

## **The history of transplantation in the world and in Poland**

Kobus G.<sup>1\*</sup>, Małyszko JS.<sup>2</sup>

1. Department of Clinical Medicine, Medical University of Białystok, Poland
2. 1 st Department of Nephrology and Transplantology, Medical University of Białystok, Poland

### **ABSTRACT**

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Transplantation is the most spectacular success of medicine in the XX century. Transplantation became the effective and standard method of treatment of end-stage organ failure. It enable not only improvement of the quality of life, but prolong survival as well. How it was a long history dating back into the ancient times. Development of clinical transplantation was possible owing to the enormous progress in surgical techniques, invention of vascular anastomoses, knowledge of immunological mechanisms underlying tolerance and rejection processes, development of immunosuppressive therapy and multidisciplinary cooperation. We learnt

about the new techniques of assessment of HLA matching, preservation of retrieved organs, new immunosuppressive regimens, more efficient antirejection therapy and prophylaxis of complications, mainly infections. The future should bring the further development of clinical transplantation, however we should be aware of new challenges as xenotransplantation, stem cells or tissue cultures or even development of artificial organs cultured in the laboratories using human cells and tissues.

**Key words:** transplantation, pioneer, history

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#### **\*Corresponding author:**

Grażyna Kobus MD  
Department of Clinical Medicine, Medical University of Białystok  
ul. Szpitalna 37  
15-295 Białystok, Poland  
Tel.: 85 685 5060  
e-mail: g.kobus@wp.pl

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Organ transplantation has revolutionized medicine, it gave an opportunity not only to improve the quality of life, but also extended the life of many patients. However, for it to happen, transplantology has come a long way. Its history dates back to ancient times.

The first mention of the attempts to transplant various parts of the body comes from China, among others. Under anaesthesia induced by strong wine, Chinese surgeon Tsin Yue-Jen (407-310 BC) performed heart transplantation in a soldier using the organ, which had been collected from another soldier; surgeon Hua-To (136-206 BC) grafted various abdominal organs under herbal anaesthesia. In ancient Egypt and India, skin grafts were applied for various deformities of the nose or face. Descriptions of autologous skin transplantation within the face can be found in the books of the Hindu (Sushruta, 600 BC) [1].

Christ was among the first people of our era who performed organ transplantation. On the hill of Gethsemane, he reimplanted the ear of Simon Peter, which had been cut off by a sword, while Saint Mark reimplanted the severed arm of a Roman soldier (Luke 22, 51, John 18, 10). In modern times, Saints Damian and Cosmas, medics from Cilicia, living and practicing in Syria in the third century, transplanted the lower limb due to malignancy in a Christian. They replaced it with a healthy leg taken from a deceased Moor [2]. The procedure of leg transplantation was immortalized by many painters and sculptors. The picture presenting Saints Cosmas and Damian transplanting leg is now in the museum in Stuttgart, and both Saints are considered patrons of transplantation medicine. Also, Saint Agatha of Catania in Sicily, who died as a martyr in the year 251 at the time of the Emperor Decius, is considered a patron of transplantation. Before her death, she experienced extraordinary restoration of the severed breasts through miraculous healing by Saint Peter [3].

In the Middle Ages and Renaissance the attempts were made to transplant autologous skin. Gasparo Tagliacozzi (1546-1599) introduced the technique of phased transfer of the skin from the arm to the nose. At the same time, excellent Polish doctor, courtier of Stefan Batory, Wojciech Oczko (1537-1599) for the first time in our country performed successful reconstruction of the nose using skin grafting [1,3].

Nose transplantations began in the fifteenth and eighteenth century. Branca de Sicile (XV) "formed" a new nose of a master using the skin of his slave; the graft was rejected after the death of the slave. Garengot (1746) reconstructed the nose of a soldier from the fold of the skin taken from the shoulder. Molinelli (1750) reimplanted the nose, which had been cut off by an executioner in a Venetian, who wisely preserved his nose in a warm loaf of bread, while Dionis (1751) reimplanted the

nose of a jealous butcher's wife from Saint-Germain [4].

