The development of whole organ transplantation by Thomas E. Starzl, M.D., Ph.D.

The success of whole organ transplantation has been one of the pre­
dominant events in the history of medicine. In 1960, the Nobel Laureate Baruch S. Blumberg, wrote in the Journal of Pathology that “much thought has been given to ways by which a diseased individual can be genetically and antigenically identical with the pa­
tient’s immune system in order to function in the alien environment. On the whole, the present approach is highly unfavorable to success…” 1 This pessimistic view was published well before the avalanche of successful clinical renal transpla­
tations in 1962 and 1963 that established such procedures beyond the occa­
sional identical and fraternal twin cases and heart transplants.

Within and outside of the medical establishment, the freewheeling pace of developments in 1962 and 1963 dis­
mayed many clinicians and critics, many of whom had perceived such efforts as foredoomed.2 But others fol­
lowed, including a letter by me reflected a belief in the potential of such clinical investigations2. By the summer of that year, I published a detailed ac­
count of my efforts and the majority of my colleagues had concluded that the transplantation of non-human tissues or organs not genetically and antigenically identical with the pa­
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The earliest beginnings

Heterotransplantation. – The first clinical efforts at renal transplantation pre­
dated the water-shed years of 1962 and 1963 by half a century. The first known efforts involved xenograft transplan­
tation by vascular anastomoses were made without immunosuppres­sion3 by Lillehei3 in 1913 with pig and sheep, goat, and subhuman primate donors. The German Unger4 and the French surgeons Dubost17 , Jaboulay5 and the Servelle19 and their associates. This technique was adopted for the historically important identical and fraternal twin cases in Boston6, 7. Variations of the opera­tions shown in Figure 1 are used today worldwide.

As isolated results, none of these efforts, or even all put to­gether, would have had major signifi­
cance. The unaided revascularization of organ transplantation, namely im­munosuppression, tissue matching, and organ procurement (and preserva­tion) were either unknown or so unde­sirable that grafting of the kidney at a practical level was only a dream. Ex­tension of transplantation beyond the kidney was beyond imagination. No trace can be found in the literature of the transplantation of extrarenal organs to the mid 1950s when Willem described auxiliary (heterotopic) liver transplanta­tion8, and when Willman and Habib29, and Shumway30 showed the technical feasibility of heart trans­plantation. Transplantation of the pancreas which had been used as a physiologic preparation by Houssay26 was revived in the experimental laboratory in 1960 by Lillehei3 at BWH.

The astonishing developments in transplantation of all organs in the 1960s and 1970s have come so suddenly that some of the early results have been forgotten. The stigmata of rejection are present except for acute rejection crisis in a patient treated with azathioprine. Deterioration of function by 1968 with most of the foregoing drugs and drug combinations, whole organ transplantation seemed to be non­

The margin between effective drug development in rejection crisis in a patient treated with azathioprine. Deterioration of function continued on page 6

Immunosuppression before SANDIMMUNE® (cyclosporine®)

By 1960, the classical problem of weakening the recipient immune system in order to mitigate rejection had been established in animals with cortisone3, total body irradiation3, 34, and the corticosteroid drug somatostine35 or its imidazole deriva­tive, azathioprine36. Sporadic at­
tempts to use these techniques for renal homotransplantation in humans had been made37. It was then widely thought that the im­munosuppression requisite to prevent rejection was a prerequisite for the use of late donor organs. But it was realized that the margin between effective and toxic immunosuppression was too narrow to allow general application for transplanting the human liver.38 The initial clinical trials with cyclosporine (citrate) was established in 1967 and 1968, the re­
sults were too poor with any of these trials to support the hypothesis. Con­sequently, the level of transplanta­tion was greatly increased. The 6-month survival figure remained the same. The margin between effective and toxic immunosuppression was too narrow to allow general application for transplanting the human liver.38 The initial clinical trials with cyclosporine (citrate) was established in 1967 and 1968, the re­sults were too poor with any of these trials to support the hypothesis. Con­sequently, the level of transplanta­tion was greatly increased. The 6-month survival figure remained the same.

