

TOP VIEW

Commemorating 50 years since the first heart transplantation in Bratislava – Czechoslovakia

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ABSTRACT

The first human-to-human heart transplantation in Czechoslovakia, and the 25th transplantation in the world, was performed in Bratislava, the second largest city in Czechoslovakia on July 9, 1968. The operation was carried out by a team led by Professors Karol Siska and Ladislav Kuzela at the second Surgical Clinic at the Comenius University of the Medical Faculty in Bratislava, Partizanska Street—only seven months after the first heart transplantation performed by Dr. Christiaan Barnard in Cape Town. Other members of the team in Bratislava included surgery recipients Siska, Kuzela, Pivkova, Holoman; surgery donors Schnorrer, Kuzela, Holoman; an extracorporeal circulation team of Treger, Carsky, Podolay; anesthesiologists Sobesky and Neumanova; operating room nurses Machkova, Homerova, Kralova, and operating room laboratory technician Malinova. The donor was P.V., a 46-year-old man, who suffered from a deadly brain trauma. The recipient was S.H., a 54-year-old woman with a failing heart, heavily affected diseased lungs, kidneys and liver. Her heart began to work, but lasted only for five hours. (Additional members of the team, Prof. Simkovic and Drs. Silvay and Sujansky were in the USA at the moment of transplantation, in Houston and New York, subsequently) (Tab. 1, Fig. 2, Ref. 62). Text in PDF www.elis.sk.

KEY WORDS: first heart transplantation in Bratislava, 2nd Surgical Clinic at the Comenius University.

Czechoslovakia

The first successful heart transplantation in former Czechoslovakia was performed many years later, in January 1984 by Professor Karel Firt at the Institute for Clinical and Experimental Medicine in Prague. The organ recipient lived for 13 years and died of the kidney failure.

Slovak Republic

In the independent Slovak Republic, the first heart transplantation was performed on March 21, 1998 at the National Institute of Cardiac Diseases in Bratislava under the direction of Professor Viliam Fischer. Heart recipient S.P. lived for 9 years and six months and died of the kidney failure.

The first human-to-human heart transplantation in the world

The first human-to-human heart transplantation in the world was performed in Cape Town, South Africa. The Groote Schuur Hospital, was placed in the front of the world's spotlight when Dr. Christian Barnard performed the first such operation there on

December 3rd, 1967. In 1967, South African laws allowed organ removal if the donor was declared dead by two physicians, one of whom had to be qualified to practice for more than five years. Neither of two physicians could have been on the transplantation team. The permission for surgery was also obtained from the relative and the coroner. The heart recipient was Mr. Louis Washkansky, a 54-year-old grocer, whose extensive coronary artery disease and three myocardial infarctions had left him with a terminally ill heart. The donor was Mrs. D.D., a 25-year-old ledger machinist, who suffered from a fatal brain injury after a car accident, in which her mother also died. Donor and recipient's blood groups were compatible and they shared a similar leucocyte antigen pattern.

The minute Barnard's team emerged from a nine-hour operation, the Groote Schuur Hospital in Cape Town became a focus of international attention.

The surgery was performed using the De Wall-Lillehei pump and bubble oxygenator for perfusion. The system was primed with six units of blood, diluted with crystalloids in 2:1 fashion. The patient was on mechanical ventilation for 25 hours. Mr. Waskansky remarkably improved following the transplantation—the signs of heart failure quickly disappeared with his edematous legs returning to the normal size by the third post-operative day. However, on day 13 after operation, Mr. Waskansky began showing the signs of pneumonia. His state gradually worsened and resulted in his death on December 21st, 1967—18 days after his operation. His new heart beat strongly until the end.

Additionally, Dr. Christian Barnard inspired by his first successful heart transplantation decided to repeat the surgery. On

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Tab. 1. The World's First 25 Heart Transplants.

