History of Organ and Cell Transplantation*

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Over the years, transplantation has fascinated the scientific community as well as the general public for a variety of reasons. The development of transplantation has involved almost all medical specialties. In the history of medicine, perhaps there is no other better example of so extensive a co-operation and exchange of knowledge and experience amongst basic scientists, surgeons and physicians in achieving a common goal.

1.1 HLA and Transplantation Immunology

The classic human skin graft experiments of Gibson and Medawar\(^1\) in 1943 demonstrated the immunologic specificity of allograft rejection — donor specific response, systemic immunity and immunological memory.

Scientific advances in the fields of immunology and genetics provided a fertile environment for the discovery and characterization of the human

major histocompatibility complex (MHC; in humans it is the human leukocyte antigen: HLA). Today, we know that HLA is a gene complex found in a four-megabase region on the short arm of chromosome 6. Three groups of major histocompatibility complex loci have been described: Class I, Class II and Class III. The first alloantibodies to Class I HLA were identified by Dausset\textsuperscript{2,3} and Miescher and Fouconnet\textsuperscript{4} in leukaemia patients who had received blood transfusions.

1.1.1 Initial use of cell culture methodologies to detect major histocompatibility complex (MHC) products

In 1964, Bain et al.\textsuperscript{5} and Bach and Hirschhorn\textsuperscript{6} reported that when mixtures of leukocytes from two unrelated individuals were cultured together for several days, large DNA synthesizing lymphoblasts appeared in the cultures. Bach and Hirschhorn\textsuperscript{6} suggested that quantitation of the degree of transformation in these cultures might measure the histocompatibility of recipient–donor combinations. These tests developed into what is now known as the mixed lymphocyte culture (MLC).

The World Health Organization (WHO) committee for HLA nomenclature is responsible for naming alleles and periodically publishing an update of new alleles. Regardless of the method used for HLA typing, the challenge continues to be the interpretation of results in light of the available sequence information.

1.1.2 Genomic organization of the HLA complex

The understanding of the HLA complex has been expanded with studies of the protein products and genomic analyses.

1.1.3 Organizations

Particularly beneficial to collaboration among early serologists was the establishment of a serum bank by the National Institute of Allergy and Infectious Diseases (NIAID).\textsuperscript{7} The National Institutes of Health (NIH) Serum Bank, housed at the NIH in Bethesda, Maryland, USA, and headed by Don Kayhoe, served as a repository for sera contributed by recipients
of NIH contracts specifically designed to procure typing reagents, as well as sera contributed by many other generous investigators. This repository provided start-up reagents to new typing laboratories and reference reagents for national and international workshops. It also supported training workshops for technologists and laboratory directors who were just starting new tissue-typing laboratories.

During the past half-century, knowledge of the structure, function and regulation of the HLA has increased at a rapid rate. Yet, its precise role in allotransplantation remains elusive and controversial. The genetic complexity of the MHC, the incompleteness of our knowledge of it, the great variety of antigens which it presents to the immune system, the interaction of the MHC with a myriad of other immune effector molecules (some of which are encoded by genes closely linked to the MHC Class I and Class II genes) – all of these factors (and more) greatly complicate our ability to fully understand the relative importance of MHC antigen-matching and avoidance of donor-specific anti-HLA antibodies for improving the likelihood of successful allotransplantation.

1.2 Organ Donation and Sharing

1.2.1 The early kidney programmes

The transplantation of the kidney paved the way for the transplantation of other organs. The first human-to-human kidney transplant was from a post-mortem donor to a sublimate-intoxicated female. Y.Y. Voronoy performed the operation in 1933 in the Ukraine. In the United States, David Hume started kidney transplantation in 1947, followed by three teams in Paris in 1950. Most of the transplants were cadaveric and for a short time successful, but for no longer than a few weeks. In France, the kidneys of a guillotined criminal were procured right after the execution and divided between two teams in two separate hospitals.

1.2.2 The exchange programmes

In 1967, the first international exchange organization, Eurotransplant, was founded in Western Europe. This exchange programme involved
West Germany, Luxembourg, Belgium and the Netherlands. There was no governmental involvement. The basis of the collaboration was the finding with HLA-typing that a good match gave a better result.

France followed suit in 1969 with the exchange programme Scandia-transplant and United Kingdom and Ireland Renal Transplant Consortium (UKIRTC) was created in 1972. An interstate kidney-sharing programme was established in Australia in the early 1980s.

