The Father of Heart Transplantation Vladimir P. Demikhov

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Abstract. The article discusses the life's work of the great Soviet scientist in the fields of transplantology, physiology and experimental surgery Vladimir Demikhov. He was the first ever to perform a heart and a cardiopulmonary system transplantation, as well as other vital organ transplantations. He was also the first to perform head transplantation on a dog. Demikhov should have become a legend of Soviet medicine, however, he did not receive the support from the government and, in particular, from the ministers of health and was undeservingly forgotten. The following article is an attempt to pay tribute to the memory of this great man, whose mind and thinking were ahead of his time by decades or maybe centuries.

Key words: Vladimir Demikhov, heart transplantation, Christiaan Barnard, forgotten personalities.

Introduction

Vladimir Demikhov: "The ultimate goal of our experiments is to make the transplantation of heart and other human organs possible".

First half of the 20th century. Is the transplantation of organs from one organism to another possible? If it was possible for a surgeon to transplant a healthy organ in place of a sick or lost one, it would open up so many new possibilities to save human lives! These were the type of radically new and groundbreaking (for its time) ideas that the great Soviet physiologist, surgeon and researcher Vladimir P. Demikhov generated and pondered throughout his entire life.

Even as a boy from a simple peasant family, born in Kuliki village in 1916, far away from the capital of the Russian Empire, he became obsessed with studying everything about the structure and functioning of animal and human organisms. His place of birth, surroundings, and trials of the Civil War were supposed to negatively affect the child but that did not happen. His mother and grandfather did everything in their power to provide a peaceful and happy childhood for the future genius, whose ideas were ahead of his time by decades (1).

Having been born in the free Cossack steppes, he incorporated the best qualities those places had to offer: independent thinking, fervour to serve without falling into servitude, confidence in oneself and one's own abilities, a habit of relying on one's own knowledge and experience, all of which were to become the defining qualities of his character. From his earliest childhood years, Vladimir was surrounded by all kinds of living creatures: a cat and a dog at home, chickens and a goat in the yard, all of which were fascinating to him. When playing, he would cure animals, and when he became a little older, Demikhov became seriously interested in the way dogs' hearts worked and how blood circulated their bodies. Neither his mother, nor his teachers at the local school were able to answer the questions that interested young Volodya. The veil over the unknown was lifted completely and unexpectedly when one day in July the boy saw a broken car by the curb. He approached the driver who was changing tyres and who told him that animals much like cars have spare parts which can be changed; for instance,

lizards can grow new tails. The driver also informed him that it was actually the heart that made the blood circulate. These thoughts made the young Vladimir Demikhov restless. As a result, he decided to cut open the chest of a dog to see how its heart worked with his own two eyes. His mother stopped him from proceeding but his interest in the way organisms work did not cease (2, 3).

In 1931 Vladimir graduated school after the mandatory 7 years schooling in the Soviet Union. Right after receiving the lower secondary education diploma, financial hardship in the family pushed Demikhov to get a job as a locksmith and a repairman at the Stalingrad Tractor Factory, where he worked until 1933. However, his intelligence and wit helped him to enroll and study while working at the Factory Plant College (FPC). It was there when V. Demikhov started to develop his transplantology ideas, having designed and produced the first workpiece of a metal heart. In June of 1933 while simultaneously working and studying, he finished his secondary education in one the schools in Lipetsk. Afterwards, he took a Komsomol voucher to enroll into the Animal Physiology Department of Voronezh State University (VSU), where, as he hoped, he would be initiated into the mysteries of the "Heart of a Dog". From the first months of his studies in Voronezh, Vladimir proved himself as an apt student up to the point that in years to come teachers would try to help him to implement some of his ideas (2).

Birth of Ideas and First Attempts at their Implementation

One of the most significant ideas in the life of Demikhov was the creation of a "mechanical heart". In order to make this idea become a reality, in 1937 he designed and created a heart-sized compact device, which consisted of two adjacent membrane pumps that functioned as two heart ventricles (4, 5). This construction was based on an improved version of the first apparatus for artificial blood circulatory assist – autojector SB-2 (Fig. 1), created in 1936 by Professor S. Brukhonenko. This device was located at the Animal Physiology Department of VSU and was used to study the central nervous system of warm-blooded animals.