Case	Date	Location	Hospital	Recipient	Donor	Surgeon	Outcome	References
1	12/3/67	Cape Town, South Africa	Groote Schuur Hospital	Louis Washkansky 54 M	Denise Darvall 25 F	Christiaan Barnard	Died 18 days, pneumonia	4,5
2	12/6/67	Brooklyn, NY	Maimonides Hospital	Infant 18 days M	Infant 2 days M	Adrian Kantrowitz	Died 6 h, metabolic acidosis	5,6
3	1/2/68	Cape Town, South Africa	Groote Schuur Hospital	Philip Blaiberg 58 M	Clive Haupt 24 M	Christiaan Barnard	Died 592 days, chronic rejection	5,7
4	1/6/68	Palo Alto, CA	Stanford University Hospital	Mike Kasperak 54 M	43 M	Norman Shumway	Died 15 days, multiple complications	5,8
5	1/9/68	Brooklyn, NY	Maimonides Hospital	Louis Block 57 M	29 F	Adrian Kantrowitz	Died 10 h, LV failure	5,6
6	2/16/68	Bombay, India	King Edward Memorial Hospital	27 M	20 F	Profulla Kumar Sen	Died 3 h, RV failure and pulmonary hypertension	5,9-11
7	4/27/68	Paris, France	Pitie-Salpetriere Hospital	66 M	23 M	Christian Cabrol	Died 51 h, pulmonary embolus	5,12
8	5/1/68	Palo Alto, CA	Stanford University Hospital	Joseph Rizzor 40 M	43 M	Norman Shumway	Died 3 days, RV failure, pulmonary hypertension	5,8
9	5/2/68	Houston, TX	Saint Luke's Hospital	Everett C. Thomas 47 M	15 F	Denton Cooley	Died 205 days, rejection after second transplant 11/21/68	5,13,14
10	5/3/68	London, UK	National Heart Hospital	Frederick West 45 M	25 M	Donald Ross	Died 45 days, pulmonary embolism	5,15
11	5/5/68	Houston, TX	Saint Luke's Hospital	James Cobb 48 M	15 M	Denton Cooley	Died 54 h, serum sickness	5,13,14
12	5/7/68	Houston, TX	Saint Luke's Hospital	John Stuckwisch 62 M	36 M	Denton Cooley	Died 8 days, multiple preexisting diseases	5,13,14
13	5/8/68	Montpellier, France	Cliniques St. Eloi	65 M	35 M	Eric Negre	Died 59 h, cerebral injury	5
14	5/12/68	Paris, France	Broussais Hospital	Damien Boulogne 57 M	37 M	Charles Dubost	Died 523 days, undetermined causes	5,16
15	5/21/68	Houston, TX	Saint Luke's Hospital	John Louis Fierro 54 M	17 M	Denton Cooley	Died 146 days, rejection	5,13,14
16	5/25/68	Richmond, VA	Medical College of Virginia	54 M	58 M	Richard Lower	Died 7 days, rejection	5,17
17	5/26/68	Sao Paulo, Brazil	Hospital Das Clinicas	23 M	41 M	Euricldes Zerbini	Died 28 days, rejection	5,18
18	5/31/68	Buenos Aires, Argentina	Clinica Modelo	54 M	47 M	Miguel Bellizi	Died 4 days, cerebral embolism	5
19	5/31/68	Montreal, Canada	Montreal Heart Institute	58 M	37 F	Pierre Grondin	Died 42 hrs, heart failure	5
20	6/1/68	New York, NY	New York Hospital	39 M	29 M	C. Walton Lillehei	Died 27 hours, heart failure	5
21	6/8/68	Dallas, TX	University of Texas SW Medical Center	46 F	26 M	Watts Webb	Died 3 hours, heart failure	5
22	6/28/68	Valparaiso, Chile	Hospital Naval Almirte	24 F	21 M	Jorge Kaplan	Died 132 days, chronic rejection	5
23	6/28/68	Montreal, Canada	Montreal Heart Institute	49 M	23 M	Pierre Grondin	Died 155 days, undetermined causes	5
24	7/2/68	Houston, TX	Saint Luke's	46 M	50 M	Denton Cooley	Died 268 days, undetermined causes	5,13,14
25	7/9/68	Bratislava, Czechoslovakia	Comenius University Hospital	54 F	47 M	Karol Sisaka	Died 5 hours	5

January 2nd, 1968, he transplanted a heart into P.B., a 58-year-old Cape Town dentist. A heart donor who suffered a massive subarachnoid hemorrhage. Mr. Blaiberg spent 73 days in the hospital post-surgery and lived for additional 18 months as an independent man with no physical limitations. He drove a car and even swam in the sea. Unfortunately, he died from a chronic heart rejection. From several other patients, Mr. D.V.Z. survived for 23 years after his heart transplantation.