The Renaissance and Enlightenment saw both skin autografts and skin grafts from animals. In 1804 Giuseppe Baronio proved that the sheep skin can be transplanted to another location, but under the condition that it is the same animal. In 1869, in Geneva Jacques Reverdin used the skin auto-grafts to treat difficult to heal wounds and found that the use of small areas of the skin were most appropriate, because they were taken. In 1874, in Leipzig Carl Thiersch applied the free, thin, lobar skin grafts to cover the large area of burns [1].

The beginning of the twentieth century brought new experiences and discoveries, which had a significant impact on the future of organ transplantation. The first reliable report on organ transplantation in animals appeared at the turn of the 19<sup>th</sup> and 20<sup>th</sup> centuries. In 1902 Emerich Ullmann from Vienna performed the first xenotransplantation. He excised the kidney from a dog and placed it in a different location of the same animal body. This autotransplantation was successful, however, when Ullmann transplanted the kidney of one dog to another, the kidney stopped working. Later, he successfully transplanted the kidney from a dog to a goat [5]. French surgeon Alexis Carrel from Lyon continued the studies initiated by Ullman. In 1908, he performed the first successful autologous transplantation in a dog. He also transplanted the kidney in a rabbit and together with Charles Guthrie (1905) performed hepatotropic heart transplantation in a rabbit [6].

Alexis Carrel (1873-1944), who is considered the father of modern transplantation, made attempts to transplant organs in animals, but above all, his works led to the development of the technique of a surgical suture for blood vessels used in transplantation, for which he received the Nobel Prize in 1912. In addition, Alexis Carrel and Charles Claude Guthrie in 1905 proved that the animal's kidney transplanted to a different location of the same animal may work long and transplanted into another animal dies quickly [7]. The achievements of Carrel in a field of vascular surgery and transplantation gave rise to return to organ transplantations in humans. The attempts to transplant the animal kidneys to humans were initiated by Mathieu Jaboullay (1906) in Lyon and E. Unger (1909) in Berlin. However, these actions were unsuccessful. The kidney secreted a few drops of urine, next the renal function stopped and an animal perished. In autografting the kidney worked for a long time. At that time, however, doctors were unaware of a different immune reaction in interspecies transplantation [7]. The devastating effects of the First World War ceased transplantation research. It was only in 1936 when Russian surgeon Voronoy, after many attempts in animals, performed kidney transplantation in a woman with acute renal

failure, who had swallowed sublimate of mercury in order to commit suicide. Unfortunately, the procedure was unsuccessful because the patient died [8]. Further attempts to transplant the kidneys were also ineffective. The outbreak of World War II interrupted transplantation attempts. After the war, kidney transplantation was resumed. In June 1950 Richard Lawler, surgeon from Chicago, collected the kidney from a donor deceased due to liver disease and transplanted the organ to a 44-year-old woman with polycystic kidney disease. The transplanted kidney was placed in a site after the patient's removed kidney. The graft functioned for 53 days without immunosuppression. The subsequent kidney transplantations performed by Parisian surgeons Charles Dubost and Marcel Servelle Failure also failed. They made eight attempts of allografts but without success. [9]

Further development of transplantation was possible thanks to the knowledge of the pathogenesis of acute renal failure, research on corticosteroids and the use of 'artificial kidney' invented by Professor Willem Kolff. The invention of Kolff allowed to improve the prognosis in patients with renal failure. Kolff donated his first four devices to centres outside the Netherlands. These were the following places: British Post-Graduate School in London at Hammersmith Hospital, Mount Sinai Hospital in New York, the Royal Victoria Hospital in Montreal and a hospital in Krakow [10].

Transplantation of the kidney derived from a twin brother was another important event in the history of transplantation medicine, which is considered the beginning of the era of organ transplantation. On 23 December 1954, in Brigham Hospital in Boston, Murray, Merrill and Harrison performed kidney transplantation in a 23-year-old man with renal failure. The kidney was transplanted into the iliac fossa, while the ureter was implanted into the bladder. The patient survived eight years, during this time he returned to work, got married and became a father of two children. He died because of the recurrence of previous renal disease in the transplanted kidney [11]. Over the next few years, Brigham hospital successfully transplanted the kidneys between twins. Similar treatments also began to be performed in other centres: in Paris, Montreal and Portland, among others. Until the middle 70s of the twentieth century, 35 kidney transplantations were performed in twins [12]. Throughout this time, studies were conducted on the possibility of organ transplantation between unrelated individuals.