The problem with the autojector was its size: it considerably exceeded the size of a dog's heart, as it was an extracorporeal device (6). In order to create an implanted version, Vladimir used his skills as a locksmith, which he acquired during his studies at the FPC. The device was designed to be placed in the thoracic cage of a dog in place of its own removed one. The shaft of the device came out the thoracic cage in order for it to be set in motion by electric motor (Fig. 2). The thoracic cage was then sewn up shut. It is known that V. Demikhov conducted 3 experiments, the results of which were extraordinary. On average, 5 minutes after the "mechanical heart" was turned on and set in motion by the electric motor, a dog would show definite signs of life (ocular, respiratory and other reflexes), including the most sensitive reflexes (5, 7).

Demikhov realized that the scientific potential of VSU did not coincide with his ambitious plans. Thus, after having consulted several professors of the Animal Physiology Department, he filed to be transferred to Moscow University (2). On September 1st of 1938 Vladimir became a fifth-year student at the Biology Department of the Moscow State University (MSU). Soon after, when his studies there began, he was immediately invited to work at the Institute of Experi-

Figure 1. S. Brukhonenko with autojector SB-2

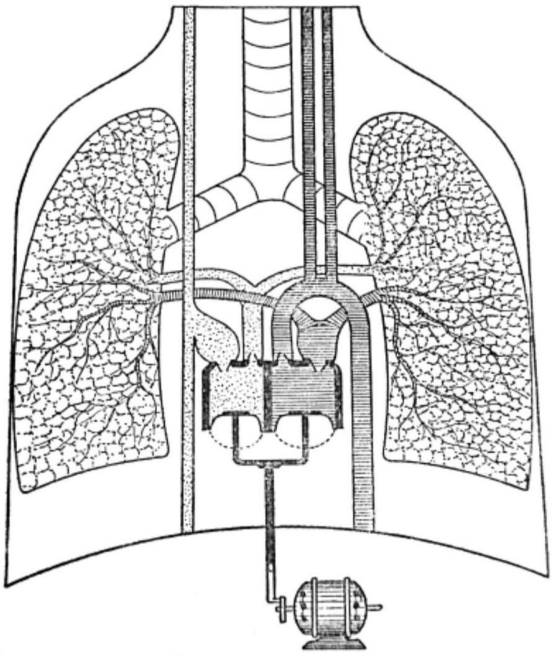

Figure 2. Functioning of V. Demikhov's "mechanical heart"

Figure 3. Heterotopic transplantation of the heart in warm-blooded animals on neck vessels using the method of A. Carrel

mental Physiology and Therapy, led by the previously mentioned S. Brukhonenko. There, during the course of 2 years, Vladimir P. Demikhov developed his apparatus that could massage the heart for an extended period of time and could be used as a device for circulatory assistance (8).

Thus, between 1937 and 1940, Demikhov proved himself as an innovator, having created two completely new and unusual devices for that time: the "mechanical heart" and the apparatus for direct cardiac massage.

Towards the Heterotopic Transplantation of the Heart in Warm-Blooded Animals

At the end of their studies, the students of the Biology Department of MSU had to defend their theses. Vladimir chose an unusual topic for his thesis: "On Heart Adaptability in the Warm-Blooded". While writing, he performed his first experiments on heterotopic heart transplantation in warm-blooded animals according to the method of A. Carrel (Fig. 3). Despite the fact that V. Demikhov relied on the method developed earlier by the French surgeon, it can be considered original owing to the perfusion of the coronary flow of the donor's heart as well as the inclusion of its right side in the bloodstream (8, 9). The abovementioned work received an excellent mark, after which in August of 1940 he received his Physiology of Animals diploma from the Lomonosov Moscow State University.

August of 1940 was special for the 24 year-old graduate not only because he received his diploma. At the end of the same month he was called to a military enlistment office to join the army. From there he was transferred to Kostroma and placed in the 527th rifle regiment of the 118th rifle division, which had just formed as part of the Moscow military district. There, the Red Army recruit Demikhov went through training and became a foot soldier. In June of 1941 the War began. Since Vladimir did not have a medical degree, he was not allowed to be a military surgeon. However, he took preliminary courses and was able to become a pathologist, which he carried out throughout the whole War (10). By the end of the War he had become the senior lieutenant of the medical corps in Manchuria and served as the senior pathologist of the Second Guards Army (4).

After the end of the War, V. Demikhov was demobilized and sent back to Moscow, where in December he became an assistant at the Physiology Depart-

ment in the Moscow Peltry and Fur Institute (MPFI). There Vladimir began to perform heterotopic heart transplantation in warm-blooded animals (1).

