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PHENOMENON OF DEMIKHOV

At N.V. Sklifosovsky Institute (1960–1986). Grishka the dog lived with a second, additional heart and a transplanted lung without immunosuppression for 142 days (1962)

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Abstract

On June 20, 1962, at the N.V. Sklifosovsky Research Institute for Emergency Medicine in Moscow, V.P. Demikhov, a biologist, physiologist, and experimental surgeon transplanted a second, additional heart together with the lung through the left thoracotomy access in the 4th intercostal space into the place of the removed two upper lobes of the left lung into the chest to the dog named Grishka. The second heart was implanted in such a way that

arterial blood circulated in it and in the transplanted lung. The donor and recipient were selected according to the blood group match. The immediate postoperative period was uneventful. On day 4, the dog became active. On day 12, the sutures were removed from the skin wound. On day 15, antibiotics (penicillin and streptomycin) were discontinued. During the daily examination, general condition and physical activity were noted, rectal temperature, respiratory rate and contractions of one's own and transplanted heart were measured; electrocardiograms were taken from both hearts. On day 13, Grishka gnawed through the electrode, which helped taking the electrocardiograms from the transplanted heart during the first 2 weeks. As a result, in place of the electrode remaining in the chest, the animal developed a fistula with purulent discharge. For this reason, as well as for coughing and wheezing in the lungs on the left, Grishka was periodically administered antibiotics. After the operation and before the withdrawal from the experiment, the dog was injected with heparin. No other pharmaceuticals were given. The dog led an active lifestyle, ate well, and displayed interest in female dogs. The second heart ceased beating 142 days after the operation, on November 8, 1962. Resuscitation measures were unsuccessful. At autopsy, in the right atrial auricle of the transplanted heart, diffuse transmural hemorrhage and a thrombus from the endocardium were revealed, which blocked the blood flow to the heart. The lower lobe of Grishka's lung was in a state of hepatization. Signs of edema and inflammation were observed in the transplanted lung. There were no blood clots at the sites of vascular anastomoses. There were no visual signs of rejection. The results of histological studies are not known.

This article for the first time introduced into scientific circulation an operation protocol, a diary of postoperative management and an autopsy

protocol for an animal that had lived with a second, additional heart and a transplanted lung without immunosuppression for 142 days, which has been a unique observation in world transplantology. Despite the long-term survival of the animal, nursing the recipient dog in the postoperative period did not meet the complexity of the operation performed, which allows us to conclude that it was impossible at that time to implement the results obtained in the experiment into clinical heart transplantation in humans.

Keywords: history of transplantation, V.P. Demikhov, experimental transplantation, dog Grishka, transplantation of an additional heart with a lung, survival after heart-and-lung transplantation

Conflict of interests Authors declare no conflict of interest

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ECG - electrocardiogram

i.v. - intravenously

s.c. - subcutaneously

Introduction

In a historical investigation, documents confirming or refuting dates, facts, and events of the past are extremely important. In 2019, describing V.P. Demikhov's life and work, we mentioned an experiment unique for Soviet and world transplantology: in 1962, a dog named Grishka operated on by V.P. Demikhov lived with a second, additional heart and a lung

transplanted with it without immunosuppression for 142 days [1]. However, at the time of publication of the article, the protocol of this operation and information about the postoperative period were not available.

In December 2021, in the collections of the Russian Museum of Medicine of the N.A. Semashko National Research Institute of Public Health (Head of the Department is N.V. Chizh), we found "Book No. 27", which described Grishka's operation, postoperative management of the animal, and the protocol of its autopsy [2].

In this article, we introduce this source into scientific circulation, reflecting the realities of organ transplantation in the USSR in the early 1960s, as well as the features of V.P. Demikhov's work as a biologist, physiologist, and experimental surgeon (Fig. 1). In the course of our narration and in the "Discussion" section at the end of the article, we commented on some provisions of this document, which has not only scientific, but also cultural and historical value.

Fig. 1. V.P. Demikhov in the operating room. 1960. [From the collection of the Russian Museum of Medicine of the N.A. Semashko National Research Institute of Public Health. Inv. No. RMM VS 738/9]

Operation

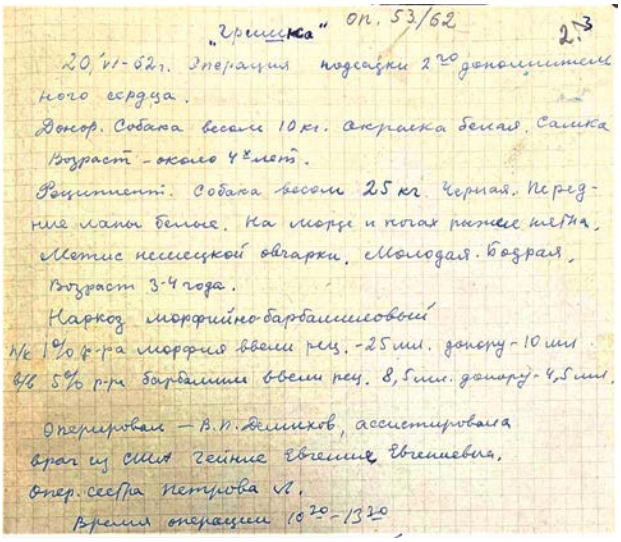
In Book No. 27, this experiment is labeled with No. 53/62. This means that the operation performed on June 20, 1962, was the 53rd performed that year. If we take into account that by this time V.P. Demikhov had performed more than 250 such operations, then operation No. 53/62 was quite routine. The protocol writes that the "the implantation of the 2nd, additional heart to the dog "Grishka" was performed". But this is not entirely true, because together with the heart, a lung was also transplanted. The operation lasted 3 hours (from 10.30 to 13.30).

The donor was an outbred 4-year-old female of white color weighing 10 kg. After explantation of the heart and lungs, she was withdrawn from the experiment. The recipient was a half-breed German Shepherd named Grishka of about the same age weighing 25 kg. Its color was black, its paws and belly were white, and there were tawny spots on its muzzle (Fig. 2).

Fig. 2. Grishka. Photo by M.M. Razgulov. 1962 [From the collection of the Cardiovascular Surgery Museum of A.N. Bakulev National Medical Research Center for Cardiovascular Surgery]

Grishka was given, as it is written in the document, "morphine-barbamyl anesthesia": 25 ml of a 1% morphine solution was administered subcutaneously (s.c.), 8.5 ml of a 5% barbamyl solution was administered intravenously (i.v.). The donor dog was given 10 ml of morphine and 4.5 ml of barbamyl.

The operation was performed by V.P. Demikhov. He was assisted, as it is written in the operation protocol, by "a doctor from the USA, Yevgenia Yevgenyevna Geinle." We do not know how Jane Henley, an anesthesiologist from Columbia University, came to our country, how she ended up in V.P. Demikhov's laboratory, and why he appointed her as an assistant for this operation. It is obvious that Jane Henley was acquainted with V.P. Demikhov before that day. In addition, this fact suggests that such "visiting surgeons" could help V. P. Demikhov during his operations. The operating nurse was L.D. Petrova (Fig. 3).


„Гришка" оп. 53/62 2.3

20.VI-62г. Операция подсадки 2-го дополнительного сердца.

Донор. Собака весом 10 кг. окраска белая. Самка

Возраст - около 4-х лет.

Реципиент: Собака весом 25 кг Черная. Передние лапы белые. На морде и пятах рыжие метки.

Метис немецкой овчарки. Молодая. Бодрая.

Возраст 3-4 года.

Наркоз морфийно-барбамиловый

н/к 1% р-ра морфия ввели рец. -25 мл. донору - 10 мл

в/в 5% р-ра барбамила ввели рец. 8,5 мл. донору - 4,5 мл.

Оперировал - В.П. Демихов, ассистировала врач из США Гейнле Евгения Евгеньевна,

опер. сестра Петрова Л.

Время операции 10^{20}-13^{20}

Fig. 3. The first page of the Operation Protocol. [From the collection of the Russian Museum of Medicine of the N.A. Semashko National Research Institute of Public Health. Inv. No. RMM KP 133/24]

Protocol of the operation (June 20, 1962)

«**The incision on the donor is transverse** (here and further the quoted speech being highlighted in bold by us. – *Auth.*) with a cross-section of the sternum and both chest walls along the intercostal space to the spine. The incision on the recipient is on the left in the 4th intercostal space.