In 1970s, the development of better antirejection drugs made heart transplantation more viable. Dr. Christian Barnard continued to perform heart transplantations and by late 1970s, many of his patients were living up to five years with their new hearts. Successful heart transplantations are being performed also today with the current problem of the shortage of organ donors.

Christian Neethling Barnard was born in Beaufort West, South Africa in 1922. His father was a Dutch Reform minister, and there were four boys in the family. He did well in school and went to study medicine at the University of Cape Town. After six years, he graduated and started his internship and residency at the Groote Schuur Hospital in Cape Town. He moved to the small town, Ceres and married his wife Outjie. The seeds of his future career were sown, when one of his patients delivered a baby boy with a heart defect, which could not be cured. The baby died, and it made Dr. Barnard think about the need for the heart surgical repair. He continued studying for his doctorate in Medicine, but heart surgery preoccupied him.

A turning point came a couple of years later when Dr. Barnard was offered a chance to work in Minneapolis, USA. The heart-lung machine, which was considered too

dangerous for surgical procedures until recently, improved and was ready to use in clinical cardiac surgery. Kidney transplantations were being successfully performed, and the idea of transplanting a heart occurred naturally. If it was possible with the kidney, why not with the heart?

Dr. Barnard learned much of surgical technique while studying in the USA. He spent three years in the University of Minnesota with Drs. Lillehei and Varco and later with the Stanford group led by Dr. Norman Shumway in Palo Alto, CA. After his three years in the USA, Dr. Barnard received an incredible gift from Dr. Wangenstein of the University of Minnesota, a heart-lung bypass machine and three-year financial support for developing of cardiac surgery in South Africa. In subsequent years, he visited the Soviet Union to discuss transplantation as well as USA to learn about the latest progress in transplantation and immunosuppression from Drs. David Hume, Richard Lower, and Thomas Starzl. Dr. Barnard came back to Cape Town, where he continued an extensive program of heart transplantation in animals and kidney transplantation in humans. On December 3rd, 1967, he performed the first human-to-human heart transplantation. Dr. Christin Barnard passed away in Cyprus, Greece on September 2001 from an acute asthma attack.

The original operating room in the Groote Schuur Hospital, where the first human-to-human heart transplantation was performed, has been turned into a museum in honor of the pioneers of transplantation medicine as well as the first donor and recipient.

I had an opportunity to visit the Groote Schuur Hospital in Cape Town twice. In March 1968, Dr. Kark, the Chairman of the Department of General Surgery at the Mount Sinai Hospital in New York (who himself was from South Africa) organized the visit for Dr. Litwak, Dr. Burrows, two Mount Sinai cardiologists and myself. Our medical group met Dr. Barnard and his second transplant patient, Mr. Blaiberg. In September 2014, I was invited to speak at the hospital by Professor Swanevelder, this time I was able to visit the heart transplant museum as well.

After the initial intensity of the media coverage of the heart transplantation, the press interest was directed towards clinical justification of such an expensive and high-risk operation. Many questioned whether all surgeons and hospitals, who had been attempting heart transplantations were equipped to do so. Dr. Cooley from the Texas Heart Institution at the St. Luke's Hospital, Houston, TX summarized his feelings about starting transplant operations himself: "My first concern was saving the lives of sick people, but it would be untrue to say that I was not eager to take part in heart transplantation, the most existing development of cardiac surgery. The delay of my entry into heart transplantation is easily explained. We couldn't find any donors, and we suspected that they were being purposely denied". In Houston, Dr. DeBakey and Dr. Dietrich started to transplant heart as well. All hotels in the area were full with the candidates waiting for the transplant. In less than a month, Dr. Cooley's team had ten and Dr. DeBakey's team performed five transplantations. Within one year since Barnard's first operation, over 100 transplantations were performed in almost 50 centers. The results were discouraging; almost 60 patients died by the eight post-operative days with the mean survival of less than 30 days.