It is important to note the unique nature of these experiments, which had been unheard of both in Russia and abroad. Singular attempts of some scientists (there were four of them: A. Carrel, F. Mann, N. Sinitsyn and B. Ognev) to transplant the heart into the neck or the inguinal region were unsuccessful, due to the fact that in those cases it was not connected to the lungs therefore, could not take an active part in blood circulation. The heart was also compressed by the adhering tissues and, as a result, would stop functioning (11, 12).

On February 24, 1946 at the Department of Pathophysiology of MPFI, Vladimir P. Demikhov performed the first-ever heterotopic transplantation of a heart into the thoracic cavity of a dog by the name of "Razboynik", using his own method (Fig. 4). The central end of the donor's aorta was stitched into the descending aorta of the recipient according to the end-to-side type, while the superior vena cava of the recipient was stitched into the donor's right atrium of the heart. An original intravenous morphine-alcoholic anesthetic was used. It included 3,0 ml of morphine and 120,0 ml of 33% alcohol. Unfortunately, after clamps were taken off from the aorta and the vena cava, the dog's blood pressure suddenly dropped, while the heartbeat was 160 beats per minute; as a result of which the dog died. During the course of the next month 3 more experiments were conducted, during which Demikhov perfected the anesthesia technique and certain steps of the operation. All of them ended tragically (7).

Vladimir realized that one of the possible reasons for these failures was the duration of the experiments. During the first 4 operations he used A. Carrel's method for stitching vessels, which required up to five hours in order to create anastomoses. For this reason, during the fifth operation on April 21st, 1946 V. Demikhov used colloidal tubes, a method described by N. Sinitsyn in 1941 (11). In addition, unlike the first operations, which only used mature specimens, 5–6 month old puppies that weighed 6–7 kg were used as donors, while the recipients were 7–8 year-old dogs with a body mass of 18–20 kg. Altogether 8 operations were performed. All of them used a new method (Fig. 5), which differed from the previous one in that the donor's heart was removed along with a lung. Moreover, in order to connect the transplant to the bloodstream, instead of using the recipient's aorta,

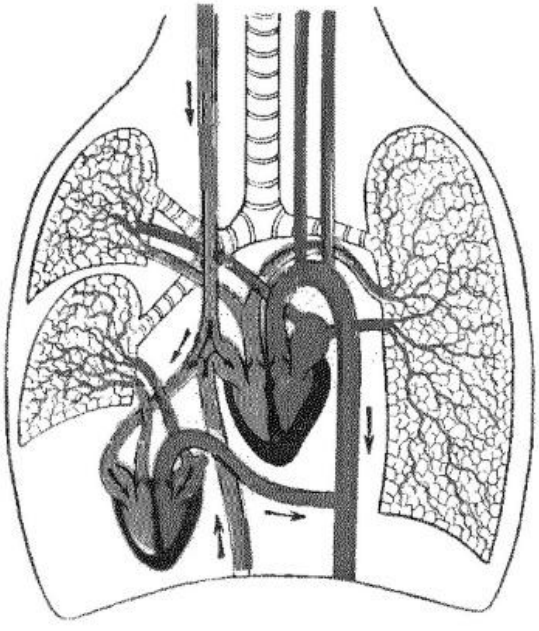

Figure 4. First-ever heterotopic transplantation of heart into the thoracic cavity conducted on 24.02.1946 in MPFI

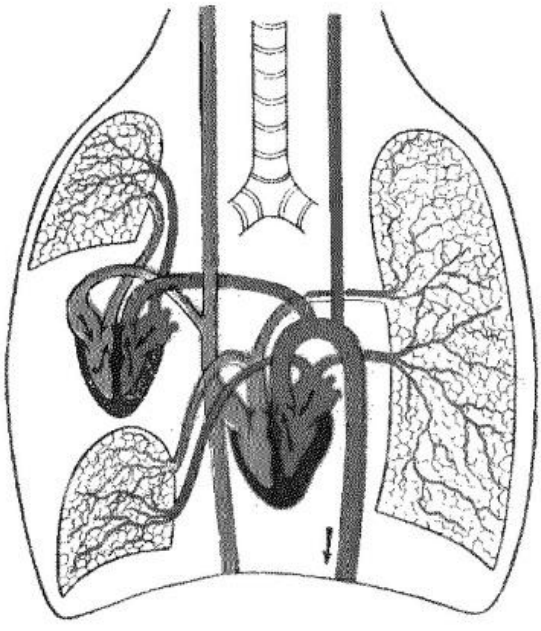

Figure 5. Heterotopic transplantation of cardiopulmonary system into thoracic cavity using the new method

Demikhov used one of its branches – the brachiocephalic trunk (7).

