History of Heart Transplantation

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While very early surgical reports documented the feasibility and safety of creating vascular anastomoses and transplanting solid organs in animal models [1], excision of a normal heart and its implantation in a recipient necessarily involve denervating the donor heart. The clinical field of heart transplantation could not exist until it was proven that a denervated heart could provide adequate circulatory support to allow normal physical activity in a heart recipient. Documentation of such physiology was first published in the early 1960s by the surgical pioneers in the field Drs. Norman Shumway and Richard Lower working in their research laboratory at Stanford University. They used the canine model and measured quite normal physiologic function in dogs with transplanted denervated hearts. Their surgical procedure was fairly simple and involved midatrial excision of both the left and right atria and of the great vessels just above their semilunar valves. This procedure was performed on both the donor and the recipient dog, and the donor heart was implanted into the recipient in the orthotopic position using the same suture lines. The recipient dogs subsequently had standard measurements of hemodynamics which were shown to be normal at rest and with exercise [2]. Such dogs were then seen to run and play normally for weeks, much to the satisfaction of the laboratory staff.

Simultaneous with this pioneering work, the field of kidney transplantation was beginning to flourish and to demonstrate the effectiveness of pharmacologic suppression of the immune system (then with azathioprine and prednisone) to prevent what was otherwise the inevitable rejection of non-human leukocyte antigen (HLA)-identical donor organs. These two converging developments set the stage for the introduction of clinical heart transplantation. At Stanford, an appropriate recipient with end-stage heart disease was identified by the surgical team and awaited the availability of a compatible donor heart from a brain dead individual. Much to the surprise of the team (and the world), the first clinical heart transplant was actually announced to have been performed in South Africa by Dr. Christian Barnard on December 3, 1967. Dr. Barnard was a heart surgeon who had observed several of the canine procedures which were done by Dr. Lower, who was then at Virginia Commonwealth University. Louis Washkansky, the recipient, lived for 18 days after the groundbreaking surgery. Stanford found an appropriate donor for their patient a month later and performed the first heart transplant in the United States on January 6, 1968. Mike Kasperak, who had had a massive heart attack, lived for 15 days after the transplant. Although he regained consciousness, was able to communicate with his wife post-transplant, and provided hope for recovery, in retrospect, his other organs were too sick, and he died of severe hemorrhage and multisystem organ failure.

Subsequent to these two very well-publicized procedures, many cardiac surgical teams were excited and quickly started heart transplant programs. There were 101 heart transplants performed worldwide in the calendar year 1968. The outcomes were abysmal, however, with survival rates measured in weeks or months, and the procedure became quite contentious, and ultimately an unofficial moratorium on clinical heart transplantation was accepted in 1970. The one program that did not follow this moratorium was Stanford, and the group continued clinical activities virtually alone during the next decade, tackling the problems that limited survival rates. Many small incremental improvements occurred in the field of solid-organ transplantation over that decade, but the signal contributions of the Stanford team included introducing the use of the endomyocardial biopsy to definitively diagnose rejection and document the effectiveness of its treatment and the demonstration of safe cold ischemic donor heart times to permit distant heart procurement. During that decade a definition of donor brain death was also accepted societally and legally, the need for which had not previously been recognized [3].

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Prior to the introduction of the endomyocardial biopsy, the diagnosis of heart rejection was made by careful observation of the recipient developing heart failure signs and symptoms and a drop in the total amplitude of QRS complexes on the surface EKG, reflecting edema and inflammation of the graft. Both of these findings of rejection were well documented in the canine model but were unfortunately late developments in the clinical course. In 1973, Dr. Phillip Caves, a cardiac surgical resident on leave from the United Kingdom at Stanford, took an older Japanese bioptome instrument and modified it to allow access to the apex of the right ventricle in order to snip off and retrieve myocardial specimens to analyze for rejection. The instrument was inserted percutaneously into the right internal jugular vein and advanced under fluoroscopic guidance across the tricuspid valve and into the right ventricle. It proved to be safe and simple to perform, able to be performed repeatedly, and productive of very useful tissue for analysis [4]. A pathological system and scale for reproducibly grading rejection were developed at Stanford by Dr. Margaret Billingham. The system has undergone a variety of iterations and now stands as the international standard for grading heart rejection [5].

The initial need to have the donor patient in an adjoining operating room usually required transport of a brain dead individual to the transplant center and, understandably, posed a major limitation on the clinical expansion of heart transplantation. In the laboratory, both Lower and Shumway demonstrated that a donor heart could be preserved in iced saline for periods up to 3 hours and then implanted and have normal physiologic function [6]. The safety of such preservation opened the way for distant heart procurement at centers other than the transplant center which, ever since, has been the major means of procuring donor hearts.

The (then) new immunosuppressive agent cyclosporine was introduced into the field of renal transplantation in the 1970s and proved to be a major improvement over the older agents. In 1980, it was introduced to heart transplantation at Stanford with similar major improvement in outcomes [7] and helped rekindle interest in the field in the medical community. Subsequently, increasing numbers of centers restarted heart transplant programs, and increasing numbers of procedures were performed. In 1982, the International Society for Heart Transplantation was formed and started a Registry of such procedures and their outcomes. The Registry remains robust and continues activity to this day and reports results to the public annually. It currently includes data on over 118,000 recipient patients.

The burgeoning number of patients over these years has led to a need for clinicians trained to provide them with highly specialized care. In the year 2010, the American Board of Internal Medicine approved the field of Advanced Heart Failure and Transplant Cardiology as a distinct subspecialty, and certifying exams are now given every 2 years. It is a subspecialty which allows clinicians the opportunity to deal with the medical issues that these patients develop as well as the psychological issues involved in their return (usually from the brink of death) to a functional lifestyle, able to exercise and study and travel and have families. Although the return to normalcy is wonderful, the interactions with family, friends, and employers can be most challenging and are the subject of this book.

Since the donor supply is clearly finite and will not likely increase in the future, we now look forward to the continued "evolution" of the field of mechanical circulatory support to eventually provide not only durable but also safe non-biological replacement of the heart.

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