The immune system should be destroyed to avoid the rejection of the transplanted organ. This was done by irradiating the whole body with X-rays, because immunosuppressive drugs were unknown at that time. In 1961, in St. Mary's Hospital in London, azathioprine and prednisone started to be administered as immunosuppressive therapy in

patients after kidney transplantation, yielding more than one year survival in more than half of patients. The subsequent years saw the development of immunology and identification of the mechanisms of skin graft rejection as well as the formation of immune tolerance. The achievements of immunogenetics allowed for the introduction of transplantation antigens typing in a donor and recipient. These findings led to a rapid increase in the number of transplantation centres. A discovery of cyclosporine in the 80s was a milestone. This was a major breakthrough in immunosuppressive therapy, which opened the way for the transplantation of other organs. However, before a discovery cyclosporine, the attempts were made not only to transplant the kidneys, but also the heart and lungs.

In Poland, on 26 January 1966, the first kidney transplant was performed. The operation was carried out by Professor Jan Nielubowicz at the First Department of Surgery of Medical University in Warsaw. At that time, it was 621st such operation in the world. The kidney was collected from the patient after a serious accident (brain injury). The collection of the kidneys required the consent of a prosecutor. This consent was obtained by the Clinic. Danusia Milewska, a 19-year-old student of the school of nursing was a recipient. However, six months later the patient died because of infection (with normal renal function). Apart from steroids, there were no other immunosuppressive drugs - she received very high doses of prednisone [13].

The 60s of the twentieth century were a turning point in the history of transplantation in the world. It saw a number of successful transplants. There were also attempts of transplantation of the lung and heart of a chimpanzee. James Daniel Hardy was the first man in the world who performed heart transplantation in a human. In 1964, a 67-year-old Boyd Rush, who had suffered another heavy heart attack and the consequently cardiogenic shock, was admitted to the cardiology department of Mississippi University Medical Centre in Jackson. The operation was performed on 23 January 1964. The implanted heart was collected from a chimpanzee. Although initially it started to work, its activity lasted only a few minutes. The first heart transplantation failed, because the patient died 90 minutes after surgery [14,15]. The failure of the surgery did not halt further attempts of heart transplantation. In December 1967, in South Africa, in Groote Schur Hospital in Cape Town, Dr. Christiaan Barnard performed the world's first successful heart transplantation. A 53-year-old Louis Washkansky with end-stage heart failure and the history of three myocardial infarctions was a recipient. The heart was collected from a 25-year-old woman. The treatment was successful and caused incredible euphoria around the world. However, pneumonia developed 15 days after the treatment. The patient died on 21 December, after 18 days of

living with the transplanted heart [16]. On 2 January 1968, Barnard performed the second heart transplantation. The treatment was successful, the patient was discharged home in March – he lived with the transplanted heart for 19 months. It was the beginning of a new era of cardiac surgery and a new chapter in transplantation [17].

In Poland, the first heart transplantation was performed by Prof. Jan Moll on 4 January 1969 at the Second Department of Surgery of Medical University in Lodz. Unfortunately, a heart recipient died a few hours after surgery. This procedure met with numerous objections, because the heart was collected from a donor in the state of brain death and the preserved circulation. At that time, there were no legal provisions for the recognition of brain death as equivalent to death. Many negative reactions dissuaded Prof. Moll from performing another surgery. It was not until several years later, on 5 November 1985, when Professor Zbigniew Religa from the Department of Cardiac Surgery in Zabrze carried out the second heart transplantation. A 62-year-old patient with extreme heart failure due to cardiomyopathy was a recipient. Unfortunately, the patient died after 6 days. Prof. Religa together with a team of doctors performed next four heart transplantations, three of them failed, and only the fourth was successful, the patient was discharged home in a good condition after 4 weeks [18]. This gave rise to heart transplantations in Poland.