Unfortunately, the result of these operations was also unsuccessful – all dogs died. After 12 failures in a row, his superiors ended up prohibiting Vladimir from performing any more operations in MPFI (8).

V. Demikhov now needed a new place, where he would be able to continue his experiments. Having found out that there was a dog pound at the military unit 74390 in Novogireevo, he went to ask its commanding officer for help as a veteran. As a result of this plea, all of the experiments until the summer of 1947 were performed there. At the beginning previous techniques (Figs. 4, 5) were used again with no success: the recipients would die due to various complications (7, 13).

The First-Ever Orthotopic Transplantation of the Heart-Lung System in Animals

Despite failures, on October 20th, 1946 Demikhov took a chance and performed the first transplantation of heart-lung system in the world. After mobilization of the transplant, the system was placed in Ringer's solution and its vessels were connected to the vessels of the recipient by means of rubber tubes with glass cannulae in such a way that after the removal of the to-be replaced system of organs, the blood circulation was set in motion by the recipient dog, while breathing continued through a tube inserted into the trachea. After placing the transplant in the thoracic cage of the recipient, its aorta and venae cavae were connected with the peripheral ends of the corresponding vessels; the heartbeat of 78 beats per minute was restored (Fig. 6). However, during the process of connecting the trachea, the dog died on the operation table due to asphyxiation (7).

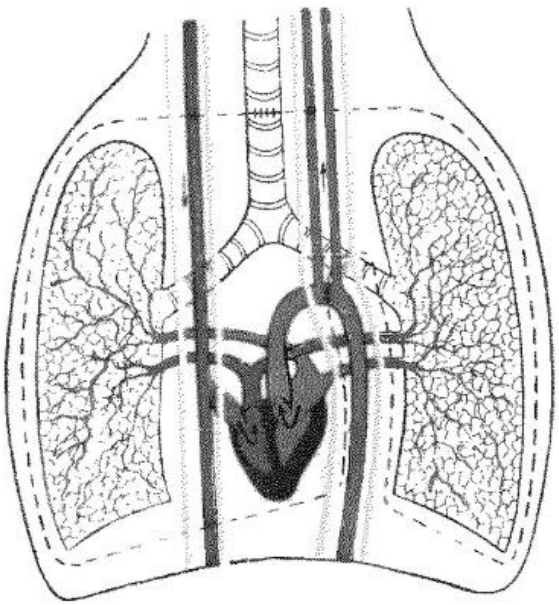

Figure 6. First-ever orthotopic transplantation of cardiopulmonary system into thoracic cavity conducted on 20.10.1946 in military unit 74390

Next, on 25th of October, 1946 another operation was performed according to the standard procedure seen in figure 3 but its result had surpassed all expectations: not only did the recipient survive but the dog seemed to feel well. Unfortunately, on October 2nd, as a result of divergence and suppuration of the tracheobronchial suture, the dog died of pneumothorax. However, it must be noted that the subject lived with an additional heart for over 7 days. Without a doubt, it was a significant success, which motivated Vladimir to perform several more similar operations, which also ended successfully (7).

Transplantation of Isolated Additional Heart without Lungs

The great scientist did not want to linger on what he had achieved and so on December 15th, 1946 he performed a transplantation of an isolated heart with lungs using a new method (Fig. 7) at the Roentgenophysiology Laboratory of the V.M. Molotov Roentgenology and Radiology Research Institute (MRRRI), led at the time by Demikhov's friend and assistant P. Mazaev. The operation consisted of connecting the following: donor's aorta with the central end of the left subclavian artery; donor's pulmonary vein with the pulmonary vein of the removed inferior lobe of right lung; donor's pulmonary artery with recipient's right branch of pulmonary artery; donor's superior vena cava with recipient's azygos vein. The transplanted heart worked for 2 days. On December 17th, the dog died from bilateral pneumothorax and asphyxiation (7).

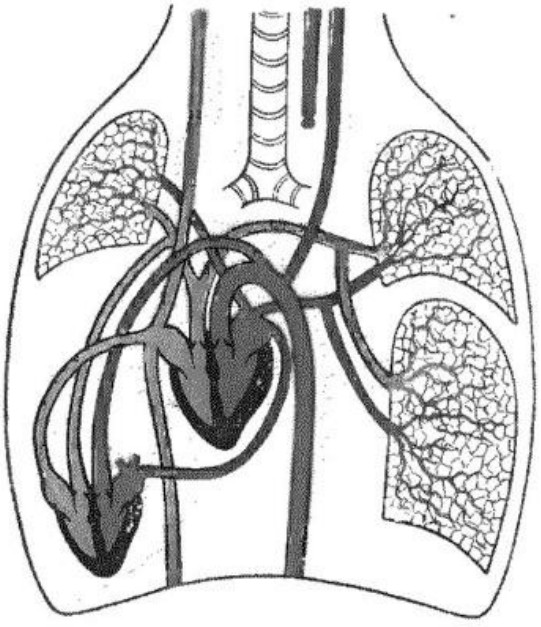

Figure 7. Heterotopic transplantation of an isolated additional heart into thoracic cavity using the new method