Scheme of connecting the vessels. The upper vena cava of the donor heart is connected to the pulmonary vein of the lower lobe of the left lung. The graft aorta is sutured to the peripheral end of the recipient's left subclavian artery[1].

The upper and middle lobes of the recipient's left lung were removed. **The bronchus of these lobes is stitched with the bronchus of the right lung of the donor**, transplanted together with the heart (3 lobes – upper, middle and lower) (Fig. 4). The blood vessels and bronchi are **sutured using** a "vasclular stapling device" [2, p. 2].

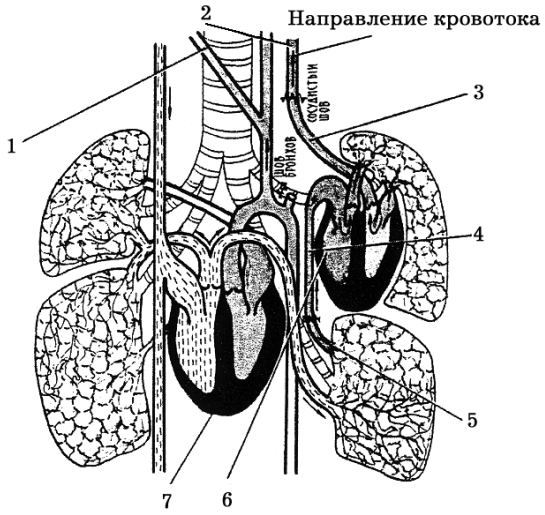


Fig. 4. Grishka's heart and lung transplant scheme: 1, right carotid artery; 2, left subclavian artery; 3, aorta; 4, donor heart; 5, pulmonary vein; 6, vena cava; 7, Grishka's native heart [1].

[1] V.P. Demikhov used this method of suturing the arterial vessels to monitor the function of the transplanted heart by the pulse on the left brachial artery.

It follows from the Protocol that through left-sided thoracotomy in the 4th intercostal space (access dimensions are not specified); an additional heart was implanted to the recipient onto the place of 2 removed upper lobes of the left lung, but not isolated one, but with the right lung consisting of 3 lobes. Moreover, the bronchus was sutured into this lung, that is, it participated in breathing. However, arterial blood, rather than venous, flowed through the right parts of the donor heart and from it to the donor lung, since the upper vena cava of the donor heart received blood from the pulmonary vein of the lower lobe of Grishka's left lung. Thus, the donor heart, which pumped only arterial blood, helped the recipient's left heart by providing auxiliary blood circulation. The " vascular stapling device " used by V.P. Demikhov to suture vessels and bronchi was obviously the device designed by V.F. Gudov of the "vascular circular stapling device (ASC)" type for circular mechanical suture.

"During the operation, the recipient was intravenously injected with 250 ml of heparinized blood taken from the donor after extracting **the cardiopulmonary complex**. Prior to heart removal, the donor was given 0.5 ml of Richter heparin (2500 IU). The heart of the graft is fixed to the recipient's chest wall. Before suturing**, 1 million units of streptomycin and 1 million units of penicillin were injected into the wound.**

The transplanted heart is located with its apex towards the head. In the area of the top of the transplanted heart**, a silver electrode** for ECG recording is sewn to the pericardium, and the end of it is brought out through the chest wall. A rubber drainage tube was drawn out of the pleural cavity through the left chest wall and left for the postoperative period. The recipient's wound is sutured tightly in layers" [2, p. 3].

Several important features of the operation follow from this document. First, we note that the technique of explantation of donor hearts and lungs is not described. However, the transbipleural approach used allows

us to judge that the cardiopulmonary complex was harvested according to V.P. Demikhov's original technique (with the pulmonary and coronary circulation contours), and as long as the surgeons prepared the recipient for transplantation, the donor organs were in a vital state: the lungs were breathing (using a ventilator), and the heart was beating. Second, transfusion of the recipient's blood from the donor indicates that the dogs had compatible blood group. Third, V.P. Demikhov had at his disposal broad-spectrum antibiotics and heparin produced by the Richter Company (Hungary). Fourth, the ECG recording of the transplanted heart after surgery was planned to be carried out from its epicardium in isolation using an electrode that had a silver tip, that is, it had prolonged antiseptic properties.

All this suggests that the technique of such interventions was developed, and that they were carried out in strict antiseptic conditions.

Three facts are noteworthy: (1) the method of fixing the heart to the recipient's chest wall is not described (in particular, for what part of the heart was it fixed?); (2) the tip of the electrode, as stated in the Protocol, was for some reason sewn to the pericardium of the transplanted heart. It is obvious that the electrode was not sewn to the pericardium, but to the epicardium in the apical region; (3) it is not clear whether such a complex technique as suturing an electrode, and even a silver one, to the heart was previously used in animals with two hearts, or whether it was first used in Grishka?[2]

The Operation Protocol is followed by daily records of the animal's condition and the results of its tests. In our opinion, these records were kept by one of the laboratory assistants, probably V.M. Goryainov. The text is given with the author's spelling preserved.

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[2] Epicardial electrodes passed through the chest wall for external electrocardiostimulation were first used in the USSR in 1961 by Yu.Y. Bredikis.

POSTOPERATIVE PERIOD

"**20.06.1962 15.00.** The condition is satisfactory. The dog is in a state of anesthesia. Breathing is calm and even 24/min. The transplanted heart is well auscultated. The native heart rate is133/min, that of the transplanted one is 84/min., t rect. 37.5°C. Pulse on the femoral artery is of good filling.

21.06.1962 10.00. The dog doesn't get back on its feet; can raise the head. It drank 300-400 ml of water. Nothing has been pumped out of the pleural cavity through drainage. **500,000 units of streptomycin and 500,000 units of penicillin were administered subcutaneously, and 20 ml of 40% glucose solution was administered intravenously.** The native heart rate is 140/min, the transplanted heart rate is 48/min. t rect. 37.8°C. Respiration rate is 32/min. **15.00.** 300,000 units of penicillin and 500,000 units of streptomycin were administered subcutaneously. **The animal got to its feet. It is unsteady on its feet. Soon lies down again. The breathing is tense.** Pulse on the femoral artery is of medium filling. The native heart rate is 144/min, the transplanted heart rate is 65/min. Respiration rate is 64/min. t rect. 38.7°C. No appetite.

22.06.1962. 500,000 units of streptomycin and 500,000 units of penicillin were administered subcutaneously.

23.06.1962 10.00. The dog is lying most of the time. Gets up on its feet rarely and for a short time. Respiration rate is 40/min, t rect. 39°C. The native heart rate is 140/min, the transplanted heart rate is 78/min. **Nothing has been pumped out of the pleural cavity through drainage.** The drain was removed. **Became more cheerful. It started walking more,** went out into the yard for a walk **(Fig. 5).** Ate some meat. 20 ml of 40% glucose solution were administered i.v. and 300,000 units of penicillin, 250,000 units of streptomycin were injected s.c.. **15.00.** 300,000 units of penicillin and 250,000 units of streptomycin were administered subcutaneously.

Fig. 5. V.P. Demikhov with Grishka on a walk. 1962 [From the collection of the Cardiovascular Surgery Museum of A.N. Bakulev National Medical Research Center for Cardiovascular Surgery]

24.06.1962. Cheerful. Walks. It responds vividly to its surroundings. Barks. Ate meat and milk. 300,000 units of penicillin and 250,000 units of streptomycin were administered subcutaneously.

"25.06.1962. The condition is satisfactory. Sedentary. Rarely gets up and walks a little. Appetite is reduced. Unwilling to eat sugar and meat. Quiet moans. A cough appeared. Breathing on the left is tapped. The transplanted heart is well auscultated. The native heart rate is 124/min, that of the transplanted heart is 120/min. Respiration rate 44/min., t rect. 39.6°C. 300,000 units of penicillin and 500,000 units of streptomycin were administered subcutaneously. 26.06.1962 The transplanted heart rate is 60/min, the native heart rate is 116/min. Respiration rate 42/min. t rect. 39.4°C. 300,000 units of penicillin and 500,000 units of streptomycin were administered subcutaneously. The pulse on the left forelimb is well palpable. General condition and appetite are satisfactory. Ate about 200 g of meat.