Fifty-one years ago, as the first human heart was successfully replaced, the world learned how progress in science and teamwork in medicine culminated in triumph of humanity over death. Dr. Barnard's achievement was followed by a series of heart transplantations in the cardiac centers around the world, in nine countries across four continents. Twelve of the transplants were performed in the USA. Of the first 25 heart recipients, 22 were man and three were women with age ranging from 18 days to 66 years of age. Of the donors, 20 were man. Outcomes were variable, and the post-transplant survival ranged from three hours to 592 days. The most common cause of death was an acute graft rejection and ventricular failure.

The ethical view of the heart transplantation was concerned with the definition and acceptance of the brain death. In 1968, a U.S. ad hoc committee and commission was established to assess and report published (JAMA 205; 85 - 90) on the ethical, legal, social and political implications of medical advances, including heart transplantation. The work of this commission eventually led to the official definition of brain death.

Long before human-to-human heart transplantation

Long before human-to-human heart transplantation was ever imagined by the public, physicians, scientists, medical and surgical researchers worked on the scientific advances, which would lead to today's success in transplantation. The field of immunology was slowly evolving through the works of several independent scientists: Landsteiner's blood group typing, Ehrlich's discovery of antibodies and antigens, and Metchnikoff's theory of host resistance. By the end of 19th century, with the advances in suturing techniques, surgeons began to transplant organs in the experimental animals. There were learned problems with rejection, blood relationship and repeat transplantation between same donors.

The history of heart transplantation started in 1905, Drs. Carrel and Guthrie at the University of Chicago, implanted the heart of a small dog into the neck of a large dog. It was done without anticoagulation, the experiment ended after blood clotted. In 1950 Dr Demikhov, Soviet researcher described more than twenty different techniques for heart transplantation. His experimental work was done before heart-lung machine was developed. By 1960, Dr Lower and Shumway in the United States had established the foundation for heart transplantation as it is performed today.

The main discovery needed for open-heart surgery and human-to-human heart transplantation was the development of the heart-lung machine. Dr Gibbon spent over 20 years in research, advancing knowledge of artificial oxygenation and pumping. After the Second World War, he realized that he needed to involve more people in this research. He cooperated with the IBM, which helped to improve the function of artificial blood oxygenation. Such association was crucial for a final development. After many trials on dogs, Dr. Gibbon reported on May 6th 1953 the first successful utilization of the heart-lung machine for open heart surgery in human.

On January 24th, 1964, Dr. James Hardy of the University of Mississippi Medical Center transplanted the heart of a chimpanzee

into the chest of a dying patient - a human heart was not available. The chimpanzee heart did function in chest for 60 minutes.

On December 6th, 1967, Dr. Adrian Kantrowitz performed the world's first pediatric heart transplantation at Maimonides Hospital in the Brooklyn, NY. The infant's new heart stopped beating after seven hours and could not be restarted.

On January 6th, 1968, Dr. Norman Shumway performed the first adult heart transplant in the United States at the Stanford University Hospital. The patient died fifteen days after the operation following multiple complications.

On May 3, 1968, a team led by Sir Donald Ross performed the first heart transplant in the United Kingdom. Sir Ross later said: "We were excited about sewing in the heart, which in fact, when you think about it technically, quite a simple plumbing job," comparing heart transplantation to other cardiac surgical procedures. The heart recipient survived for 45 days.

In 1984, the world's first successful pediatric heart transplant was performed on a four-year old boy at the Columbia University in New York. The patient received a second transplant in 1989 and lived until succumbed to the other medical issues in 2006.

Despite a growing number of patients with the end stage heart failure, the annual volume of heart transplantation has been constant at 3,000-4,000 heart transplants per year for the last decade. According to the International Society for the Heart and Lung Transplantation registry, from January 2009 to June 2015, the leading diagnosis for the heart transplantation were non-ischemic cardiomyopathy (11,629 cases) and ischemic cardiomyopathy (8,223 cases).