1.2.3 The donors

The first human kidney transplant with long-lasting success was performed in 1954 in Boston, USA. The crucial point in this case was the fact that donor and recipient were identical twins, proven by skin transplants. The kidney lasted for eight years. The technique was the same as the one developed by the Paris teams in 1950: end-to-side artery and vein to the external iliac vessels and an ureteroneocystomy. This technique has survived until the present day.

1.2.4 Brain death

The concept of coma dépassé originated in France and opened the possibility to procure organs for transplantation while the heart is still beating. In 1963, the Belgian surgeon Guy Alexandre was the first to start coma dépassé, followed by the team co-ordinated by Hamburger in Paris in 1964.

1.2.5 The nonrenal organs

Successful liver transplantation only became possible when heart-beating donation became a reality and when cyclosporine, a stronger immunosuppressant drug, became available (1980 onwards). When a liver was too large for a small recipient, reduced-sized livers were used.

The heart has a special position in organ donation and sharing — only after the acceptance of the concept of brain death can heart transplantation become possible. Short preservation time restricts sharing and again there is
not much to win with matching for the heart transplant as matching does not affect success rate.

1.3 The History of Kidney Transplantation

1.3.1 1902–1912: Experimental efforts of Ullmann and Carrel

At the Vienna Medical Society meeting in January 1902, Hungarian surgeon Emerich Ullmann reported the first case of kidney transplantation, in which a dog’s kidney was implanted into another dog’s neck.\(^{11,12}\)

Also in 1902, French surgeon Alexis Carrel, apparently unaware of Ullmann’s work, published a paper in the journal *Lyon Médecine* entitled ‘The Operating Technique for Vascular Anastomosis and Organ Transplantation’.\(^{13}\)

In 1904, Carrel left Lyon for the United States. From 1905 to 1906, he worked in Chicago in close collaboration with Charles Guthrie, where the two investigators made significant contributions in the field of vascular grafts and organ transplantation.

1.3.2 1906–1913: Initial kidney transplants from animals to humans

The French surgeon Mathieu Jaboulay was the first to clearly document kidney transplants from animals to humans.\(^{14}\) In 1906, he transplanted the left kidney of a pig into the left elbow of a woman suffering from nephrotic syndrome. However, this graft failed because of early vascular thrombosis.

1.3.3 1936: First unsuccessful kidney transplant between humans

In 1936, in Kherson, Russia, Voronoy reported the first kidney transplant between humans using a cadaveric kidney.\(^{15}\) The recipient was a 26-year-old woman who was admitted in a uraemic coma after swallowing mercury in a suicide attempt. Voronoy retrieved a kidney from a 60-year-old man who had died from a fracture of the base of the skull.
1.3.4 **1943–1944: Medawar’s explanation of graft destruction due to ‘biological incompatibility’, as described by Carrel**

During World War II, the British Medical Research Council (MRC) focused on the problem of skin grafting for the treatment of burns. They asked Peter Medawar, an Anglo–Lebanese professor of zoology, to work with Thomas Gibson, a plastic surgeon, to attempt to perfect skin auto- and, if possible, allotransplantation in humans.\(^\text{16}\) In the laboratory, Medawar observed a persistent finding in experiments with mice or rabbits: if an initial skin graft was taken from animal A and placed on animal B, it survived for about seven days. Then, if a second skin graft was taken from animal A and placed on animal B in exactly the same fashion, it was destroyed in about half that period of time.

Medawar characterized this finding as the ‘second set response’ and defined its immunologic origin.\(^\text{17,18}\) Carrel’s description of graft destruction due to ‘biological incompatibility’ was now explained as rejection due to an immunologic response.

Medawar, in collaboration with Brent and Billingham, proceeded to unravel many aspects of tissue immunology. Medawar’s historic achievements established the field of modern transplant immunology, and he shared the Nobel prize in medicine with Sir Frank Macfarlane Burnet in 1960.\(^\text{18–21}\)

1.3.5 **1947–1953: Initial unsuccessful allotransplants after World War II**

In 1947, a young woman was admitted to the Peter Bent Brigham Hospital in Boston, USA. The decision to have her undergo a kidney transplant was made by a team led by David Hume.\(^\text{22}\) The hospital administration objected to the use of an operating theatre for such an experimental procedure, so the operation was performed in the middle of the night under difficult conditions, in a small room, using only two lamps.