27.06.1962. 500 000 units of streptomycin, 300,000 units of penicillin, and 350,000 units of colimycin were administered subcutaneously. 20 ml of 40% glucose solution was

administered intravenously. t rect. 40°C. The native heart rate is 144/min, the transplanted heart rate is 72/min. Respiration rate 60/min.

29.06.1962 10.00. t rect. 39.9°C. The native heart rate is 120/min, that of the transplanted heart is 72/min. Respiration rate 34/min. The pulse on the left brachial artery is well palpable. No cough. 500,000 units of penicillin and 500,000 units of streptomycin were administered subcutaneously. 15.00. 500,000 units of penicillin and 500,000 units of streptomycin were administered subcutaneously.

30.06.1962 10.00. The condition is satisfactory. t rect. is 40°C. The native heart rate is 132/min, the transplanted heart rate is 72/min. Respiration rate 60/min. The appetite is satisfactory. Eats meat. Refused porridge and milk. 500,000 units of penicillin, 500,000 units of streptomycin were administered subcutaneously, and 20 ml of 40% glucose solution was administered intravenously. 14.00. 500,000 units of penicillin and 500,000 units of streptomycin were administered subcutaneously" [2, p. 3-5].

10 days after surgery (June 30, 1962)

The operator's technique (no hemothorax), postoperative care and nutrition (meat, milk, sugar), antibiotic therapy (twice a day subcutaneously) had the proper effect. On day 3 (after removing the drainage from the pleural cavity), the dog was taken out into the yard. On the 4th day, Grishka felt "quite satisfactory": it was alert, barking reacted to others. The transplanted heart contracted about twice less frequent than the native one. Ten days after the operation, the animal's condition was consistently satisfactory. Antibiotics were prescribed again for the cough. Thus, the first milestone of the possible occurrence of a rejection reaction of the transplanted organ, which at that time was calculated as the 7^{th} day, was passed. Further, the diary of Grishka's postoperative follow-up was filled out once a day.

"01.07.1962. The condition is satisfactory. Walks. Caressing. Reacts vividly to others. Ate meat willingly. Pulse on the left brachial artery is of medium filling. Breathing is

calm. 300,000 units of penicillin and 500,000 units of streptomycin were administered subcutaneously.

02.07.1962. The condition is good. The native heart rate is 120/min, the transplanted heart rate is 96/min. Respiration rate is 36/min. t rect. 39°C. The tongue mucosa is red. Breathing is calm. 500,000 units of penicillin and 500,000 units of streptomycin were administered subcutaneously. **Cutaneous sutures were removed on the postoperative wound**. The skin edges healed by primary tension.

03.07.1962. The condition is good. 400,000 units of penicillin and 500,000 units of streptomycin were administered subcutaneously twice a day. **The dog chewed off the end of the wire that runs from the electrode attached to the pericardium of the transplanted heart. The end of the wire remained under the skin.**

04.07.1962. The condition is satisfactory. <…> [Antibiotics are canceled].

05.07.1962. t rect. is 38.6°C. The native heart rate is 104/min, the transplanted heart rate is 90/min., respiration rate is 40/min. The pulse on the left brachial artery is clearly palpable. Breathing is free. The tongue mucosa is red. The condition is good. It responds vividly to its surroundings. There is a sexual attraction to a female dog. The appetite is good. <…> **At the end of the bitten-off wire, a fistula formed, from which pus is discharged.** The surface of the fistula is washed and sprinkled with streptocide."

From July 6 to July 11, 1962, Grishka's condition, as noted in the diary, was "good". The dog was active, running, barking. Postoperatively, the ECGs were recorded several times at a rapid pace. The rectal temperature ranged from 38.7° C to 39.8°C. The respiratory rate ranged from 28 to 52 per minute. The native heart rate ranged from 96 to 120 beats per minute, and that of the transplanted heart ranged from 84 to 108 beats per minute. The pulse on the left brachial artery was clearly palpated [2, p. 5-6].

21 days after surgery (July 11, 1962)

Twenty one days passed after the operation. Two more "classic" milestones of the rejection reaction were overcome: on the 14^{th} and 21^{st} days. The dog was cheerful, very active and demonstrated a sexual instinct. The transplanted heart was contracting more slowly than the native one.

During this three-week period, the following events occurred. On day 12, sutures were removed from the thoracotomy wound that had healed by primary tension. After another 2 days (i.e. 2 weeks after the operation), the antibiotics were canceled. But there was an "emergency": Grishka bit the wire of the epicardial electrode. In place of the remaining end, a purulent fistula formed, which was washed out and "sprinkled with streptocide" instead of surgical debridement.

From July 12 to July 20, 1962, Grishka's condition was described as good. The body temperature, respiratory rate and the native and transplanted heart rates were within the range observed from July 6 to July 11. The pulse on the front left paw (from the transplanted heart) was clearly palpable. On July 20, it was noted that the dog "limps slightly on the left front leg when moving, possibly due to pain in the fistula area at the site of the bitten off end of the wire" [2, p.6-7].

1 month after surgery (July 20, 1962)

A month after the operation, Grishka's condition was still satisfactory, or, as they wrote in their diaries, "good." The rhythm of the transplanted heart was distinct, but rarer than the rhythm of the native heart. The body temperature and respiratory rate were normal. Apparently, the fistula at the place of the broken wire bothered the dog, which caused him to limp. But

otherwise Grishka was active and had a good appetite. The surveillance was continued.

"**21-23.07.1962.** The condition is good. t rect. is 38.6-38.8°C. The native heart rate is 82-100/min, that of the transplanted heart is 96-100/min. Respiration rate is 22-28/min. The pulse is palpable well.

24.07.1962. The condition is good. **The dog was demonstrated to a delegation of doctors from Romania, a doctor from Venezuela, doctors from the Institute of Thoracic Surgery [USSR Academy of Medical Sciences] and Yakutsk** (Fig. 6).

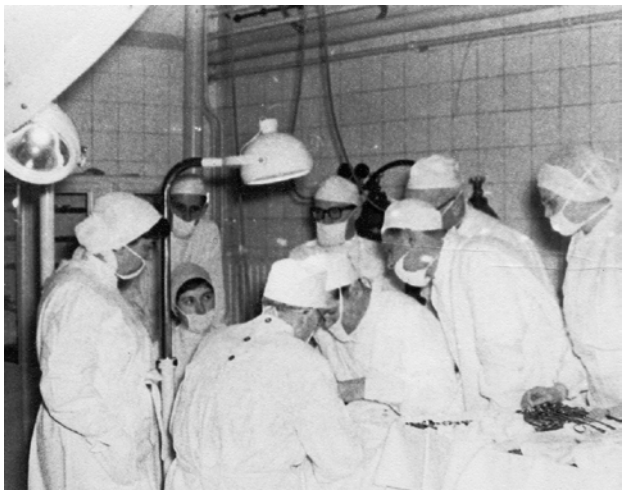

Fig. 6. A group of doctors watching the operation performed by V.P. Demikhov (the 4th from the right). 1960's. [From the collection of the National Museum of the History of Medicine. Stradynya. Inv. № MVM Fototeka. Negativa №15947-4. Riga, Latvia]

25.07.1962. A rare cough appeared. t rect. is 39°C. < ... > 10.00. 250,000 IU of penicillin and 250,000 IU of streptomycin were administered subcutaneously. 15.00. 250,000 IU of penicillin and 250,000 IU of streptomycin were administered subcutaneously.

26.07.1962. t rect. is 38.7°C. The rhythm of the native heart is 110/min, and that of the transplanted heart is 100/min. Respiration rate is 44/min. Rare cough. The state is still the same. Eats meat willingly. Cheerful. **The dog was repeatedly photographed by foreign doctors from the VIII Anti-cancer Congress, by the Sklifosovsky[3] Institute Communist Party Leader, and by Petrov B. A.[4]**

27-31.07.1962. The condition is good. Rare cough. t rect. is 38.8-40.3°C. Respiration rate is 36-44/min. The rhythm of the native heart is 100-120/min that of the transplanted heart is 108-112/min. <…> **Playful. Playing at night, tears the sofa lining, breaks a broom, tears rags.**

01.08.1962. The condition is good. Cough. A small abscess at the body site of the broken wire. Runs fast, jumps. Willingly eats meat (Fig. 7). The surgical field is so overgrown with hair that it does not stand out from other areas. The dog's hair looks shining. The pulse on the left brachial artery is palpable. The transplanted heart is clearly auscultated. 160,000 IU of streptomycin diluted with ½% novocaine solution was administered subcutaneously.

