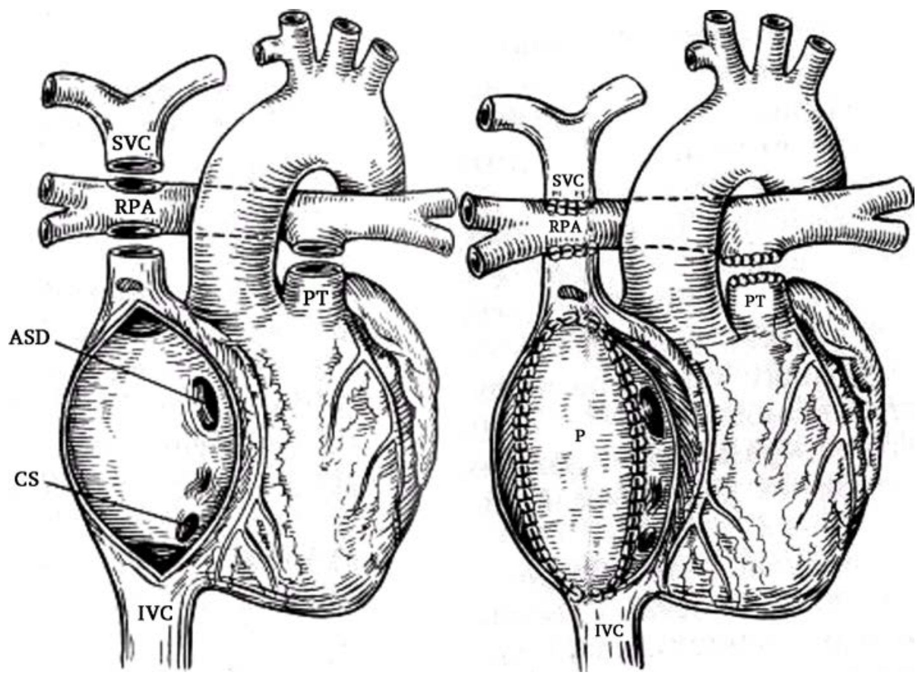

Fig. 3 a, b. The scheme of the surgery for a complete cava-pulmonary anastomosis with the normal location of the main vessels: A. The right atrium (RA) has been opened and the superior vena cava (SVC) transected. Two longitudinal incisions have opened the right pulmonary artery (RPA), the pulmonary trunk (PT) has been crossed; B. The proximal and distal ends of the intersected PT are closed. The proximal and distal ends of the SVC are sewn into the RPA incisions. The tunnel made of xenopericardium patch (P) leads from the inferior vena cava (IVC) to SVC; the opening of the coronary sinus and the foramen ovale remain outside of the patch. [Podzolkov V.P., Chiaureli M.R. *Hemodynamic correction of congenital heart defects.* Moscow: Medicine Publ., 1994] (the signature is in accordance with the original)

Nevertheless, V.P. Demikhov confirmed with his experiments that:

> "... the main force driving the blood in the body is the heart. It creates the movement of blood along *arteries, capillaries and veins* (italics by S.G.).
>
> [Moreover,] the force of heart ventricle contractions is sufficient for not only driving the blood along the circulatory system of one body, but also for the blood movement in two bodies" [2, p. 218].

But, if the first, cardiocentric conclusion had been known, in principle, since the days of W. Harvey, and V.P. Demikhov only confirmed it, the second was the original one. And although, the cross circulation technique for cardiac surgery developed in the US in 1950-1954 was applied by W. Lillehei earlier than by V.P. Demikhov, he, in contrast to V.P. Demikhov, did not risk providing blood circulation in two organisms by using a single heart and included a finger pump in the "donor-recipient" system as an additional blood drive (Fig. 4). In Demikhov's scheme, there was no such pump.