In 1950, at the Presbyterian Hospital in Chicago, Richard H. Lawler replaced the left kidney of a woman who had a compromised prognosis because of complicated polycystic kidney disease. By six months post-transplant, the graft was completely destroyed. The recipient lived for some time with just her right polycystic kidney.
In January 1951, in Paris, two kidney transplants were performed on the same day by two different teams. Charles Dubost and Nicolaos Oeconomos used a kidney that had been retrieved from a prisoner immediately after his execution by guillotine.23 Later that same month, also in Paris, René Küss performed a kidney transplant in a 44-year-old woman with advanced renal failure.24 This case was most likely the first kidney transplant from a living donor.

1.3.6 1959: First successful kidney transplant between nonidentical twins

In January 1959, the first successful kidney transplant between dizygotic twins was performed, again at the Peter Bent Brigham Hospital in Boston, USA, by a team led by Murray.25

1.3.7 1960: First successful kidney transplant between nontwin siblings

In January 1960, the first successful kidney transplant between nontwin siblings took place at the Foch Hospital in Surenes, France, and was performed by a team led by René Küss.26

1.3.8 1960–1961: First successful kidney transplant between nonsiblings

In 1960 and 1961, at the Foch Hospital, Küss performed two kidney transplants between nonsiblings. An episode of rejection occurred at five weeks post-transplant. It was treated with low doses of total body irradiation, steroids and, based on the results of the experimental studies conducted by Roy Calne, 6-mercaptopurine, a new agent with a highly immunosuppressive effect in animals.27

1.3.9 1961–1962: First kidney transplants using azathioprine

Experimentation with 6-mercaptopurine began in 1959 in London, where Roy Calne demonstrated prolonged kidney graft survival in dogs.27
This drug was first used in humans in 1960, as a complement to initial total body irradiation.

1.3.10 1962: First successful cadaveric kidney transplant using immunosuppression

In April 1962, at the Peter Bent Brigham Hospital, Murray performed the first successful human cadaveric kidney transplant, using an immunosuppressive regimen of azathioprine and actinomycin C.\textsuperscript{28} The graft functioned for more than one year — a record for a cadaveric kidney at that time.

1.4 The History of Liver Transplantation

In the USA, in the late 1950s and early 1960s, two independent attempts at orthotopic liver transplantation in the dog were made. These were by Dr Francis Moore at the Peter Bent Brigham Hospital in Boston and by Dr Thomas Starzl in the Northwestern University of Chicago.\textsuperscript{29,30} As Starzl has pointed out, the Boston group were continuing their interest in organ transplantation following their unique and extensive experience of kidney transplantation, whereas in Chicago Dr Starzl was particularly interested in the metabolism of the liver and especially a comparison of systemic venous blood and portal venous blood entering the liver. A major obstacle in performing the orthotopic operation was the fatal result of clamping the portal vein and inferior vena cava (IVC) in the dog during the recipient hepatectomy.

The early cases of liver transplantation in Denver, where Starzl moved in 1961, proved to be formidable surgical undertakings. By October 1963, the Denver group had had no long-term success and had decided to have a moratorium on orthotopic liver transplantation, which lasted for more than three years. In 1967,\textsuperscript{31} the Denver group resumed orthotopic liver transplantation obtaining some long-term successes.

In 1968, Roy Calne achieved the first technically successful liver transplant in Europe.\textsuperscript{32} A lady with a primary malignant growth in her liver was referred to Calne. She was anxious to go through this new and experimental operation, even after she had been told the numerous dangers — she said
she had nothing to lose. Most of Roy Calne’s colleagues at Addenbrooke’s Hospital were opposed to him doing a liver graft for a variety of reasons. Then, on 2 May 1968, a child with a viral brain infection became comatose, with irreversible destruction of the brain stem.

Calne convened a meeting of his colleagues to discuss the case. That morning, Francis Moore had phoned him. By extraordinary good fortune, he happened to be in Cambridge visiting his son, a graduate student in molecular biology. Calne asked Moore to join the meeting. When the details of both the recipient and potential donor had been presented, Calne asked each of his colleagues for an opinion. They were unanimous in opposing the operation.