Fig. 7. Grishka after surgery. Photo by M.M. Razgulov. 1962.

[3] The Party Committee Leader (The Secretary of the Local Party Organization) of the N.V. Sklifosovsky Institute was N.K. Permyakov, Doctor of Medical Sciences, the Head of the Pathologoanatomical Department, (See footnote # 7).

[4] Petrov B.A. (1898-1973), a Soviet surgeon, Professor, Full Member of the USSR Academy of Medical Sciences. In 1928-1948, he headed one of the surgical and trauma departments; in 1949-1973, he was the Chief Surgeon of the N.V. Sklifosovsky Institute. Honorary Fellow of the American College of Surgeons (1966).

[From the collection of the Cardiovascular Surgery Museum of A.N. Bakulev National Medical Research Center for Cardiovascular Surgery]

02-03.08.1962. The condition is still the same. <…>

04-06.08.1962. The condition is good. Rare cough. t rect. ranges 38.6-39.1°C. Respiration is 38/min. The native heart rate is 130-140/min, the transplanted heart rate is 120/min. Runs, jumps. Frequent erection. Eats meat willingly. On November 4**, M.M. Tarasov saw the dog**[5] **with a group of foreign doctors.**

07.08.1962. The dog was seen and photographed by a French professor who came accompanied by Professor Alexandrov[6]. After a walk, the t rect. was 39.7°C. After 40 minutes, it decreased to 38.7°C rect. The transplanted heart is clearly auscultated. The pulse on the left front leg is clearly palpable <...>. Rare cough. The native heart rate is 120/min, the transplanted heart rate is 118/min. Respiration rate is 32/min. Runs around. Barks. Playful. Caressing. Eats meat willingly. Frequent erection. Overall condition is good. Subcutaneously, 250,000 IU of penicillin and 250,000 IU of streptomycin were administered.

08-09.08.1962. t rect. ranges 38.9-39.3°C. Respiration rate is 36-48/min. The native heart rate is 120-128/min, the transplanted heart rate 120-128/min. The pulse on the left brachial artery is palpable. The sounds of the transplanted heart can be auscultated. <...> The dog eats sugar and meat willingly. Drinks milk unwillingly, refuses porridge. Rare cough.

10.08.1962. t rect. is 39.7°C. By 15.00 it has increased to 40.1°C. The limp on the left front leg increased. <...> The dog ran a lot in the morning. By the end of the day, it became more boring. The movements probably caused the increase of the inflammation in the fistula area... **The pus discharge from it increased**. 15.00. 250,000 IU of

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[5] M.M. Tarasov (1904-1973), a surgeon, the veteran of the Great Patriotic War, worked as the Director of the N.V. Sklifosovsky Institute from 1952 to 1968.

[6] Aleksandrov M.S. (1885-1965), a Soviet doctor, gynecologist, Professor, Head of the Gynecology Department of the N.V. Sklifosovsky Research Institute for Emergency Medicine.

penicillin and 250,000 IU of streptomycin were injected subcutaneously into the fistula area. <…>

"Grisha" was seen while walking in the morning by Permyakov, the Secretary of the Sklifosovsky Institute Party Organization[7].

11.08.1962. The condition is good. < ... > 250,000 IU of penicillin, 500,000 IU of streptomycin, 180,000 IU of colimycin, and 200,000 IU of mycerin were injected twice into the fistula area subcutaneously. The pus discharge from the fistula decreased. The appetite is good. A rare cough persists. The limp became less frequent. Subcutaneously, 200 ml of a 4% glucose solution with saline was administered.

12.08.1962. <...><...> **The fistula closed**. 250,000 IU of penicillin, 500,000 IU of streptomycin, 180,000 IU of colimycin, and 200,000 IU of mycerin were administered subcutaneously. Subcutaneous injection of 20 ml of 4% glucose solution with saline.

13.08.1962. The condition is good. The animal is playful. Runs fast chasing the cats, sparrows, healthy dogs. Does not drink much. Ate 300 g of meat. Eats sugar. On the left, intermittent **wheezing** is heard at auscultation over the pulmonary fields, and there is **a slight dulling of percussion sound**. < ... > 200 ml of 4% glucose solution with saline and 750,000 IU of penicillin were administered subcutaneously.<...><...>.<...>

14-18.08.1962. <…> Twice daily subcutaneous injections of 250,000 IU of penicillin were administered.

20.08.1962. t rect. is 38.4°C in a resting position (immediately after running during a walk t rect. was 40.3°C). The native heart rate is 120/min that of the transplanted heart is 118/min. Respiration rate is 36/min. Cough. **Intermittent dry wheezing over the pulmonary fields on both the right and left** sides. The appetite is good. 180,000 IU of penicillin, 180,000 IU of streptomycin, and 140,000 IU of mycerin were administered" [2, pp. 7-11].

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[7] Permyakov N.K. (1925-1999), a Soviet and Russian physician, pathologist, Honored Scientist of the RSFSR (1978), Laureate of A.I. Abrikosov Prize of the USSR Academy of Medical Sciences. (1983), the USSR State Prize winner (1984), Full Member of the USSR Academy of Medical Sciences – RAMS (1988), Director of the Institute of Human Morphology of the USSR Academy of Medical Sciences (RAMS) (1988-1999). Meanwhile, from 1951 to 1999, he was the lecturer at the I.M. Sechenov 1st Moscow Medical Institute and worked at the N.V. Sklifosovsky Research Institute for Emergency Medicine (Physician, Senior Researcher, Head of the Department of Pathomorphology with Electron Microscopy, Consultant). Publications in the field of general pathology, morphology of visceral organs in various diseases (specifically, in sepsis), pathology of extreme conditions (critical care pathology).

2 months after surgery

Two months have passed since the operation. During this time, a lot of new events happened in the lives of Grishka and V.P. Demikhov. The dog was taken out almost daily to the yard, where the animal chased sparrows, cats and dogs (Fig. 8). Grishka was constantly bothered by the fistula with purulent discharge, cough began appearing periodically; wheezing was heard at auscultation over the left half of the chest, and a dulling of the percussion sound was noted. Antibiotics had to be resumed.

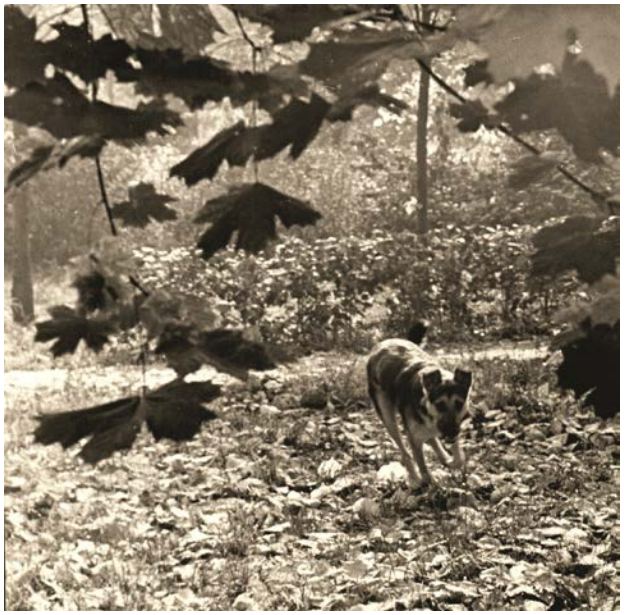

Fig. 8. Grishka on a walk. 1962 [From the collection of the Russian Museum of Medicine of the N.A. Semashko National Research Institute of Public Health. Inv. No. RMM VS 133/24]

But all this was nothing compared to the fact that Grishka became a celebrity. Doctors from Romania, Venezuela, and France, foreign delegates of the VIII Anti-Cancer Congress and foreigners who visited the

N.V. Sklifosovsky Institute at other years, all wanted to see the dog and take a picture of it. Among the Soviet specialists, Grishka was seen by surgeons from the Institute of Thoracic Surgery of the USSR Academy of Medical Sciences and by doctors from Yakutsk; by M.M. Tarasov, Director of the N.V. Sklifosovsky Institute, and other Institute staff: Professor B.A. Petrov, the Head Surgeon, pathologist N.K. Permyakov, and Professor-gynecologist M.S. Aleksandrov.