The results achieved throughout the 2 years of experimentation (94 experiments were performed altogether) were presented in 1947 by Vladimir at the First All-Union Conference on thoracic surgery. Members were able to visualise the technique used during the operation in a special film. Demikhov's paper was highly received by one of the members of the conference – a prominent Soviet surgeon A. Bakoulev who thought the experiments were "a big achievement for our Soviet medicine and surgery" (13).

A New Turn in the Development of V. Demikhov's Experiments

Vladimir understood that performing experiments in the military unit or at the MRRRI is far from ideal. Thus, despite the fact that the USSR Academy of Medical Sciences Institute of Surgery was going through hard times of reorganization, it was there that Demikhov continued his remarkable research. At first he performed a series of heart transplantations with the use of earlier methodologies (Figs. 4-6) (1, 7, 14).

In addition, in May of 1948 V. Demikhov developed an original version of the heart-lung preparation, which allowed to significantly simplify and improve the method of heart and lung transplantation in dogs (Fig. 8). Unlike I. Pavlov, N. Chistovich (1883) or E. Starling (1912), Demikhov abandoned the systemic circuit in his preparation and used the coronary one instead (15). The idea was truly unique in its brilliance and simplicity, since it became possible to sustain the activity of the isolated heart and lungs for several hours without additional adjustments. 25 experiments were performed: 13 ended with death; in fourteen case there were signs of life prolongation: heart-lung preparation continued to function in the thoracic cage of the recipient dog for 7 hours; in the 11 experiments that followed, dogs with transplanted heart and lungs lived from several hours to 2 days (7).

At the same time, Vladimir continued to develop and improve new methods of cardiopulmonary system transplantation. Thus, from June, 1948 until November, 1949 12 previously non-existent types of operations were tested. The results were disappointing: animals lived from 2 to 12 days after surgery and then died from asphyxiation, infection or bleeding. There

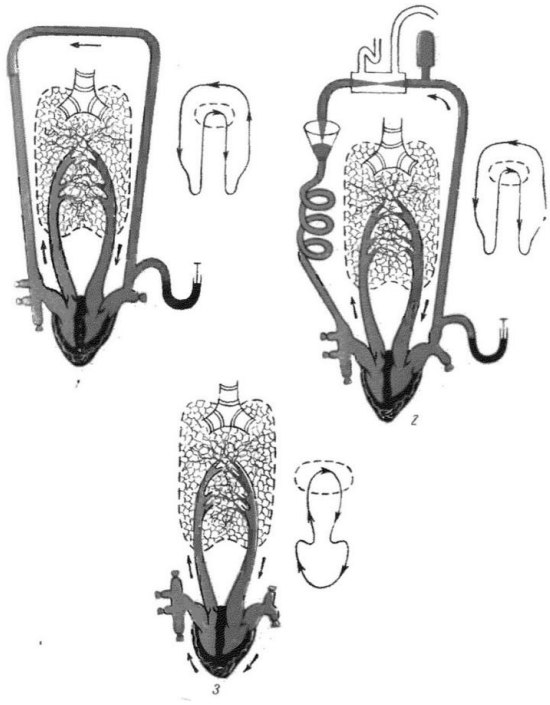

Figure 8. Diagram of heart-lung preparations. 1 – according to Pavlov and Chistovich; 2 – Starling's method; 3 – Demikhov's method

were, however, some break-throughs. Primarily, for the first time in cardiac surgery the left heart bypass with a biological prosthesis (Fig. 9) was developed (the operation was performed on the 21st of September, 1948). It is widely applied today with the use of pneumatic or electrical artificial heart ventricles instead of donor hearts. Secondly, apparatus for circular machine vessel suture developed by V. Gudov (Fig. 10) began to be used. It allowed to reduce operation time and, as a result, to increase the survival rate of test subjects (16). Demikhov shared the results of his work on November 12th, 1949 during the symposium at the USSR AMS Institute of Surgery, dedicated to A. Vishnevsky, where the problem of organ transplantation was discussed for the first time in the USSR. Afterwards, there were several other positively-met presentations, including those at the symposiums at the Academy of Sciences and the USSR Academy of Medical Sciences. Besides this, V. Demikhov published several articles on the problems of heart and heart-lung system transplantation (7, 14).