Calne introduced the world-famous Dr Moore, who, together with Starzl, was one of the pioneers in liver grafting. Moore’s response was short and typical of him: ‘Roy, you have to do it.’ Their patient woke up shortly after the end of the operation, and all were delighted. Sadly, two and a half months later, she developed a fatal pneumonia due to the immunosuppressive drugs given to prevent organ rejection.

### 1.5 Multi-Visceral Transplants

Multi-visceral transplants in which the liver is a component organ have figured experimentally and clinically over the years. With the introduction of cyclosporine there has been a number of attempts at intestinal and liver transplants, when the patient has had liver disease in addition to the need for small bowel replacement.

### 1.6 The History of Pancreas Transplantation

The idea of pancreas transplantation as a treatment for diabetes has been present ever since the disease was recognized as a deficiency of insulin secretion in the pancreas. In the 1920s, when insulin was isolated and parental administration for treatment of the disease became widespread, vascularization of pancreas allografts was also performed in dogs.

In the next few decades, various investigators worked out some of the surgical details of pancreas transplantation in animal models, thus setting the stage for clinical application.
1.6.1 Clinical chronology

The first human pancreas allograft was performed by doctors William D. Kelly and Richard C. Lillihei on 16 December 1966 at the University of Minnesota. The International Pancreas Transplant Registry (IPTR) was formed at the Lyon meeting in 1980. The progressive improvement in pancreas transplant outcomes over time has been well documented by the IPTR through annual reports. By 2000, more than 15,000 pancreas transplants had been reported to the IPTR, (80% from the United States), with more than 1,000 annually since the mid 1990s.

1.6.2 Evolution of recipient selection and programme development

In addition to the observations on secondary complications, studies in the 1980s documented an improvement in the day-to-day quality of life of a diabetic patient by the insulin independence induced by a functioning pancreas graft. Follow-up studies confirmed this benefit, providing an impetus to consider pancreas (or islet) transplantation at any stage of diabetes.

1.7 The Development of Islet Transplantation

1.7.1 The first successful islet isolation and transplantation

The transplantation of vascularized organs (such as the kidney) was gaining much attention by the late 1950s, with the phenomenon of allograft rejection documented and under intense investigation. The possibility of transplanting endocrine tissue (parathyroid) as a free graft was first investigated as a scientific endeavour by Russell, who raised the intriguing possibility that such tissue might show reduced immunogenicity. The improved yields of islets obtained using the collagenase digestion technique allowed Moskalewski (working with Hellman in Uppsala, Sweden), to report the first study of survival of transplanted isolated islets. However, the real credit for realizing the full potential of isolated islet transplantation goes to Lacy in St Louis, who took the collagenase digestion technique reported by Moskalewski and combined it with a pre-digestion process of intraductal distension with mechanical mincing of the pancreatic tissue in order to
improve the efficiency of the collagenase. Using this technique, Lacy and co-workers\textsuperscript{52} were able to obtain sufficient islets to demonstrate an effect on plasma glucose following isologous islet transplantation to the peritoneal cavity of streptozotocin diabetic rats. By today’s standards, these first islet transplants showed minimal function, but nevertheless the results were greeted with much excitement.

1.7.2 Development of techniques for identification, tissue culture and cryopreservation of islet tissue, and assessment of islet viability and function

A number of ancillary techniques developed over the years have been important in facilitating advances in islet isolation and transplantation. The ability to easily identify islet tissue \textit{in vitro} is a facility now taken for granted as the use of dithizone allows visualization of islet tissue, causing the zinc-containing islets to stain bright red. The affinity of dithizone for islet tissue was noted many years before it was rediscovered as useful in isolated islet identification.\textsuperscript{53,54}

For rapid islet viability assessment, many groups used dye exclusion techniques common to all tissue culture labs, but the use of supravital fluorescent dyes requiring active uptake provided a more accurate definition of viability and was first introduced and validated for islets by Derek Gray from Morris’ group in Oxford, UK.\textsuperscript{55}

1.7.3 Clinical islet transplantation

The ultimate goal of all the aforementioned experiments has been to successfully transplant islets into diabetic patients, producing as close to a true cure by replacement as it may be possible to get. Early attempts to achieve this goal using tissue obtained from techniques designed for rodent pancreas were uncritical in terms of definition of exactly what was being transplanted, and the results were very poor. Indeed, clinical islet transplantation more or less ceased (ignoring sporadic reports that were not repeatable) until a repeatable technique, which could regularly isolate large numbers of islets from the human pancreas, became available, with the aforementioned advances in automation.