The Department of Cardiovascular Surgery at Icahn School of Medicine at Mount Sinai, New York, NY. obtained the Certificate of Needs in 1991. Until present, November 1, 2018, 530 heart transplants were performed there (Tab. 1).

Parallel Progress behind the "Iron Curtain" Heart Transplantation in Eastern Europe and Bratislava, Czechoslovakia

It is difficult to describe and understand the enthusiasm of generation of the Slovak physicians for a development of cardiac surgery. The political problems in every day work and life, meddling between members and not members of the communist party was creating a suboptimal situation for research. The traveling out of Eastern Europe for the majority of population was rarity. Literature played the key role in the medical information and progress. However, an access to the foreign medical literature in former Czechoslovakia was limited. Internet did not exist. The diffusion of medical information was censored by the communist regimen as was the importation of surgical devices and instrumentation. The government did not have in plan to buy a heart-lung machine. However, such circumstances did not interfere with the group of the emerging physicians, led by Dr. Ivan Simkovic - Drs. Smrecansky, Schnorrer, Hubka, Kuzela, Silvay, Sujansky and Slezak (later all working at the Second Surgical Department and the Experimental Surgery at the Slovak Academy of Sciences in Bratislava) (Figs 1 and 2).

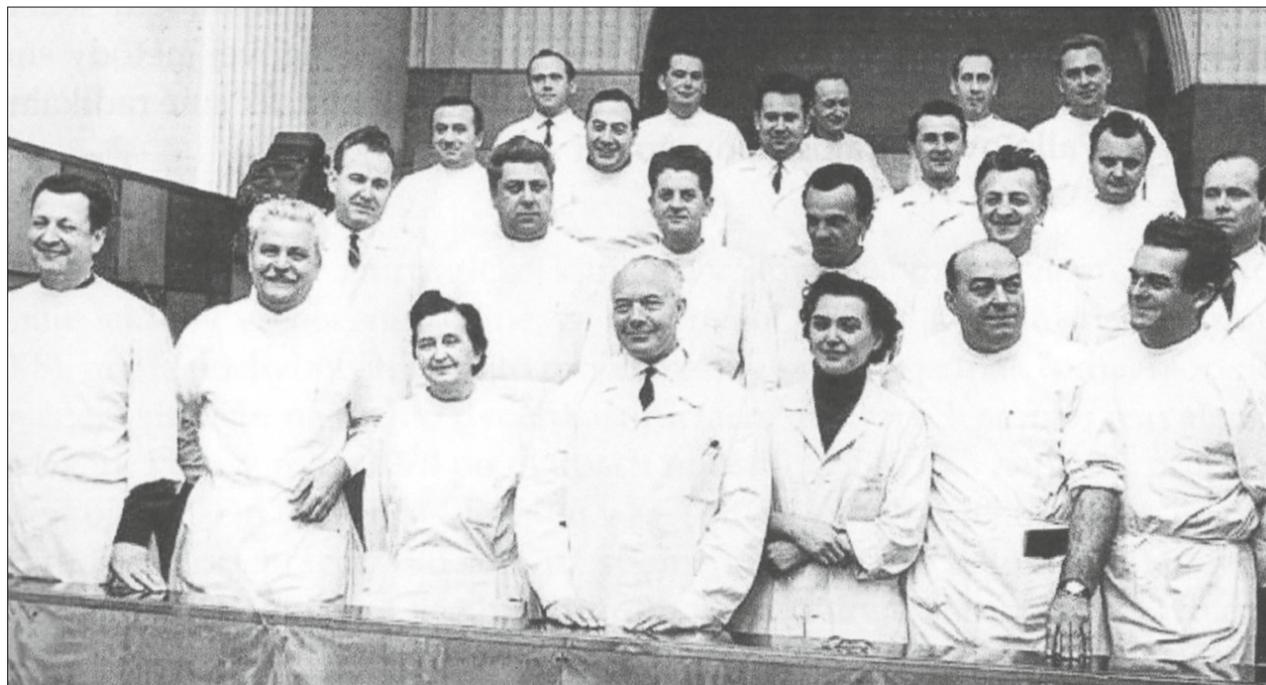


Fig. 1. The team of doctors on Second Surgical Department in the University Hospital in Bratislava. From the left in the upper row: Treger, Holoman, Licko, Mikulas, Kuzela, Sevcik, Cervenakov, Dimov, Silvay, Schnorrer, Krajcovic, Tumara, Trancik, Demjan, Misek, Oravec, Simkovic, Kostolny, Pivkova, Siska, Vanzurova, Hutan, Papp.



