History of cardiac transplantation: Tracings up to the first clinical homotransplantation

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Abstract

Christian Barnard captured the imagination of the whole world when he performed the first clinical homotransplantation of the heart on December 3, 1967. However, the origins of this intervention date back to the early twentieth century and its journey from being a nascent idea to practical feasibility makes for interesting reading. We present a chronological thread of the development of heart transplantation, stressing on the relevant advances, experiments and people. Carrel and Guthrie conducted the first experiments with heart transplantation in dogs and demonstrated that a heart could be transplanted into another body where it regained its capacity to contract. Later Mann et al extended their work and were able to achieve longer survivals in their dogs. They attributed death to "some biological factor". Throughout the forties and the fifties, Demikhov in Russia conducted experiments with heterotopic as well as orthotopic heart transplants. His experiments were reported in 1962. Marcus et al (1951 to 1953) tried imaginative techniques of transplantation. The fifties saw a whole array of researchers dabbling with transplantation and coming up with solutions to individual problems of donor preservation, surgical techniques, immunosuppression and the like. All of this was integrated into a single protocol by Shumway, Lower and Stofer. In 1964, in a poignant fallout of the lack of suitable laws, Hardy transplanted a chimpanzee’s heart into a man’s chest. After the initial excitement following Barnard’s feat, heart transplantation fell into disrepute owing to poor results; primarily because of inadequate immunosuppression and graft rejection. The advent of cyclosporine A in 1980 bolstered immunosuppression, and since then heart transplantation has become a globally accepted modality of treatment. (Ind J Thorac Cardiovasc Surg, 2005; 21: 182–193)

Key Words: Cardiac transplantation, Heart, graft

Introduction

“This Heart Transplant Remains a Fantastic Speculation for the Future” Emanuel Marcus, 1951
“Dr Christian Barnard performs the first heart transplant” Headline on December 4, 1967

The details of perhaps the first documented transplantation can be found in the Siva Puran, a holy book of the Hindus- lord Siva transplanted the head of a baby elephant onto the body of the young lad guarding Parvati’s private chambers. The young boy who rose was made the general of Siva’s forces and christened Ganesh.

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This story is at best apocryphal, but one thing that is clear is that since time immemorial, man has been fascinated by the ability to transplant organs.

For hundreds of years, the heart was considered to be the seat of the soul. For this very reason and the fact that the earliest attempts at cardiac surgery were almost invariably fruitless, the heart was considered inviolate. Fabricius summed up the feeling about heart injuries prior to the last century: “If the heart is wounded the fear is desperate. It is, therefore, unnecessary to attempt treatment.” However, men are rarely bound by the limits of the contemporary society; and so, attempts at cardiac surgery continued. The first cardiac surgery is generally imputed to Dr Ludwig Rehn, a German doctor, who on September 9, 1896 sutured a myocardial laceration successfully. However, if the term heart surgery is broadened to include pericardial procedures, then the first intervention was made by Francisco Romero, a Spanish physician, who became the first heart surgeon when he performed an open pericardiotomy to treat a pericardial effusion in 1801.
Cardiac transplantation has evolved through the separate but interrelated streams of surgical techniques and organ preservation, immunologic advances; and ethico legal issues regarding the same. The timeline of its history can be divided into the experimental transplantation period, and the clinical transplantation period. We will briefly analyze in this treatise the work up till the first successful transplantation by Dr Barnard and present the history as one single thread with the allied advances in other fields mentioned wherever appropriate.

**Earliest Efforts**

Alexis Carrel and Charles Claude Guthrie were the first to attempt organized experimental studies in heart transplantation; working in conjunction, they reported the first experimental heart transplantation in a dog model in 1905. The first cardiac transplantation was completed when they excised the heart of a puppy and transplanted it into the neck of a larger dog. They anastomosed the cut ends of the jugular vein and the carotid artery to the aorta, pulmonary artery, one of the venae cavae and a pulmonary vein. One hour and 15 minutes after the cessation of the heart beat, circulation was re established through the heart and 20 minutes after re establishment of circulation, blood was actively circulating through the coronary system. The ventricles of the transplanted heart resumed contractions about 1 hour after the operation. Fig. 1.

![Fig 1. The possible anastomoses of the transplanted heart in the experiments conducted by Carrel & Guthrie. Note that the donor heart receives blood from the arterial system of the host and pumps out blood into the venous system of the host.

a - proximal carotid artery of the host; a' - distal carotid of the host
b - Proximal jugular vein of the host; b' - distal jugular of the host](image)

Since no special aseptic techniques were adopted, coagulation occurred in the cavities of the heart after 2 hours, and the experiment was interrupted. One of the problems of this arrangement was the hemodynamic disharmony. Atrial inflow under arterial pressure and aortic outflow against venous pressure resulted in poor coronary perfusion.

However, this experiment at once demonstrated that the heart could be separated from its blood supply and sutured into the circulation of a second animal where it recovered its ability to contract. Further, this experiment threw up a number of questions, such as preservation of the donor heart during the transfer period and various other physiological phenomena, requiring further research to be undertaken on these issues.

Meanwhile, understanding of the concept of immunity and rejection was in a nascent stage. George Shone in 1912 surmised that a) Transplantation into a foreign species invariably fails b) Allogeneic transplantation usually fails, c) Autografts almost invariably succeed, d) There is a primary take and delayed rejection of the first graft in an allogeneic recipient, e) There is an accelerated rejection of the second graft in a recipient who had earlier rejected a graft from the same host. f) The closer the ‘blood relationship’ between donor and recipient, the more likely the graft success. Researchers therefore understood that transplantation was not only about surgical techniques, but also about acceptance into the recipient’s body of a foreign organ.

The next notable presence felt in heart transplantation was that of Frank C. Mann, James T. Priestly, J. Markowitz and WM Yater in 1933. They were able to achieve a mean post operative survival of 4 days with a longest survival of 8 days in their dogs.

Mann and colleagues made innovative anastomoses, whereby the right ventricle functioned as a pump. Here the aorta was anastomosed to either the proximal or distal cut end of the carotid artery, establishing arterial inflow into the coronary circulation, while the pulmonary artery was anastomosed to the recipient’s jugular vein, establishing venous outflow via the coronary sinus. Thus the problem of coronary perfusion was solved. There was however another problem - with the host’s carotid anastomosed to the aorta of the donor, there was no cross circulation, and since the carotid blood flow was excessive for the coronary arteries to take away; the aorta would be under tremendous pressures, Fig. 2.

The researchers surmised that ventricular distention and coronary embolism needed to be circumvented for