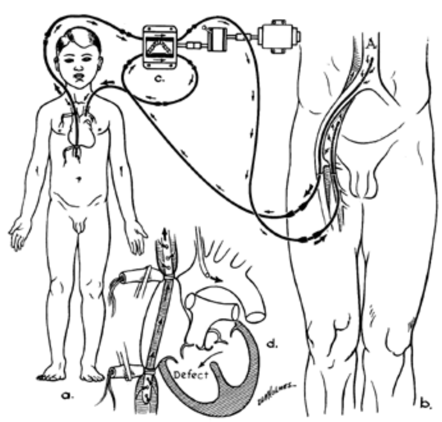

Fig. 4. The scheme of controlled cross-circulation between the child (A) and the man (B), where the child's heart (D) with a congenital defect has been stopped, and the blood movement in his body is provided by the men's heart and the finger pump (C). [Lillehei C.W., et al. The results of direct vision closure of ventricular septal defects in eight patients by means of controlled cross circulation. *Surgery, Gynecology & Obstetrics*. 1955;101:446–466]

At the end of the last, "physiological" chapter of his book, V.P. Demikhov again, as an experimenter and a specialist in the physiology of blood circulation, completely rejected all the arguments about the presence of blood depot in the spleen, lungs, liver, uterus and other organs and tissues, which was much written about in those years, especially abroad (in particular, by J. Barcroft, the creator of the blood oxygenation doctrine); and he also proposed to revise "the so-called E.Starling's heart law"[5], however, without going into the details of the topic, but referring a reader to his article with the similar title published in the *Bulletin of Experimental Biology and Medicine* 1950, No. 5.

Thus, the results obtained by V.P. Demikhov coupled with a critical analysis of available literature, which he laid out on 224 pages of his book "Experimental Transplantation of Vital Organs" convincingly showed that:

> "... from a physiological and surgical point of view, the problem of organ transplantation is real, but further complex studies are necessary for its final solution" [2, p. 225].

And Demikhov, in his opinion, proved with his experiments. that:

> "Homoplastic transplanted heart, lungs, and other organs retain their function for some time in another body and at the same time can maintain the life of the recipient while removing his/her own organs.

[5] The study of the dependence of the cardiac contraction force in the systole on the expansion degree of its chambers in the diastole showed that the strength of each cardiac contraction depended on the volume of the venous influx and was determined by the final diastolic length of the myocardial fibers. That dependence was called "heterometric regulation of the heart" and is known as E.H.Starling law: "The force of the cardiac ventricle contraction, measured in any way, is a function of the length of the myocardial fibers before contraction" (1918), i.e. the cardiac output is increased with the increases in cardiac chamber filling. (http://fundamed.ru/nphys/145-zakon-franka-starlinga-bolshe-rastyazhenie-serdechnoj-myshtsy-bolshe-sila-sokrashcheniya.html). Over time, it turned out that this law is valid only for normal myocardium.

> In the absence of infection and other complications, the acceptance of a homoplastic organ transplant occurs within 1-2 weeks. The death of these organs in the absence of thrombosis at the sites of vascular sutures often came from inflammatory complications. Such inflammation of the graft (in the absence of infection) can be explained as resulted from the combination of trauma during surgery, denervation with a vasodilating effect and, apparently, *inadequate compatibility of donor and recipient tissues* (italics by S.G.), which needs further study" [2, p. 225].

And here is the so-called author's unacceptance of the tissue biological incompatibility between the donor and recipient allegedly incriminated to him! Of course, from the point of modern transplantation, the "acceptance" of homoplastic organs without immunosuppression within 1-2 weeks is nonsense. But the fact that "the graft inflammation (in absent infection)" can be explained by "inadequate compatibility of donor and recipient tissues", as well as the fact that this question "needs further study" can not be regarded as wrong.

Therefore, the following V.P. Demikhov's proposal is perceived as completely reasonable:

> "Proceeding from the fact that the ultimate goal of resolving the problem of organ transplantation is to achieve the possibility of transplanting organs in humans, further research on organ transplantation should apparently be carried out in a human in permissible cases with studying the *inherent specific immunological responses* (italics by S.G.)" [2, p. 226].

To overcome a possible incompatibility reaction in clinical experiments, V.P. Demikhov proposed to select donors with respect to blood groups, and for the time of the transplanted organ engraftment, also to create a cross blood circulation between the donor and the recipient.

Thus, the requirements for successful organ transplantation in a human formulated by V.P. Demikhov in 1960, were reduced to three main ones:

1) Appropriate immunological match between the donor and recipient (with respect of blood groups and *additional factors*);

2) Creation of cross circulation between the donor and the recipient *until the graft acceptance* (earlier the cross circulation was proposed to be set up *before the operation*; but in 1960, it was a question of the whole period of engraftment until acceptance; compare that with modern immunosuppression!);

3) Sufficient methodological substantiation of the operation (from physiological and surgical points of view).