However, it is surprising that all of them *looked* at Grishka, but no *one examined him*. In any case, there is no record of anyone examining him *as a patient* in the diaries. There is also no record that he was tested for blood and urine, X-rays were taken, and that Grishka was consulted by specialists. Especially his condition would be interesting to immunologists, because for some unknown immunological reasons, Grishka kept on living.

"**21.08.1962.** The condition is good. <…>

22.08.1962. The status without any special changes. t rect. is 39°C. Respiration rate is 48/min. The native heart rate is 128/min, the one of the transplanted heart is 128 /min. subcutaneous injection of 125,000 IU of penicillin, 125,000 IU of streptomycin, 100,000 IU of mycerin was made. Eats meat and sugar willingly. Rare cough. **Had shortness of breath after running.** The dog was restricted to running. They began to take the dog out into the yard on a leash. **The dog was seen by an Indian professor and the Director of the Institute Tarasov M. M.. An Indian professor photographed the dog.**

23.08.1962. The condition remains the same <...>.<...>

24.08.1962. N.K. Permyakov saw the dog [for the third time]**.** <...><...>

25-29.08.1962. The condition is good. The dog is active. the appetite is good. <…> I ate meat, brown bread, and cheese curd. Runs fast, jumps, stands on its hind legs and puts its front legs on the chest of laboratory employees. < ... > Daily < ...>since 20.08 received antibiotics (penicillin, streptomycin, micerin). <…>

30.08.1962. The dog was seen by the Director of the Institute Tarasov M.M. <...><...>

31.08.1962. t rect. is 38.5°C. Respiration is 40/min. **There was a cough and wheezing in the area of the transplanted lungs.** During the day, 500,000 IU of penicillin and 500,000 IU of streptomycin were administered twice. The pulse from the transplanted heart is clearly palpable on the left front leg. The transplanted heart is clearly auscultated.

01-10.09.1962. [Condition unchanged (good). Cheerful, running. The appetite is good. Physical parameters are normal. Periodically antibiotics were administered].

11.09.1962. The dog was seen by an Indian Professor Baliga[8], by **M.M. Tarasov, the Director of the Institute, by Professor P.O. Androsov.**[9] Professor Baliga was presented with an ECG from Grishka and a photo of the dog. The dog's t rect. Is 39°C. Respiration rate is 36/min. In the electrocardiography room of the Sklifosovsky Institute, **doctor Lidia Ivanovna Petrova** recorded ECG on the device "Elema" before dog's running and after running. A small amount of pus is released from the fistula. Behind the fistula (close to it), a dense swelling of a chicken egg in size appeared. The dog is in good condition. Runs around. It responds vividly to its surroundings.

16.30. The dog was shown to doctors from Guinea, Tarasov M.M., the Director of the Institute and the Novosti Press Agency (APN) photo reporters. By evening, Grisha became less active. He began limping on his left front leg, probably due to pain in the area of the fistula, in which depth there is the end of the wire from the electrode attached to the transplanted heart.

12.09.1962. <...> The discharge of pus from the fistula increased. The surface of the wound is sprinkled with streptocide and washed with hydrogen peroxide. <…>

13.09.1962. t rect. is 38.4°C. Respiration rate is 36/min. The transplanted heart rate is 108/min, and the heart rate of the native heart rate is 108/min. The swelling behind the

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[8] Baliga A.V. (1904-1964), an Indian surgeon and public figure, Professor, was the President of the All-India Society for Cultural Relations with the USSR. He was the Head of the Surgery Department in the Bombay University Hospital. He was a delegate of the XXVI All-Union Congress of Surgeons, made a presentation on Heart Surgery, he was elected an Honorary Member of the All-Union Society of Surgeons.

[9] Androsov P.I. (1906-1969), a Soviet surgeon, Professor. From 1943 to 1969, he headed one of the surgical departments of the N.V. Sklifosovsky Institute.

fistula increased, became more soft. The dog licks the surface of the fistula covered with a purulent film more intensively than usual. <…>

14-18.09.1962. [The condition is still the same. The dog is active. The appetite is good. The temperature, respiratory rate, and pulse of both the transplanted and native hearts are normal. 17.09. "**A small abscess has formed in the lower corner of the postoperative wound.**" Antibiotics were administered periodically]

19.09.1962. t rect. Is 38.6°C. The rhythm of the native heart is 120/min, and that of a transplanted heart is 108/min. respiration rate is 40/min. The condition is good. The dogs runs around. It jumps. Caressing. The dog was **filmed by doctor Petrovsky from the Sklifosovsky Institute.**

21.09.1962. < ... > The dog feels well, willingly takes food, runs, barks, does not get tired. Breathing is clear without coughing. **Reporters from the *Sovetskaya Rossiya* newspaper came for interviews.**

22-23.09.1962. t rect. is 38.7-38.8°C. Respiration rate is 28-32/min. The native heart rate is 116-129/min, the transplanted heart rate is 101-108/min. The dog's condition is normal.

24.09.1962. The condition is good. **The dog was seen by Professor Maisky**[10]**, the Director of the Institute of Biology, by Tarasov M.M., the Director of the Sklifosovsky Institute, by Kapichnikov M.M., a Researcher from the Institute of Biology, an English surgeon Kessel**[11] (Fig. 9).

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[10] Maisky I.N., a Soviet biologist, immunologist, Professor, Director of the Institute of Experimental Biology of the USSR Academy of Medical Sciences. Author of the monograph "On the biological foundations of anticancer immunity" (Moscow: Medgiz Publ., 1955).

[11] Kessel A.W.L. (1914-1986), Professor, University of London (UK).

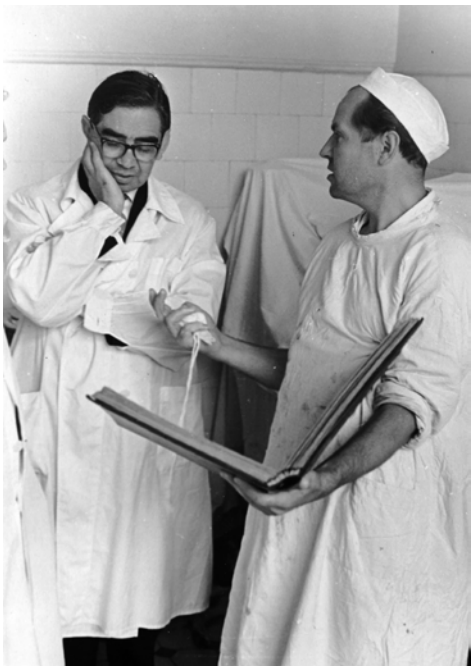

Fig. 9. Professor A.W.L. Kessel (Great Britain) in V.P. Demikhov's Laboratory 1962 [From the collection of the National Museum of the History of Medicine. Stradynya. Inv. № MVM Fototeka. Negativa № 15948. Riga, Latvia]

25.09.1962. t rect. is 38.4°C. The native heart rate is 140/min, the transplanted heart rate is 108/min. respiration rate is 32/min.

26.09.1962. t rect. is 36°C. Respiration rate is 34/min. The native heart rate is 126/min, the one of the transplanted heart is 110/min. The dog's condition is still good, and his appetite has not worsened. The fistula is open and the area around it has softened. Breathing with a slight wheeze. **The dog was seen by a Berlin reporter.**

27.09.1962. t rect. is 38.4°C. Respiration rate is 29/min. The heart rate of the native heart is 131/min, the transplanted heart rate is 106/min. The dog feels good, willingly takes food. **The suppurative sac of the fistula was deliberately opened. A purulent fluid was released.** 250,000 IU of penicillin, 500,000 IU of streptomycin, and 200,000 IU of mycerin were administered subcutaneously.

28.09.1962 (one hundred days). T rect. is 38.5°C. Respiration rate is 26/min. The native heart rate is 134/min, the transplanted heart rate is 104/min. The condition is good.