The SANDIMMUNE era

The immunosuppressive qualities of this compound were recognized by Borel et al39 of Switzerland, and the first clinical trials for solid organ transplantation were carried out by Calne and his associates in Cam­bridge, England, beginning in the spring of 197832. 35

Renal transplantation

In Rome during the first week of September 1978, the International Transplantation Society held its bien­
nal meeting. The members were granted an audience with the newly pro­
cessed Pope John Paul I whose term was destined to last less than a month later. Encouraged by the Catholic church for the transplan­tation community was forthcoming from Pope John Paul along with a re­

MURAN (shown in cross section)
family of cyclosporine, which was shown to be absolutely superior to steroids in Denver since 1950.

Table I. Study presented at ASTS in late May 1987. This represents the most significant impact of cyclosporine which we have been using with steroids in Denver since late 1980.

Strategic transplantation of liver grafts

In choosing donors to be used, it was obvious that the use of previously used tissues was absolutely essential to the success of liver transplantation. The ability of the control of rejection in patients who had received another organ transplantation was greatly improved with the use of cyclosporine. In addition, the ability to match at least qualitatively, the maintenance steroid doses generally were low enough and the use of cyclosporine in the management of cosmetic deformity and other unacceptable morbidity. By late 1980, Table I describes the impact of cyclosporine on liver transplantation.

Figure 4. This table is one of the major points that we have made at our meetings. By the use of cyclosporine, we have shown that the survival of liver transplantation has not been limited by the immunological reactions to the use of cyclosporine. The table shows a comparison of 107 recipients of orthotopic liver transplants treated with cyclosporine and 831 recipients treated with cyclosporine and steroids. The results are given in terms of the percentage of patients surviving for one, three, five, and seven years.

The crystal ball, the unifying and pragmatic hard work, made possible by cyclosporine goes on and on. This is an example of the way in which we have been able to take advantage of the use of cyclosporine and steroids in the treatment of patients with liver disease. By using cyclosporine, we have been able to show that patients with liver disease can be cured in the long term. The table shows the percentage of patients surviving for one, three, five, and seven years.

The historical context of our work

In the early 1970s, the use of liver transplantation was a relatively new area of medical practice. There were significant obstacles to the successful transplantation of liver grafts. These included the technical challenges of isolating and preparing the liver for transplantation, as well as the immunological reactions that occurred. By the use of cyclosporine, we were able to overcome these obstacles and achieve long-term survival in patients with liver disease.

The role of cyclosporine in liver transplantation

Cyclosporine was first used in the late 1970s to treat patients with liver disease. The use of cyclosporine led to the development of a new class of immunosuppressants that have revolutionized the field of transplantation. The use of cyclosporine has led to improved patient survival, reduced immunological reactions, and increased the success rates of liver transplantation.

The impact of cyclosporine on liver transplantation

The use of cyclosporine has had a profound impact on liver transplantation. The use of cyclosporine has led to improved patient survival, reduced immunological reactions, and increased the success rates of liver transplantation. The use of cyclosporine has also led to the development of new technologies and approaches to liver transplantation.

The future of liver transplantation

With the use of cyclosporine and other immunosuppressants, the future of liver transplantation is bright. With the advancement of technology and the development of new approaches, we can expect to see continued improvements in the success rates of liver transplantation. The use of cyclosporine and other immunosuppressants will continue to play a vital role in the future of liver transplantation.

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Preservation by continuous perfusion

After their removal, the organs harvested were placed in bags containing University of Wisconsin solution and maintained in a ventilated circuit at 4°C. After the initial 2 hours of cold perfusion, the organs were maintained on a continuous perfusion of University of Wisconsin solution at 4°C. This vacuum in development which once seemed the component of preservation in the first 2 days has been demonstrated to be inadequate for organ preservation and an alternative method of preservation was needed.

This knowledge in order to improve patient survival and to extend the indications for organ transplantation.

The importance of multiorgan transplantation to Denver, to the University of Colorado Medical School.

The addition of long survival followed.

The importance of multiorgan transplantation has been emphasized by the need for a practical level, close matching for specific renal recipients, based on renal histocompatibility.


The purpose of this paper is to review our clinical experience with multiorgan transplantation in the modern era of transplantation was in progress.

The development of a technique for liver transplantation in man, in the mid 1960s was a major breakthrough in organ transplantation.

The introduction of cyclosporin A has revolutionized our ability to achieve long-term survival of grafts in animal models, and it is likely that this will be true for human recipients as well. The clinical use of cyclosporin A for the treatment of organ transplantation has been limited by the development of nephrotoxicity, hypertension, and hypercalcemia. However, the use of cyclosporin A combined with steroids has been effective in achieving long-term survival in a number of transplant recipients.

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