If we compare the above requirements with those formulated by V.P. Demikhov a year earlier [11], it is clearly seen that they were the same, only the technical requirement moved from the second to the third place, and two purely immunological requirements took the priority. V.P. Demikhov considered the *selection of donors* to be another important task that had to be overcome on the way of implementing the method into practice; and he suggested using the corpses whose organs could be revived. If the revived organs could not be transplanted at once, it was necessary to maintain their vital functions for some time, in other words, "to create a necessary reserved pool for the selection of donor organs and tissues". In other words, it was a question of creating a *bank of organs for transplants* .

Our first systematic review of V.P. Demikhov's book *"Experimental Transplantation of Vital Organs"* (Medgiz Publ., 1960) showed that (in a broad sense) *for 1960* it had been a complete and perfect methodological manual for finding approaches to homoplastic human organ *transplants in clinic*. Its only "drawback" (from today's point of view) was the author's purely biological approaches to overcoming an allo-tissue and organ incompatibility, the approaches arising, on the one hand, from his original Michurin-Pavlovian worldview and the tasks of contemporary biology of that time posed and solved in the book, and on the other hand, due to no recognized at that time evidence that would have demonstrated the possibilities of acquiring immunological tolerance, or pharmacological means for its realization. However, the review of his book showed that V.P. Demikhov had closely approached the solution of these natural-scientific problems.

In addition, the book (in the narrow sense) can be considered as a guide for experimental transplantation of isolated organs and their complexes, for experimental physiological, extracorporeal and assisted blood circulation, as well as for thoracic, cardiac, coronary, and vascular surgery, cardiac anesthesiology, and cardiac life support.

Instead of a conclusion, let us list V.P. Demikhov's achievements described in the book, by formulating them in the form of hypothetical names of *experimental dissertational studies*, characterized by a high relevance, problem-oriented nature, methodological originality, unquestionable scientific novelty, and great practical significance, indicating the volume of the material studied (if such was known). These *are the* topics *we propose*:

1. Mechanical suture of the main vessels (500 observations).
2. Cardiopulmonary complex: the preparation technique, homoplastic transplantation and prospects of using (300 observations).
3. Pharmacologically (potassium) induced cardioplegia in cardiac surgery.
4. Cardiac fibrillation in heart surgery and ways to cope with it.

5. Ways to reduce mortality at surgery on thoracic organs (250 cases).

6. Revitalization of an isolated cadaveric human heart for its subsequent homoplastic transplantation (15 cases).

7. Intravenous anesthesia in warm-blooded animals in the experiment (more than 300 observations).

8. Artificial respiration in warm-blooded animals in the experiment (more than 300 cases).

9. Transplantation of the second, additional, heart with a pumping function in the experiment (250 cases).

10. Temporary and permanent bypass of the left heart as a method of treatment for heart failure (more than 200 cases).

11. Implantable mechanical heart for the replacement and auxiliary treatment of heart failure (an experimental study).

12. Irreversible cardiopulmonary failure and the transplantation of a cardio-pulmonary complex in dogs (67 cases).

13. Orthotopic transplantation of a beating heart in dogs (22 experiments).

14. Lung transplantation in dogs (about 8-10 experiments).

15. Kidney transplantation in dogs (30 experiments).

16. Head transplantation in warm-blooded animals in the experiment as a model for studying the effect of recipient's central nervous system on donor's higher nervous activity (20 experiments).

17. Transplantation of half of the trunk in warm-blooded animals to study the feasibility to transplant a complex of organs and tissues with preserved morphological, neurohumoral, and lymphatic links (concept, technique, results).

18. A whole-body transplantation (implantation) of the warm-blooded animal to another body without vital organs to maintain its vital activity (concept, technique, results).

19. Parabiosis as a way to overcome immunological incompatibility in organ transplantation (concept, technique, results).

20. Immunological (serological and cellular) responses at organ transplantation, their detection and correction.

21. Selection of donors and patient match selection for organ transplantation by considering blood groups and additional immunological signs.

22. The use of artificial (assisted) blood circulation in heart failure.

23. The use of artificial (extracorporeal, cross) blood circulation in operations on heart.

24. The use of artificial (extracorporeal) blood circulation for organ storage and transplantation (to create a bank of organs).

25. Mammarocoronary anastomosis on a beating heart as a method of surgical treatment for coronary heart disease (15 cases with a maximum survival of 7 years).

26. Treatment of coronary failure by making mammarocoronary anastomoses[6] (including the use of ITA, autologous vessels, and nylon prostheses, as well as V.F. Gudov's vascular anastomosis device).