In the morning, the dog ran fast and hard (Fig. 10), which did not affect the health. Around the fistula during the night, a soft swelling formed again. The fistula site was sprinkled with streptocide [2, p. 11-16].

Fig. 10. Grishka 100 days after heart and lung transplantation. Photo by M.M. Razgulov. 1962. [From the collection of the Cardiovascular Surgery Museum of A.N. Bakulev National Medical Research Center for Cardiovascular Surgery]

100 days after surgery (September 28, 1962)

As indicated in the postoperative record of September 28, 1962, "100 days" had passed since the operation. From the point of view of transplantology at that time, this was an absolute victory. Such results were achieved by American surgeons only in the second half of the 1960s after the implementation of immunosuppressants (in particular, anti-lymphocyte serum). Once again, reporters of Soviet and foreign newspapers and news agencies were hovering around Grishka, and once again the "two-hearted" dog was visited by foreign surgeons and employees of the N.V. Sklifosovsky Institute.

Here is a quote from our previous article about Grishka:

"It was a sensation. <...> When the flow of journalists subsided, and the newspapers spread the news about the "double-hearted" Grishka everywhere, the Director of another Institute came to the Organ and Tissue Transplantation Laboratory of the Moscow Sklifosovsky Research Institute of Emergency Medicine. He examined Grishka for a long time, listened in silence to the explanations of Demikhov, the Head of the Laboratory, and then asked quietly:

– Do you realize what you've done?

Demikhov was taken aback.

– This is an atomic bomb for immunology!

Demikhov just shrugged his shoulders: what can I do? Of course, immunologists should study how the body defends itself against the invasion of an alien tissue; but what if Grishka's body does not want to defend itself against a foreign heart? [3]"

In that article published in No. 1 of the "Transplantologiya. The Russian Journal of Transplantation" journal in 2019, we expressed a regret of not knowing the name of this director. But, judging by the above data, it could be Professor I.N. Maisky, the Director of the Institute of Experimental Biology of the USSR Academy of Medical Sciences, who visited the Laboratory of V.P. Demikhov on September 24, 1962. Note that in the same note from which we took this quote, it is said that V.P. Demikhov as a lecturer of the All-Union Society "Znanie" demonstrated Grishka in the Polytechnic Museum, and the sounds of the two hearts of the dog were amplified through a microphone by loudspeakers.

"Knock-knock, knock-knock...", Grishka's own heart was beating. Fast and not very regular.

"Knock, knock, knock...", the second heart measured out clear beats. They were confident, full-bodied. Silence was bursted out with applause.

And at that moment, quite different sounds occurred to my mind. Those very ones that that shocked the whole world five years ago: "Beep-beep... Beep-beep... Beep-

beep..."

I listened to the heartbeats, and the signals of the first Soviet satellite were ringing in my ears. The coincidence was too startling! After all, the second heart is also a satellite. And if in 1957 the first satellite opened a new era, the era of space flight, then why Dr. V.P. Demikhov's experiment on the successful engraftment of another's heart could not have been the beginning of a new era in biology and surgery?" [3].

Unfortunately, the experience of Dr. V.P. Demikhov did not become the beginning of a new era in biology and surgery, and the document we found does not mention anything about the demonstration of the caudate patient in the Polytechnic Museum. Therefore, we cannot verify this fact.

All this is good, but what is the result? And the result is this. Recall that in early 1963, V.P. Demikhov wrote a letter to the Moscow City CPSU Committee, from where it got to the USSR Ministry of Health, which created a Commission to inspect the activities of V.P. Demikhov's Laboratory. By the way, that Commission included M.M. Kapichnikov from the Institute of Experimental Biology of the USSR Academy of Medical Sciences, and Professor I.N. Maisky was present at the Meeting of the Ministry's Board following the results of the Commission's work.

All this, as we wrote earlier [4], ended in nothing. And the outstanding result of the dog Grishka did not inspire anyone to search for the causes of his phenomenon.

But one of Grishka's visitors may have been more impressed than others. Let us recall the record of August 22, 1962, about the Indian professor's visit to Grishka. Twenty days later, on September 11, Professor Baliga from Bombay visited V.P. Demikhov. If he were the previous visitor, then he would have been recorded under this name for that visit. But we know that there was another Indian surgeon and scientist from Bombay,

visited the V.P. Demikhov's Laboratory; that was Professor P.K. Sen, who performed the 6th human heart transplantation in the world and the 1st one on the Asian continent on February 16, 1968 [5].

We read the diary further.

"**29.09-27.10.1962.** The condition is good. Jumps, runs, slightly limping on the left front leg when running. Willing to eat meat. T rect. is 38.4-39.1°C. Respiration rate is 28-42/min. The native heart rate is 108-129/min, the transplanted heart rate is 108-102/min. Breathing is clear. The pulse on the left front leg is well palpated. The condition of the fistula is the same. It was periodically washed and sprinkled with streptocide.

28.10.1962. The condition is good. The pulse from the transplanted heart is clearly palpable. The tones of the transplanted heart are clearly auscultated. **There is no discharge from the fistula. An abscess formed near it.** The appetite is good. T rect. is 39.1°C. Respiration rate is 40/min" [2, p. 16-17].

130 days after surgery (October 28, 1962)

Another month passed. Grishka's condition changed very little. He still led an active lifestyle, ate well, and took a lot of walks in the fresh air.

As expected, an abscess formed at the site of the fistula that was the consequence of non-performance of the wound surgical debridement in a timely manner. If a patient with a fistula in the area of a catheter fixed to the apex of the heart had received a proper management, then it should have been necessary to find out, at least, how deep the fistula extended, by using vulnerography, for example.

It is noteworthy that Grishka had no visitors in the past month. It seems that no one except V.P. Demikhov and his Laboratory staff was interested in the fate of the long-lived recipient.

"**10.29.1962.** The condition is good. T rect. is 39.3°C. Respiration rate is 50/min. The native heart rate is 120/min, the one of the transplanted heart is 110/min. **An abscess was opened on the left chest wall.**

30.10.1962. <...> The condition is still the same.

01.11.1962. Shot in a movie by the documentary film studio (cameraman is R.A. Belesova) On the night of 01.11.1962, an incident occurred. Mechanic Skrzhinsky in a drunken state broke the glass in the window on the 2nd floor in the room where the dogs were kept after the operation and climbed from the street. The doors were locked. The reason why he got in is not clear. After that, for several nights, the dogs spent the night in the next cold room, until the bars on the windows were made in the preoperative room (where the dogs were previously located).

02.11.1962. t rect. is 38.8°C. Respiration rate is 42/min. **When lying on the right side, breathing increases to 100/min. A cough appeared.** 500,000 IU of penicillin, 500,000 IU of streptomycin were administered subcutaneously in 2 injections each.

03.11.1962. t rect. was 39.4°C. Rare cough. **When lying on the right side, breathing becomes faster and reaches 100/min. Exhalation is difficult as with bronchial spasm** (Doroshchuk[12]). The pulse on the left brachial artery is palpable. The transplanted heart is auscultated. Breathing on the left is audible, but weaker than on the right. The tongue is bright red. A small amount of pus is discharged from the fistula. There was a single vomiting in the morning; vomit with mucus and bile. The reaction to the environment is lively. Runs with a slight limp on the left front leg. Plays with the dog "Sputnik", willingly ate chicken bones and meat. 1,000,000 IU of penicillin and 1,000,000 of streptomycin were administered in 2 injections each.

04.11.1962. Re-shooting by the documentary film studio (cameraman is R.A. Belesova). t rect. is 39.5°C. Respiration rate is 84/min. No cough. The native heart rate is 120/min, that of the transplanted heart is110/min. Pulse on the left brachial artery is weak. The dog runs, plays with other dogs. Ate meat willingly. 500,000 IU of penicillin and 500,000 IU of streptomycin were administered subcutaneously in 2 injections each.

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[12] V.P. Doroshchuk, an employee of V.P. Demikhov's Laboratory.

05.11.1962. t rect. is 39.2°C. Respiration rate is 66/min. The appetite is good. Live reaction to the environment. There is no discharge of pus from the fistula. 500,000 IU of penicillin and 500,000 IU of streptomycin were administered subcutaneously in 2 injections each.