Fig. 2. Professor Silvay in an interview with President Kovac.

George Silvay was a laboratory technician at the First Surgical Department in the University Hospital, since he was not recommended to have a secondary education, because his father refused to join the communist party. He was recruited to Dr Simkovic's team as a laboratory technician, measuring oxygen saturation and hemolysis for testing artificial oxygenation. The research started at the Anatomical Department of the School of Medicine, where there was an available operating room for dogs. Simkovic very wisely convinced Professor Bolf from the Engineering Department of the Slovak Academy of Sciences for the collaboration to work on improving the function of the oxygenator and building a heart-lung machine. In 1956, Professor Simkovic was able to visit Paris and Stockholm, where he observed experimental and clinical work with the heart-lung machine and open heart surgery. After overcoming multiple technical issues, the Simkovic-Bolf heart-lung machine was built and set for an experimental evaluation. The extensive testing proved that the Simkovic-Bolf heart-lung machine was ready for a clinical use. The device became commercially available by Prema Co. and was utilized in several hospitals in the Soviet Union and Eastern Europe hospitals. Shortly after, the first successful open heart operation, with the Simkovic-Bolf heart-lung machine, for the closure of an intracardiac defect was performed on July 8, 1958 by a surgical team of Professor Karol Siska and professor Ivan Simkovic. It was the first successful open-heart surgery in Eastern Europe.

In 1959, Professor Siska performed the first open mitral valve surgery in Czechoslovakia utilizing the Simkovic – Bolf heart-lung machine. In 1969, the first coronary-artery bypass surgery with the heart-lung machine was performed by Professor Simkovic.

For the aortic and mitral valve replacement, the Simkovic – Bolf heart-lung machine was utilized routinely.

A reconstruction of the Evangelic hospital in Bratislava into the Second Surgical Clinic of the Comenius University was accomplished under the craftsmanship of Professor Karol Siska. He was able to arrange to build an additional floor, which became home for the Institute of Experimental Surgery of the Slovak Academy of Sciences. The institute was providing an exclusive possibility with an operating room and space for experimental surgery, postoperative

care and evaluation of the experimental animal. The situation was ideal for cardiac research, heart transplantation and complex cardiac valve and aortic surgical procedures. A series of experimental projects led to the development of an advanced clinical surgical practice, culminating with the ability to perform dog-to-dog heart transplantation. Dr. Hubka was a leading surgeon of the project for heart transplantation on dogs. His team was able to transplant a heart from a related dog and use blood from a donor to prime a heart-lung machine. In May 1968, they transplanted a series of dogs, survived over 1/2 year after surgery. One dog, named Strelka, survived over 10 months. During the occupation of Czechoslovakia on August 21, 1968, Dr. Hubka rescued Strelka to his home. Important histopathological studies were continuously performed by Dr. Slezak.

Professor Simkovic summarized all information about experimental and clinical cardiac surgery in his book entitled "Surgery of the Heart" published in 1996 with coauthors Fischer, Reich, Silvay and Vrsansky.

Conclusions

Heart transplantation has been established as the gold standard in the treatment of patients with end-stage heart failure around the world. Because of the stagnating number of available donor hearts, transplantation remains an option only for a limited number of patients. Mechanical circulatory support could become an alternative. Additional improvement in preventive medicine, discovery of newer immunosuppressive strategies, pharmacological treatments and application of new medical methods of treatment may improve the present situation. The future will use personalized medicine, where genomic and molecular science will determine customized treatment for optimal outcomes. The future is being challenged on all sides – recipients, donors, immunosuppression, tolerance, genomics and xenotransplantation. Only the future will provide a new explanation and will reveal new challenges.

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Received August 28, 2018.
Accepted November 11, 2018.