Most reports of successful islet transplantation utilized several donors to obtain sufficient islets in order to obtain insulin independence, and
most of the centres took the approach of trying to reduce the number of donors required to one, the Giessen group being the most successful in this aim.56−59 However, the importance of being able to achieve insulin independence, albeit using multiple organ donors, was highlighted by the extraordinary interest generated from the report by Lakey and Shapiro from Rajotte’s group in Edmonton, who obtained insulin independence in seven consecutive patients by using islets from multiple donors, combined with a novel, steroid-sparing immunosuppressive regimen.60

1.8 The History of Intestinal Transplantation

1.8.1 The world experience

Between April 1985 and May 2001, 651 patients worldwide received 696 intestinal transplants at 55 centres,61 180 (28%) of which were performed at the University of Pittsburgh, USA. The number of centres involved and procedures performed increased each year. The kind of allografts used were isolated intestine (42%), combined liver–intestine (43%), and multi-visceral (14%). In children (61% of the recipients), the underlying diseases were gastrochisis (21%), volvulus (18%), dysmotility syndromes (18%), necrotizing enterocolitis (12%), intestinal atresia (7%) and microvillus inclusion (6%). For adults (39% of total cases), the indications for transplantation were intestinal vascular occlusive disease (22%), Crohn’s disease (13%), gastrointestinal neoplasms (13%) and trauma (12%). The retransplantation rate was 7% for children and 5% for adults.

1.8.2 The Pittsburgh experience

At the University of Pittsburgh, a total of 165 transplants were given to 155 consecutive recipients between May 1990 and February 2001. The actuarial patient survival for the total population was 75% at one year, 54% at five years, and 42% at ten years, with achievement of full nutritional autonomy in more than 90% of survivors.62

1.8.3 Future prospects

The emergence of intestinal transplantation has depended on the development of more potent immunosuppression, and particularly the advent of
tacrolimus. This progress has culminated in the qualification of these procedures for funding as a service by the US’s Health Care Financing Administration (HCFA) as of 4 October 2000. The further maturation of the field will almost certainly be contingent on better timing and more discriminating doses of immunosuppressants.

1.9 The History of Heart Transplantation and Heart Valve Transplantation

The possibility of human heart transplantation was first entertained in the early 1900s, starting with a heterotopic heart transplant performed by Alexis Carrel and Charles Guthrie in 1905 at the University of Chicago. Such experiments were performed to establish the techniques of vascular anastomoses. This first reported heart transplant was performed by transplanting a smaller dog heart into the neck of a larger dog. The transplanted heart survived for about two hours.

Orthotopic heart transplantation was first performed by Petrovich Demikhov in the early 1950s. He devised a method of sequential anastomoses to maintain both donor and recipient perfusion during orthotopic heart-lung transplantation without use of cardiopulmonary bypass.

1.9.1 Clinical heart transplantation in humans

The era of clinical human heart transplantation began in 1964 when James D. Hardy, at the University of Mississippi Medical Center, performed a chimpanzee-to-human orthotopic heart transplant. On 3 December 1967, Christian N. Barnard performed the first successful human orthotopic heart transplant at Groote Schuur Hospital in Cape Town, South Africa. The recipient survived for 18 days before succumbing to Pseudomonas pneumonia.

1.9.2 Heart valve transplantation

Early heart valve replacements were performed with crude mechanical valves that were highly thrombogenic. This led to the implantation of homografts, first inserted in 1962 by Donald Ross in London and Brian Barrett-Boyes in Auckland. In the 1960s and early 1970s, homografts were the biological valve of choice. However, there were difficulties in
harvesting as well as limited lifespan of the homograft. This stimulated further research efforts for alternative bioprostheses, paving the way for the introduction of porcine, and later, pericardial bioprosthetic valves.

1.10 Lung Transplantation

The world’s first human lung transplant was performed at the University of Mississippi Medical Center by Dr James D. Hardy in 1963. This procedure was performed in a 58-year-old prison inmate who was suffering from chronic infection, abscess and atelectasis formation in his left lung. The patient survived for 18 days and maintained excellent arterial oxygen saturations for the first week post-transplant. Immunosuppressive therapy had not been developed and was not used in this first human lung transplant.