In between writing his first works, Vladimir continued to create and test new methods of heart transplantation. At the end of 1951 he developed 3 more types of operations. The orthotopic transplantation of an isolated heart performed in early October of 1951 is of special interest, since it was the first in the world to not use artificial blood circulation (16). Unfortunately the experiment could not be finished, because the subject died on the operation table. This was the last homotransplantation of additional heart. Demikhov did not perform this operation from 1952 to 1954, since he was developing and performed the first-ever mammacoronary bypass surgery. Today this method is widely used in clinical practice all over the world (18, 19).

Return of the Heart Transplantation Experiments and World Recognition

1954 was marked by resumed experiments on heart transplantation. On December 30th, V. Demikhov was finally able to complete a replacement of the recipient's heart with that of the donor, which was first performed in 1951. It was the fourteen operation. The next 5 resulted in the animals' deaths as a result of technical mistakes. However, on January 11th, 1955 the most successful (in Vladimir's opinion) experiment was conducted. Not only did the recipient wake up after anesthesia but it also lived until 8 AM of the following day. Unfortunately, only 2 out of 22 operations

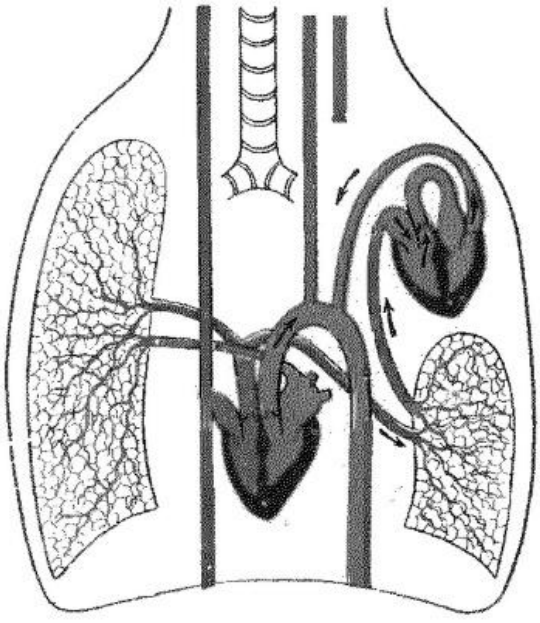

Figure 9. Left Heart Bypass method with a biological prosthesis

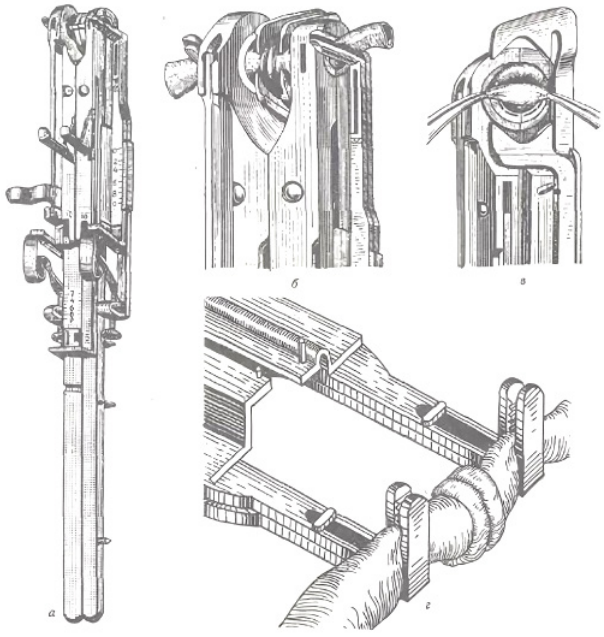

Figure 10. Vascular Stapler of V. Gudov

can be called successful. Demikhov perfectly realized that neither he, nor the medicine of that time were ready for transplantations of such type. Thus, he focused on transplantation of a second additional heart which could be introduced into clinical practice in a much easier and safer fashion. Thus, in the spring of 1955, Vladimir developed his twentieth method of additional heart transplantation with a lung lobe (Fig. 11). It was tested on the 22nd of March. The recipient dog died after 8 days (7, 20).