06.11.1962. t rect. is 39.3°C. The native heart rate is 120/min, the transplanted heart rate is 120/min. Respiration rate 96/min. The dog runs, plays. The appetite is satisfactory. Pulse on the left brachial artery is weak. The sounds of the transplanted heart are muffled. 500,000 IU of penicillin and 500,000 IU of streptomycin were administered subcutaneously in 2 injections each.

07.11.1962. t rect. Is 39.2°C. Respiration rate is 70/min. The native heart rate is 120/min, the transplanted heart rate is 120/min. The pulse is weak on the left front leg. **The sounds of the transplanted heart are muffled.** 500,000 IU of penicillin and 500,000 IU of streptomycin were administered subcutaneously in 2 injections each.

08.11.1962. The pulse on the left brachial artery is not palpable. In the morning, when walking, the dog ran around the yard. The ECG recorded after the walk shows very rare altered QRS complexes from the transplanted heart. **The sounds of the transplanted heart were not heard at auscultation.** After several hours of rest **and intravenous administration of 2 ml of heparin**, the rhythm of the transplanted heart's contractions became more frequent and muffled tones began to be heard. At 17 o'clock, 1 ml of heparin and 20 ml of 40% glucose solution were administered intravenously. 500,000 IU of penicillin and 500,000 IU of streptomycin were administered in two injections each" [2, pp. 17-19].

142 days after surgery (November 9, 1962)

"**09.11.1962. The chest cavity was opened under morphine-barbamyl anesthesia and controlled respiration.** After examining the chest cavity, the dog was slaughtered. Before thoracotomy, 15 ml of a subcutaneous 1% morphine solution and 6 ml of an intravenous 5% barbamyl solution were administered" [2, p. 19].

The last 10 days of Grishka's life. Please note that on Saturday, November 3, while lying on his right side, the dog developed shortness of

breath up to 100 breaths per minute. From that day on, rapid breathing was recorded (from 66 to 90 respiratory movements per minute). All these days, Grishka kept a high temperature from 39.2 to 39.5°C, and the rate of the transplanted heart contractions increased acutely and almost equaled the rate of the native heart contractions (120 beats per minute).

Shortness of breath in the dog's position on *the right side* could indicate an impaired respiratory function of the lungs located in **the left half of the chest**, and tachycardia of the transplanted heart could indicate an impaired blood supply. However, no measures were taken to find out the causes of the growing cardiorespiratory failure: no electrocardiogram was taken, no X-ray was performed, and blood was not sampled for the white blood cell count.

On November 9, under anesthesia and controlled respiration (that is, the dog was intubated), Grishka's chest was opened (we believe that V.P. Demikhov operated on the dog). Grishka's autopsy report, quoted below, begins with a description of what he saw. Could the surgeon have done anything when he saw the dark color and hepatic density of the lower lobe of the left lung and the non-contracting transplanted heart? We believe that he could. For example, he could try to create an anastomosis between the vena cava of the donor's heart and the recipient's aorta, start a stopped heart, and then remove the affected lobe of the lung. But V.P. Demikhov preferred to withdraw the animal from the experiment. Most likely, in order to find out the cause of the transplanted heart arrest.

AUTOPSY REPORT

"**On** 09.11.1962 at **11.10**, in the presence of **N.K. Permyakov,** Doctor of Medical Sciences, the Head of the Pathologoanatomical Department of the Sklifosovsky Institute,

I.A. Chervova[13], an Associate Professor of the Histology Department of the II Medical Institute, the Candidate of Medical Sciences **Pafomov G.A.**, Researcher **V.M. Goryainov,** and **V.P. Doroshchuk** (the invited experts: Professor I.N. Maisky, the Director of the Institute of Biology of the USSR Academy of Medical Sciences, and Professor B.A. Petrov, the Deputy Director of the Sklifosovsky Institute were not present) **the chest of the dog Grishka was opened under anesthesia and controlled respiration.**

The native heart and right lung were functioning. **The transplanted heart did not contract. The lower lobe of Grishka's left lung and the lung transplanted with the heart did not inflate at controlled respiration.**

The lower lobe of the left lung of Grishka is of hepatic density, enlarged in size, airless, of a mottled appearance at section, against the background of gray hepatic density, there are many areas of black and red color, up to 2 centimeters in diameter. The gray part of the lung and dark red areas without the presence of gas bubbles at section are not yield to squeezing. **Three lobes of the transplanted lung are of uneven density, gray in color at section, with smaller (compared to the previous lobe) foci of red color**. Gray areas of the lung are compressible and a large amount of foamy liquid flows out of them. The transplanted lung is fused with fibrous adhesions to the lower lobe of the left lung and to the surrounding pleura of Grishka. <...> The transplanted heart is slightly enlarged in size compared to the preoperative period. Its epicardium is fused by fibrous adhesions with the pericardium at many sites, which outer side is tightly fused with the surrounding tissues of the dog Grishka.

At the site of the vascular suture of the graft superior vena cava with the pulmonary vein of the lower lobe of the recipient's left lung, there is a very good fusion covered with intima, without the presence of blood clots. The vascular suture of the graft aorta with the recipient's left subclavian artery is also in a very good condition, without signs of blood clots, and is well fused. At the sites of the

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[13] Chervova I.A. (1924-2016), a Soviet and Russian physician, morphologist and histologist, Professor, a student of T.A. Grigorieva. She was the Head of the Morphology and Histology Department of the MBF of the 2nd MOLSMI (now the Pirogov Russian National Research Medical University); she studied the structure of muscle and nerve components of the myocardium in animals of different species in the normal and experimental conditions. She published the monograph "The Heart as a self-regulating system "(Moscow: Meditsina Publ., 1968).

brachiocephalic artery and the left subclavian artery ligations, from the intima side on the aortic arch of the donor, parietal blood clots of gray color, tightly attached to the sites of transposition of the ligated vessels.

In the wall of the right atrium auricle of the transplanted heart, there is a site of diffuse hemorrhage for the entire thickness, dark red in color of about 1 cm^2 area; a black blood bundle with the volume of a walnut is glued to this site from the intima side, covering the mouth of the vena cava and blood access through the lower lobe of the left lung. A small area of hemorrhage in the adjacent chest wall of the dog Grishka approaches the site of hemorrhage in the auricle. The pulmonary artery (left branch), through which blood flowed to the lower lobe of Grishka's left lung, is free of blood clots.

The intima of large vessels and the endocardium of the transplanted heart are pale, smooth, shiny, and outwardly indistinguishable from similar tissues of a recipient dog. There is a small area of hemorrhage dark red in color under the endocardium of the left ventricle of the transplanted heart. The muscle of the right ventricle of the transplanted heart is thickened, its thickness being 5 mm, gray-red in color on the section, unevenly filled with blood. The muscle of the left ventricle of the transplanted heart is about 1 cm thick, of a dense consistency, pale pink-red appearance on the section, also insufficiently evenly colored, somewhat anemic, the surface on the section is shiny. The valves of the transplanted heart are pale, smooth, shiny, elastic, without visible abnormalities. <…>

The recipient's right lung is everywhere airy, fluffy, gray-red on the section, without visible abnormalities. The dog's native heart is about an average man's fist in size, fused to the pericardium on the right and left in some places by fibrous adhesions. Heart muscle, valves and endocardium are without visible abnormalities. <...> The spleen is in a contracted state, dense, pale red on the section, without pulp scraping. The liver and kidneys have no visible abnormalities, and are quite healthy in appearance.

Pieces of organs were taken for histological examination by Associate Professor I.A. Chervova.

A macropreparation of the chest along with two hearts, head and front paws of Grishka was taken for preservation in formalin" [2, p. 20-22].

Discussion

In 1962, in the USSR an event occurred that showed for the first time the probability of long-term survival after lung and heart transplantation. The dog Grishka lived with a second heart and a transplanted lung without immunosuppression for 142 days. In a very short time, the survival time of recipients with transplanted hearts will be calculated by many months. This will happen in the late 1960s, when effective and fairly safe drugs will appear to suppress the immune system of recipient's body. But in 1962, no one in the world achieved such results.