In addition to heart transplantations, the 60s saw the attempts of liver transplantation. The history of liver transplantation begins on 1 March, when the team of Prof. Thomas E. Starzl from Denver in the United States, for the first time performed liver transplantation in a child with biliary atresia. Unfortunately, this attempt was unsuccessful, as seven consecutive. It was only in July 1967 when the same surgeon made another attempt, this time successful. A 1.5-year-old girl with hepatocellular carcinoma was a recipient, she survived 13 months after surgery [19]. The first attempt to transplant to a child the reduced liver taken from a deceased adult donor took place in 1984. The year 1988 was another page in the book on liver transplantation, as it saw the method of dividing the liver taken from a deceased donor into two recipients - an adult and a child. Also, the year 1989 was relevant in the history of transplantation, because then the first successful liver transplantation from a related donor was performed [8].

The first liver transplantation in Poland took place in 1987 at the Department of Surgery of Medical University in Szczecin, and was carried out by Professor Stanisław Zieliński. Professor Piotr Kaliciński is a pioneer of liver transplantation in children, who since 1990 has been performing liver transplantations at the Children's Health Centre in Warsaw. Nine years later, in the same centre, with

the help of the French transplantation team, the first family liver transplantation was carried out [20].

The history of pancreas transplantation began on 16 December 1966 in Minneapolis, where Kelly and Lillehei simultaneously transplanted the kidney and pancreas. The patient did not require insulin treatment only for 6 days [21]. In Poland, the first successful simultaneous transplantation of the pancreas and kidney was conducted on 4 February 1988 by Prof. Jacek Szmidi at the Department of General, Vascular and Transplantation Surgery of Medical University in Warsaw. A year later, the professor with his team received the Ludwik Rydygier Prize – the highest surgical award in Poland - granted by the Association of Polish Surgeons. The patient survived almost 15 years after transplantation without insulin therapy and dialysis, she died of stroke [20].

Isolated islet transplantation is an alternative to the transplantation of the whole pancreas and is a safe surgical method, which does not overload the patient. In Poland, this method has been implemented by a team of doctors from the Department of General and Transplant Surgery of Military Institute of Medicine in 2008 [22].

First transplantation of the lung and heart was performed by B. Reitz of Stanford University in California, who in 1981 transplanted the heart and both lungs to a 45-year-old Mary Golke with primary pulmonary hypertension. The recipient lived until May 1986. Successful transplantation of the single lung was performed in 1983 by Dr. J. Cooper [14]. In Poland, the first transplantation of the single lung was carried out in Zabrze under the leadership of Prof. Marian Zembala in 1997. It was transplanted to a 32-year-old woman with an extreme form of respiratory failure in the course of severe lymphangiomyomatosis. At the same time in Szczecin, a team led by Prof. Thomas Grodzki transplanted a single lobe of the lung taken from a related donor. Unfortunately, none of these two treatments were completely successful. It was only in 2001, when Prof. Marian Zembala performed in Zabrze the first successful heart and lung transplantation in Poland in a 38-year-old patient with severe post-infarction heart failure and irreversible pulmonary hypertension. The year 2003 brought another success of the clinic in Zabrze, when a team led by Prof. Zembala successfully transplanted the single lung [23,24].

Two years later also in Zabrze, Prof. M. Zembala performed the first transplantation of both lungs in a 49-year-old patient, who was born with a genetic defect leading to the rapid development of chronic obstructive pulmonary disease.

Upper limb transplantation have been performed since 1997 in nine centres in the world [25]. The first hand transplantation in Poland took place on 2 April 2006 in the Saint Jadwiga of Silesia

Hospital in Trzebnica. It was carried out by a team under the leadership of Professor Jerzy Jabłecki. The recipient, a 32-year-old man returned to work after 16 months of treatment [26]. Since then, six successful hand transplantations have been performed. In June 2010, also under the leadership of Prof. Jabłecki, both upper limbs were transplanted at the level of the shoulder. The procedure was done in a 56-year-old woman, who had lost the limbs in a traffic accident. [27] Limb transplantation is an example of a complicated tissue grafting, which is associated with the transplantation of a complex of tissues such as the skin, muscles, tendons, blood vessels, nerves, bone marrow and lymphatic system components. This new method of reconstruction was created thanks to an effective combination of the microsurgical techniques with the latest developments of transplantation immunology. In clinical practice, upper limb transplantation has very good cosmetic, functional and psychological results [28].