1.10.1 Living-related lobar lung transplantation

The success of human lung transplantation has improved due to advancements in surgical technique, donor organ preservation, prevention and treatment of rejection, and management of infection. This has resulted in an expansion of recipient selection criteria and increased demand for donor organs. Starnes et al. have reported the results of eight patients with a variety of diagnoses, including primary pulmonary hypertension, post-chemotherapy, pulmonary fibrosis, bronchopulmonary dysplasia, idiopathic pulmonary fibrosis and obliterative bronchiolitis. Overall survival at one year was 75%. These results support an expanded role for living-donor lobar lung transplantation. Survival at four years post-transplant is approximately 50% for paediatric and adult lung transplant recipients combined. Continuing research efforts, donor and recipient selection and management, and clinical trials using a variety of new immunosuppressive agents will potentially improve the overall results of lung transplantation.

1.11 Bone Marrow Transplantation

1.11.1 Early attempts at BMT

The first published attempt at human bone marrow transplantation was by the doyen and Nobel-prize winner E. Donal Thomas in 1957. Although
this attempt was unsuccessful, it did demonstrate that large amounts of marrow could be safely infused intravenously.

1.11.2 The new era

In 1968, the team of Robert Good carried out a bone marrow transplant in Minneapolis based on results of histocompatibility tests in a child with severe immunological deficiency.69,70

The major clinical problems are finding histocompatible sibling donors, prevention of graft rejection, support care with blood products, antibodies antivirals and antifungals, prevention and treatment of graft-versus-host disease and veno-venous occlusive disease of the liver and longterm management of gonadal failure and sterility in adults.69,70

1.11.3 New developments

To obtain adequate amounts of bone marrow for transplantation, approximately one litre of marrow is removed from the iliac crest of the donor. This is a relatively cumbersome procedure and usually requires general anaesthesia.

1.12 Arm Transplantation

Earl Owen, world-renowned pioneer of microsurgery, first voiced the idea of a hand transplant more than 30 years ago in a speech at Edinburgh University, but it was not until the mid 1990s that he decided it was both technically and immunologically possible. The only reported hand transplant attempt had taken place in Ecuador in 1964 and had failed due to initial absence of any anti-rejection drug use, allowing immediate severe rejection.

With this in mind, and with encouraging results of successful skin, nerve and joint human transplants, he approached Nadey Hakim in 1998, who contacted the Royal College of Surgeons and the UK’s Transplant Service Authority to ask for permission for such an operation to go ahead. However, British authorities were unconvinced and had doubts about the ethics of the procedure for a single limb. They believed that putting a healthy patient on potentially dangerous immunosuppressants could not be justified at this stage, despite the long-term successes with experimental animal composite tissue transplants with a cocktail of recently proven powerful drugs.
Owen was keen to form a team of experts in preparation for the procedure, so Hakim suggested that he contact Max Dubernard, head of transplantation and urology at Lyon’s Edouard Herriot Hospital. Dubernard had carried out France’s first pancreas transplant in 1976 and was not only one of France’s top surgeons, but also a prominent local politician who ran his own hospital department. He was excited by Owen’s suggestion and agreed that the proposed forearm transplant could go ahead in his department in Lyon. Owen quietly began assembling a skilled international team composed of transplant, orthopaedic and hand microsurgeons, anaesthetists, a psychiatrist and a psychologist specializing in body image disturbances.

A gentleman called Clint Hallam was well known to Owen and was one of three people shortlisted for a hand transplant. Hallam, determined for many years to have the operation, had contacted Owen and confirmed his willingness to travel for the surgery anywhere, anytime.

The surgical team was drawn from around the world and therefore its members needed to agree on a time to convene and then wait for a donor to become available. The date was set for the beginning of September, 1998. The operation went very smoothly, and the team went on to perform the first successful double arm transplant — another global first. The recipient of the new hands, Denis Chatelier, was a 33-year-old house painter and father of two, whose hands were blown off when a home-made model rocket he was showing to his nephews exploded prematurely.

References

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15. Voronoy, Y. (1936). Sobre el bloqueo del aparato reticuloendotelial del hombre en algunas formas de intoxicacion por el sublimado y sobre la transplantacion del rinon cadaverico como metodo de lo anuria consecutiva aquella intoxicacion, Siglo Medico, 97, 296–298.