27. Selection of patients for the mammarocoronary anastomosis surgery.

28. Coronaroangiography as a method for evaluating the efficacy of the direct myocardial revascularization (an experimental study).

---

[6] In 1971, a Doctoral Thesis under such title was defended by E.V. Kolesov, the son of V.I. Kolesov.

29. Transplantation of vital organs as a model for studying the normal physiology of blood circulation (arterial "peripheral heart", blood circulation in capillaries and veins, etc.).

30. Transplantation of vital organs in warm-blooded animals as a model for studying the pathological physiology of the extracorporeal and assisted blood circulation (more than 300 cases).

Total 30 major topics, each of them could have been the subject to write and defend a Candidate or Doctoral Thesis in 1960s; and every of them could have become a new trend in cardiac and vascular surgery in those years[7]. So, not far from the truth were those V.P.Demikhov's contemporaries who believed that, indeed, several dissertations were "hidden" under the cover of his book[8]. We have counted about three dozens.

Thus, the approaches to heart transplantation in humans had been developed, the ways to overcome the biological incompatibility outlined. It remained to overcome the last frontier: to start heart transplants in clinic. And it was for that purpose, in our opinion, V.P. Demikhov came to work in N.V. Sklifosovsky Institute for Emergency Medicine in 1960.

But this will be covered in our next articles.

Conflict of interests. Authors declare no conflict of interest.

Financing. The study was performed without external funding.

---

[7] The first specialized Institute of Cardiovascular Surgery in this country was opened in 1961.

[8] According to L.A. Buzinova (Tushmalova), the employee of the Operative Surgery and Topographic Anatomy Department of the 1st MOLMI named after I.M. Sechenov that circumstance prevented V.P. Demikhov's book contents from being the topic for defending a single dissertation only.

References

1. Glyantsev S.P. Phenomenon of Demikhov. In the Vishnevsky Institute of Surgery (1947–1955): Development mammaro coronary anastomosis (1952–1953). Organ transplantation in the light of the Michurin theory (1953). *Transplantologiya. The Russian Journal of Transplantation.* 2015;2:39–48. (In Russian).

2. Demikhov V.P. *Experimental Transplantation of Vital Organs*. Moscow: Medgiz Publ., 1960. 259 p. (In Russian).

3. Bokeriya L.A., Rabotnikov V.S., Glyantsev S.P., Alshibaya M.D. *Essays on the history of coronary surgery*. Moscow: Scientific Center for Cardiovascular Surgery n.a. A.N. Bakulev RAMS Publ., 2002. 244 p. (In Russian).

4. Glyantsev S.P. Phenomenon of Demikhov. In the Vishnevsky Institute of Surgery (1947–1955): Two-headed dogs from V.P. Demikhov (1954-1955). XXVI All-Union Congress of Surgeons (1955). *Transplantologiya. The Russian Journal of Transplantation*. 2015;3:89–100. (In Russian).

5. Bokeriya L.A., Glyantsev S.P. Professor Vasily Ivanovich Kolesov: parade of priorities (To the 50 anniversary of the world’s first operation of mammary-coronary artery anastomosis and the 110 anniversary of the 53 birth of its author – V.I. Kolesov). *Annaly khirurgii*. 2014;3:53–62. (In Russian).

6. Pletnev D.D. *Selected*. Moscow: Medicine Publ., 1989. 220 p. (In Russian).

7. Borodulin V.I. *History of Medicine of Russia. Clinic of internal diseases in the 2nd half of the XIX – 1st half of the twentieth century*. Moscow: Medpress-inform Publ., 2011. 55 p. (In Russian).

8. Schumacker H. *The Evolution of Cardiac Surgery*. Indianapolis: Indiana Press, 1992. 78–85.

9. Bokeriya L.A., Podzolkov V.P., Glyantsev S.P., Kokshenev I.V. Operation of cavapulmonary anastomosis. Part 1. From idea to its embodiment. *Children's heart and vascular diseases*. 2005;4:5–12. (In Russian).

10. Bokeriya L.A., Podzolkov V.P., Glyantsev S.P., Kokshenev I.V. Operation of cavapulmonary anastomosis. Part 2. From the embodiment of the idea to its improvement. *Children's heart and vascular diseases*. 2005;5:7–13. (In Russian).

11. Demikhov V.P. *Organ transplantation: is it possible?* Moscow: Znanie Publ., 1959. 32 p. (In Russian).