What caused the donor heart to arrest? It follows from the diary that "On the night of 01.11.1962<...> Mechanic Skrzhinsky in a drunken state broke the glass in the window on the 2nd floor in the room where the dogs were kept after the operation and climbed in from the street" What happened next, we do not know, but it is obvious that the dogs, including Grishka, suffered a lot of stress. It is possible that at that time there was an injury to the dog's chest wall in the area adjacent to it (fixed?) auricle of the right atrium. This is indicated by the phrase: "A small area of hemorrhage in the adjacent chest wall approaches the site of hemorrhage in the auricle." Bruising of the auricle led to transmural hemorrhage, in the place of which a blood clot began forming on the epicardium, starting from November 3; cardiopulmonary insufficiency (tachycardia, shortness of breath) began to increase, which led to a donor heart arrest on November 8. The changes in the transplanted lung were not fatal.

The reader may have three questions about the transplant technique. (1a) Why did V.P. Demikhov prefer to transplant the donor heart as a second, additional one, and not replace the biological heart with it? (2a) Why was the second heart included as an additional one in the arterial circuit, and not

parallel to its own one? (3a) Why was the second heart transplanted along with the lung?

The answers to these questions can be as follows. (1b) Transplantation of a second, additional heart, according to V.P. Demikhov, was more promising, since if this heart stopped due to rejection, it could be replaced with a new one, but the recipient would not die, since his own heart would work [6]. Paradoxically, for some reason this principle was not applied in the case of Grishka. (2b) Previously, V.P. Demikhov experimentally established that the blood return to the right heart took place owing to the contractility of the left ventricle [6]. Therefore, the inclusion of a donor heart in the arterial circuit makes it possible to use its contractility more effectively. (3b) Heart transplant together with a lung had a threefold purpose. First, the number of vascular anastomoses was reduced to 2 (vena cava and aorta). Second, the lung acted as a "trap" capturing blood clots that could form at the site of a proximally located veno-venous anastomosis. Third, it is known that mast cells of the lungs are able to produce heparin and, thus, reduce blood clotting, preventing thrombosis at the site of a distally located aorto-arterial anastomosis. As follows from the protocol of Grishka's autopsy, no blood clots were found at the site of vascular anastomoses.

About antibiotic therapy. V.P. Demikhov considered the infection prevention to be the main thing in organ transplantation, in addition to preventing thrombosis. For this purpose, during the postoperative follow-up, Grishka was administered: penicillin 20,105,000 units, streptomycin 20,465,000 units, colimycin 710,000 units. and mycerin 3,710,000 units. This number of drugs suggests that the supply of V.P. Demikhov's laboratory with these drugs, which were in short supply at that time, was sufficient. We consider the presence of a fistula with purulent discharge going into the

chest cavity to the transplanted heart, which was never surgically debrided, to be a negative background for the postoperative period. It is also possible that the injury in the area of the right auricle of the transplanted heart was caused by a fragment of the ECG electrode remaining in the chest.

A few comments about the autopsy procedure. Despite the fact that the autopsy was attended by Doctor of Medical Sciences N.K. Permyakov, the Head of the Pathology Department of the N.V. Sklifosovsky Institute, we believe that the autopsy of Grishka was performed by V.P. Demikhov who had many years of experience as a pathologist. He was assisted by his collaborators V.P. Doroshchuk and V.M. Goryainov. Associate Professor I.A. Chervova was invited to collect the material for histological examination. G. A. Pafomov was present as the Head of the N.V. Sklifosovsky Institute Laboratory, which was engaged in the collection of cadaveric material: blood and tissues. Director of the Institute of Experimental Biology of the USSR Academy of Medical Sciences I.N. Maisky and Chief Surgeon of the Sklifosovsky Institute B.A. Petrov did not attend the autopsy.

We repeat that the autopsy began under anesthesia under conditions of controlled respiration. And the first thing the audience saw was that Grishka's native heart was contracting, his right lung was breathing, and the transplanted heart with a lung and the remaining lobe of Grishka's lung were not functioning in the left half of his chest. Theoretically, V.P. Demikhov could have removed everything that was on the left, leaving Grishka to live with what was on the right. However, he, again, preferred to withdraw Grishka from the experiment.

First, the lower lobe of the left lung and the transplanted heart with a lung were studied. The lower lobe was in a state of numbness, the

transplanted lung fused to it showed signs of edema and inflammation, and a blood clot was found in the right auricle of the transplanted heart preventing blood from entering it. The vessels in the areas of the anastomoses were completely patent, and their complete acceptance was observed. No other visible morphological abnormalities were found.

Among the autopsy shortcomings, we note that the hearts and lungs were not weighed and measured. The site of the donor heart fixation to the chest wall is not described (the operation protocol says that "the heart of the graft is fixed to the recipient's chest wall"). The passage of the purulent fistula and the fate of the ECG electrode that caused it, which, apparently, was never removed, were not described. Finally, the external surface of Grishka's chest was not examined for the presence of trauma (edema, hemorrhage).

Conclusion

This article introduces for the first time the operation protocol, postoperative management diary and autopsy protocol of an animal (Grishka's dog) that lived with a second, additional heart and a transplanted lung without immunosuppression for 142 days, which is a unique observation in the world transplantology.

The following internal factors contributed to Grishka's long-term survival (142 days): the selection of a donor and recipient by blood type, a brilliant operator technique, careful monitoring and care in the postoperative period, proper feeding, administration (if necessary) of large doses of antibiotics. Immunosuppressants were not administered to the animal.

No immunological studies were performed on Grishka, and no histological data could be found, so the reason for such prolonged immunological tolerance remained unknown.

It is important to emphasize that the cardiac arrest of the transplanted heart, according to V.P. Demikhov, was not due to its rejection (macro-signs of the reaction, in particular, inflammation and infiltration, were not found at the autopsy), but due to the formation of a blood clot in its right atrium, which prevented blood flow to the heart. For the same reason, a venous infarction of the lower lobe of the recipient's left lung occurred, which aggravated the exsanguination of the donor heart. The cause of blood clot formation could be an injury caused to the heart by an electrode located in the chest or by an external blow to the chest wall of the animal at the site where the transplanted heart was fixed to it.

In our opinion, Grishka could have lived much longer with the transplanted organs. External factors may have contributed to this, for example, not only attention to this experiment from the press, but also help from the medical and academic communities. V.P. Demikhov could have saved the animal's life even after the cardiac arrest of the transplanted heart by removing it from the chest along with the affected lungs.

Despite the long-term survival of the animal with a transplanted heart and lung, its care in the postoperative period did not correspond to the complexity of the operation performed on it. This allows us to conclude that the implementation of the results obtained by V.P. Demikhov into the clinic was impossible in the early 1960s.

References

1. Glyantsev SP. Phenomenon of Demikhov. In the Sklifosovsky Institute (1960–1986). Scientific revolution in transplantation (1960–1964). Achievements of the USA and the USSR in the feld of transplantation and transplant immunity (1962). *Transplantologiya. The Russian Journal of Transplantation.* 2019;11(1):71–87. (In Russ.). https://doi.org/10.23873/2074-0506-2019-11-1-71-87

2. Book № 27. Laboratoriya transplantatsii organov NII SP im. N.V. Sklifosovskogo GUZM MZ RSFSR. Protokoly opytov. *Iz sobraniya Rossiyskogo muzeya meditsiny FGBNU «Natsional'nyy NII obshchestvennogo zdorov'ya imeni N.A. Semashko»*. Inv. № RMM KP 133/24.

3. Gushchev S. Chto eto? Proryv fronta biologicheskoy nesovmestimosti? *Tekhnika – molodezhi*. 1963;(1):32–34.

4. Glyantsev SP. Phenomenon of Demi-khov. In the Sklifosovsky Institute (1960–1986). Research Coordination Council of the USSR Healthcare Ministry: Missed opportunities. Part 1 (1963). *Transplantologiya. The Russian Journal of Transplantation.* 2019;11(3):244–258. (In Russ.). https://doi.org/10.23873/2074-0506-2019-11-3-244-258

5. Rowe HT. *Der Chirurg von Kapstadt.* München: Verlag R.S. Schultz; 1968.

6. Demikhov VP. *Peresadka zhiznenno-vazhnykh organov v eksperimente.* Moscow: Medgiz Publ.; 1960.

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