The differences between V. Demikhov and that of the Institute's directors and A. Vishnevsky in particular, became a barrier for future experiments. As a result, he was dismissed. Then Vladimir began to work at the I.M. Sechenov First Moscow State Medical University, where continued to develop and improve new methods of transplantation. During his work there (1956–1960) he created the cross circulation method, which was to help to overcome the biological incompatibility (Fig. 12). Demikhov also tested 4 completely new types of cardiopulmonary system transplantations several times. This time the results were positive: animals successfully underwent surgery and lived from 14 to 32 days (7).

Gradually, the works of the Soviet experimenter became known abroad and consequently he would get invited to international symposiums in the US and Europe increasingly more often. However, Demikhov only made 3 trips abroad at the end of 1958–1959: to Eastern and Western Germany (after which he was banned from travelling) (17). The success of his lectures and especially of his demonstrative operations was huge in the world of medical science. Vladimir received an honorary doctorate at the Leipzig University, became a member of the Royal Society of Sciences in Uppsala, Sweden, as well as of the Hannover University and the American Mayo Clinic (21).

The publishing of his monograph "Experimental Transplantation of Vital Organs" in 1960 became Demikhov's triumph, since it became the first transplantology guide in the world (Fig. 13). His work was much appreciated abroad and his book was immediately translated into several languages and re-published in New York, Berlin, and Madrid. Unfortunately, Vladimir's work went almost completely unnoticed in the USSR (22). The main idea of the book was to communicate

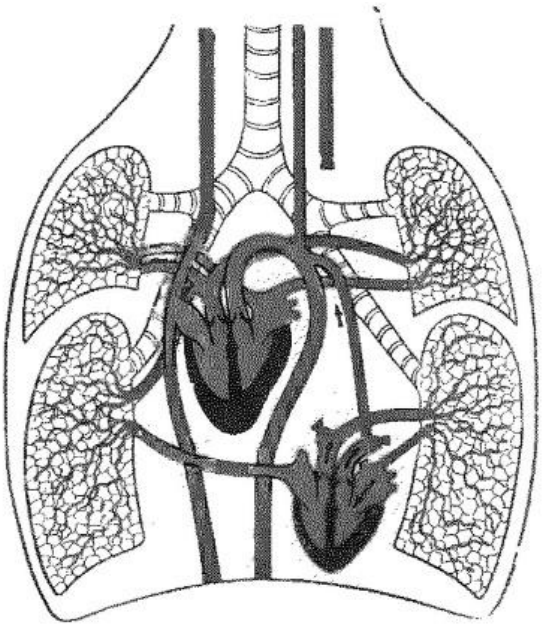

Figure 11. Heterotypic transplantation of cardiopulmonary system into thoracic cavity using the new method

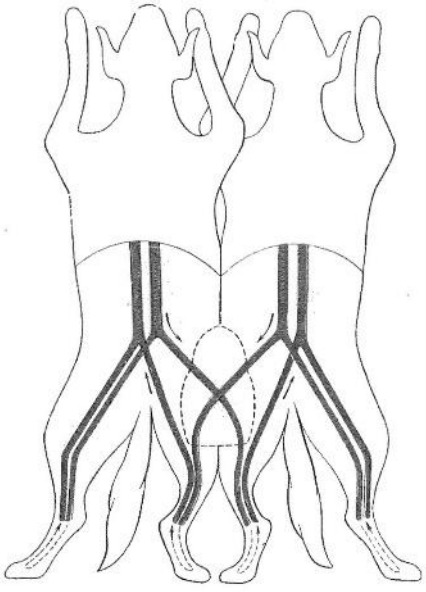

Figure 12. Cross-circulation method

to the leadership that it was necessary to begin organ transplantations in a clinical setting. However, it was impossible to do at his Department, so in the summer of 1960 Demikhov appealed to transfer his laboratory to the Sklifosovsky Institute in order to perform a heart transplantation on a human. In November, 1962 Vlad-

imir transplanted a heart to a monkey. In December he told the Times magazine that he would be able to do the same on a human. Unfortunately, USSR Ministry of Health strictly prohibited the Institute to perform such heart transplantation, since it considered such methods to be contrary to Communist ethics (23). As a result, V. Demikhov began to develop a physiological method of preserving vital isolated organs (heart, cardiopulmonary system, etc.) in a functioning state by means of connecting them in a transparent thermostatic case to the circulatory system of a living or a brought-back-to-life organism. He was able to connect up to four cardiopulmonary systems to one animal and keep them functioning up to seven days (7).

Consequently, the first clinical heart transplantation was performed in 1967 by Christiaan Barnard from Cape Town, RSA, after which he received many awards and prizes in different countries, while Vladimir continued to work at the Sklifosovsky Institute until 1986 and then honorably sent to retirement (24, 25).