Transplantology does not only involve the transplantation of organs and limbs, but also stem cells. The idea of treating with the bone marrow was born in the twentieth century. Undoubtedly, the laurel of priority in this regard should be given to the three scientists: Osgood, Riddle and Mathews, who in 1939 described the first intravenous transfusion of the bone marrow. In 1938 the Poles: Jan Stefan Raszek and Franciszek Groer, practicing at the Jan Kazimierz University of Lwow, performed the first bone marrow transplantation. The procedure consisted in the intramedullary administration of the healthy bone marrow. To do this, the bone marrow was collected from healthy donors and injected to the sick, unfortunately, the treatment failed. Because of the outbreak of the Second World War, they stopped further research, and described their method only in 1948 [29]. The first attempts of allogeneic bone marrow transplantation in humans were made in the 50s of the twentieth century. The successful bone marrow transplantation in humans (from a related donor) was carried out by a team of E.D. Thomas in 1957 in New York [30]. The year 1969 saw the first successful attempt of allotransplantation from a sibling. Ten years later, the first transplantation from an unrelated donor was carried out in a 10-year-old girl diagnosed with leukaemia [31]. In Poland, the first successful bone marrow transplantations were performed in Warsaw by Prof. Witold Jędrzejczak in 1984 - allogeneic in a child with Fanconi's syndrome, and in 1985, autologous. The first transplantation from an unrelated donor took place in 1997 in Katowice (Prof. J. Hołowiecki), and the first simultaneous transplantation of the bone marrow and umbilical cord blood was done in 1996 by A. Lange (Wrocław) and Prof. W. Jędrzejczak (Warsaw) [30]. The first transplantation of umbilical cord blood from an unrelated donor was carried out in 2000 by Prof. Jacek Wachowiak. The first

simultaneous transplantation of two units of umbilical cord blood, which had been collected from two different donors, was carried out by Professor Jędrzejczak in 2003 in Warsaw [32].

A beginning of the twenty-first century brought further progress in the development of transplantation. A team of surgeons under the leadership of Professor Jean-Michel Dubernard and Professor Bernard Devauchelle carries out in Amiens (France) on 27 November 2005 the world's first partial face transplantation in a human. The transplantation covered only the fragments of the face, including the nose and mouth, among others. Three years later (2008), in Cleveland in the United States a Pole, Dr. Maria Siemionow transplanted more than 80% of the face together with the palate, nose, cheeks and eyelid. The year 2013 was special for the development of face transplantation in Poland. In May 2013, at the Oncology Centre in Gliwice, a team of surgeons led by Prof. Adam Maciejewski performed the first Poland's face transplantation. The procedure was carried out in a 33-year-old man, whose face had been damaged. In this case, transplantation was not only a cosmetic procedure, which prevented from permanent defacement, but a life-saving surgery. The operation, which was performed at the Oncology Centre in Gliwice by a team led by Prof. Adam Maciejewski was the world's first face transplantation carried out in order to save life. The first Polish face transplantation has been recognized the best world's reconstructive surgery of the year 2013. On 4 December, the same team performed the second face transplantation in Poland. The procedure was carried out in a 26-year-old woman, who since birth suffered from neurofibromatosis type I. The disease made it impossible for the patient to function normally. The treatment was also successful.

Transplantation is one of the most spectacular medical achievements of the twentieth century. Organ transplantation has become an effective and routine treatment for patients with organ failure. Before it happened, medicine has come a long way, it required effort and hard work of many people. The progress of transplantation became possible thanks to the development of surgical techniques, understanding of the immune response mechanisms, the use of new immunosuppressive preparations and close cooperation of many specialists. The new histocompatibility testing techniques appeared and the ways of storage of the collected organs improved as well as the immunosuppression methods. Moreover, the process of rejection began to be diagnosed earlier and effectively treated. Also, the methods of preventing infections and treating complications ameliorated. What the next years will bring to transplantation? In the face of permanent shortage, will the organs bred in laboratories replace those collected from people or maybe xeno-

transplantation is our future? One thing is certain, transplantation medicine will continue to develop.

## Conflicts of interest

None declared

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