Discussion

The life of V. Demikhov is full of unfortunate examples of poor judgement and shortsightedness of the

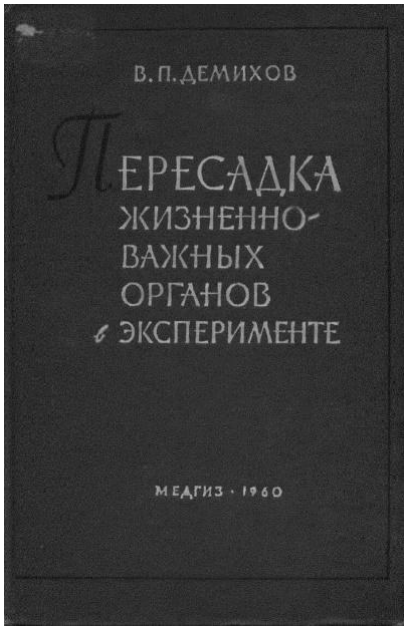

Figure 13. Cover of Demikhov's monograph "Experimental Transplantation of Vital Organs"

Soviet medical officials, who did not appreciate his scientific and practical potential as an outstanding scientist as well as depriving their country from becoming the first in the world to host the transplantation of the heart. All of the fame from scientific breakthroughs, which can be compared to the first flight on the moon, went to an outstanding surgeon of the mid-20th century C. Barnard, who performed many surgeries based on the methods described in Vladimir's book (17, 21).

However, it must be noted that the position of some of the officials of the Soviet healthcare system can be explained not only by the inertia of their thinking but also by looking at the moral and ethical system of that time period. One can look at the events of the spring of 1964 as an example. Demikhov defended his Candidate of Biology degree thesis in a very tense situation around him. Some of those present (B. Petrovsky, V. Kovanov, G. Falkovsky and other esteemed scientists) were aggressively trying to stop Vladimir, since they deemed his work immoral and looked at Demikhov himself as a daydreamer and a charlatan (26). The majority of those present in the auditorium of MSU were able to fight back the naysayers. The official opponent – P. Androsov was allowed to give his word and he said the following: "This work is worthy of receiving not simply a Candidate degree but the Doctor of Science degree". The second opponent – A. Gurvich also agreed. As a result, on the 12th September, 1964 V. Demikhov received the Doctor of Biological Science degree from the Highest Attestation Commission under the Ministry of Higher and Secondary Education of USSR (27).

The works of the great pioneer were being discussed not only in the Soviet Union but also abroad. Starting from 1947 foreign doctors and correspondents were able to observe his operations on multiple occasions and wrote about him from time to time. However, Vladimir's experiments received widespread attention only in the winter of 1958. On December 8th, 1958 Demikhov traveled to German Democratic Republic (it was the first out of the 3 aforementioned trips), where he gave a lecture on the future development of the transplantology as well as conducted an artificial heart transplantation of a heart into thoracic cavity and the front part of a juvenile dog unto the neck vessels of an adult dog. The previously mentioned

experiments shocked both the specialists and regular people who knew nothing about medicine. Doctors, philosophers and theologians had heated debates about the ideological as well as the moral and ethical side of said experiments. One of such discussions took place in April of 1959 in the office of Stuttgarter Zeitung newspaper. Based on the published materials, one can see that the assessment of Vladimir Demikhov's works by the members of the round table varied from strictly negative to moderately positive (28). It is quite probable that the experiments demonstrated by the Soviet researcher in GDR, pushed the world's scientific community to study ethical, philosophical, religious and other aspects of transplantation in more detail.

The historical significance of Demikhov's life cannot be overstated, regardless of the recognition his input into global science during his lifetime received. Essentially, owing to Vladimir, today a considerable amount of heart transplantations are performed all over the world and thousands of patients with incurable heart diseases get a second chance, in most cases not even knowing that they owe their life to the Soviet physiologist, who was fanatically devoted to his ideas and was a pioneer in things his contemporaries had never dreamed of.

The work that allowed to prolong lives of seriously ill patients became the greatest achievement for scientists of Russia and abroad in the field of heart transplantation. However, for us the greatest name in the history of medical science is and will be Vladimir P. Demikhov.

Conclusion

The name of the great Soviet scientist is not well known today not only among a wider audience but also among many doctors. It should be added, that there is hope that such an injustice will be corrected and the name of Demikhov will be recognized among such pioneering doctors as Pirogov, Botkin, Mechnikov, Pavlov, Vishnevsky, Sklifosovsky, who are well-known not only in their native country but all over the world and who are a pride of Russia.

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