HEART TRANSPLANTATION

AN ESSAY

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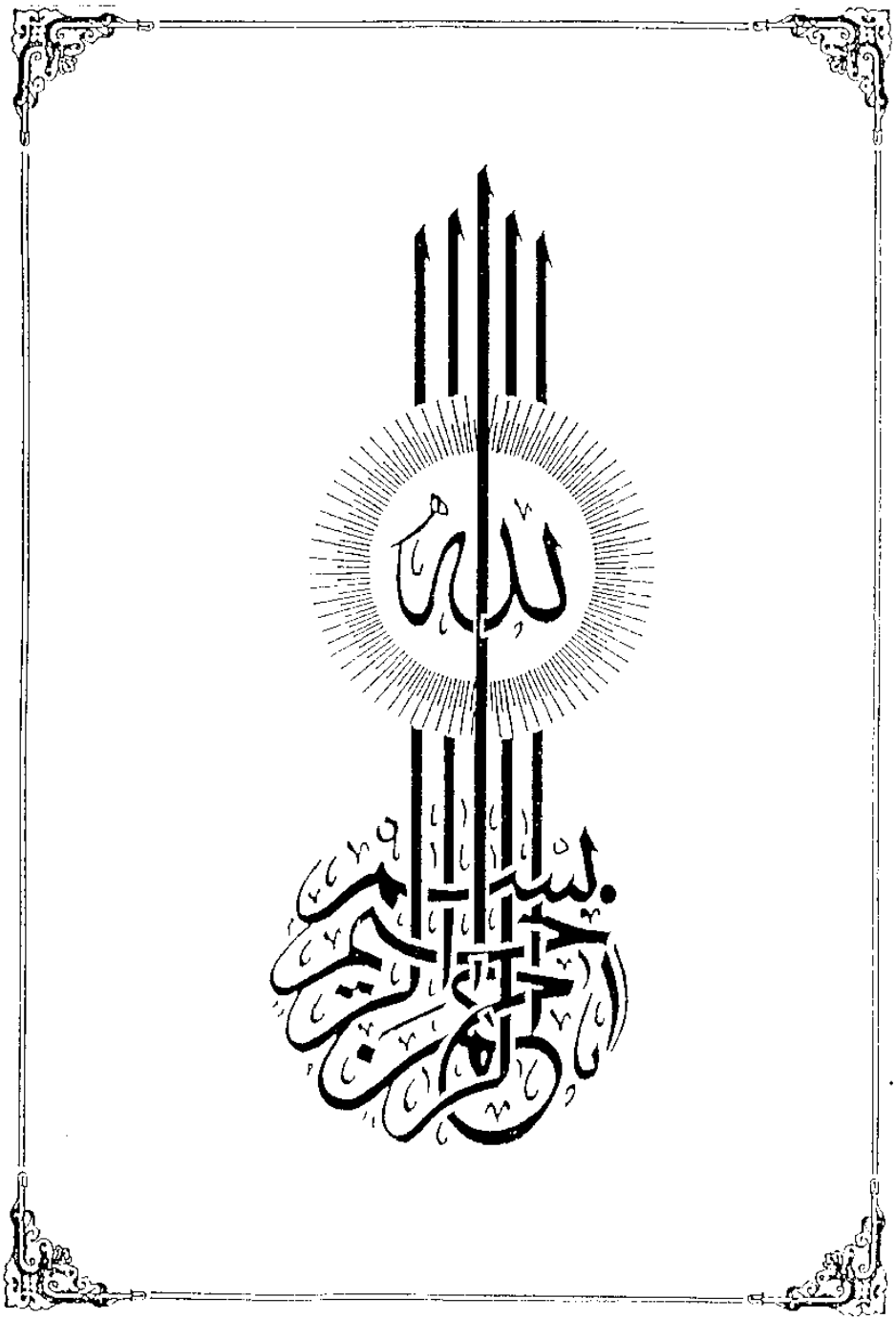

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INTRODUCTION

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Cardiac transplantation became a daily routine in many centers all around the world. The results of clinical cardiac transplantation became of therapeutic value in the past few years. It is no longer a topic for experimental clinical research. However, there is still much to be learned about transplantation of the heart, namely the development of more effective and selective immunosuppressive regimens (Bolman, 1985). In our country, some steps have been taken forwards very successfully in the field of renal transplantation, but not in the field of cardiac transplantation.

This work will review the subject of cardiac transplantation as regards:

1- The history of experimental and clinical development of cardiac transplantation.

2- The indications and contraindications for cardiac transplantation, and how to select a suitable recipient.

3- The problem of organ donation, and donor heart preservation and transportation.

4- The operative technique and postoperative care for these critical patients.

5- The major problem of immunosuppression which is considered by all centers to be the most limiting factor for cardiac transplantation programs.

6- The different complications of the operation, as well as complications due to the postoperative medications and procedures.

7- The results of the most active centers will be reviewed in order to stand on the progress achieved in this field.

8- A rapid review of the subject of heart-lung transplantation.

This is followed by discussion of some of the important subjects in the review and pointing out the difficulties facing our centers in Egypt to proceed forewards in this field.

HISTORICAL BACKGROUND

Human heart transplantation was the product of a substantial tradition of experimental surgery and transplantation immunology, as well as of other advances of twentieth century science and medecine that are too numerous and desparate to be cataloged here. This chapter will review primarily the evolution of the surgical technique which made human heart transplantation possible.

The history of heart transplantation can be divided into experimental efforts of three types; (1) those involving placement of the exised donor heart in a heterotopic position in the recipient in such a way that the heart beats but does not make any significant contribution to the circulatory work of the recipient; (2) those in which the heterotopic heart graft is placed in parallel to the recipient's own heart and assumes part of or all of the circulatory work in the recipient, depending on the function of the recipient's heart; and (3) those involving orthotopic placement of the heart graft with removal of the recipient organ. (Griepp and Ergin,1984.).

HETEROTOPIC HEART TRANSPLANTATION:

The first heart transplant was performed in 1905 by Carrel and Guthrie at the University of Chicago. The authers described the following experiment:

"The heart of a small dog was extirpated and transplanted into the neck of a larger one by anastomosing the cut ends of the jugular vein and carotid artery to the aorta, the pulmonary artery, one of the venae cavae and a pulmonary vein. The ischemia time was 1 hour and 15 minutes. After re-establishment of the circulation by 20 minutes, blood was actively circulating in the coronary system. Afterwards, contractions of the auricle appeared, and about 1 hour after the operation, effective contractions of the ventricles began. The transplanted heart beated at the rate of 88 per minute, and the rate of the normal heart was 100 per minute. Coagulation occurred in the cavities of the heart after about 2 hours of coordinated beating and the experiment was terminated."(Baumgartner,et al,1984.).

This is the most complete account of their single experience with heart transplantation. The exact way in which the anastomosis were arranged is not known with certainty, but figure 1 shows the most likely possibility. In retrospect, this experiment's importance lies in its having demonstrated that a heart can be removed, separted

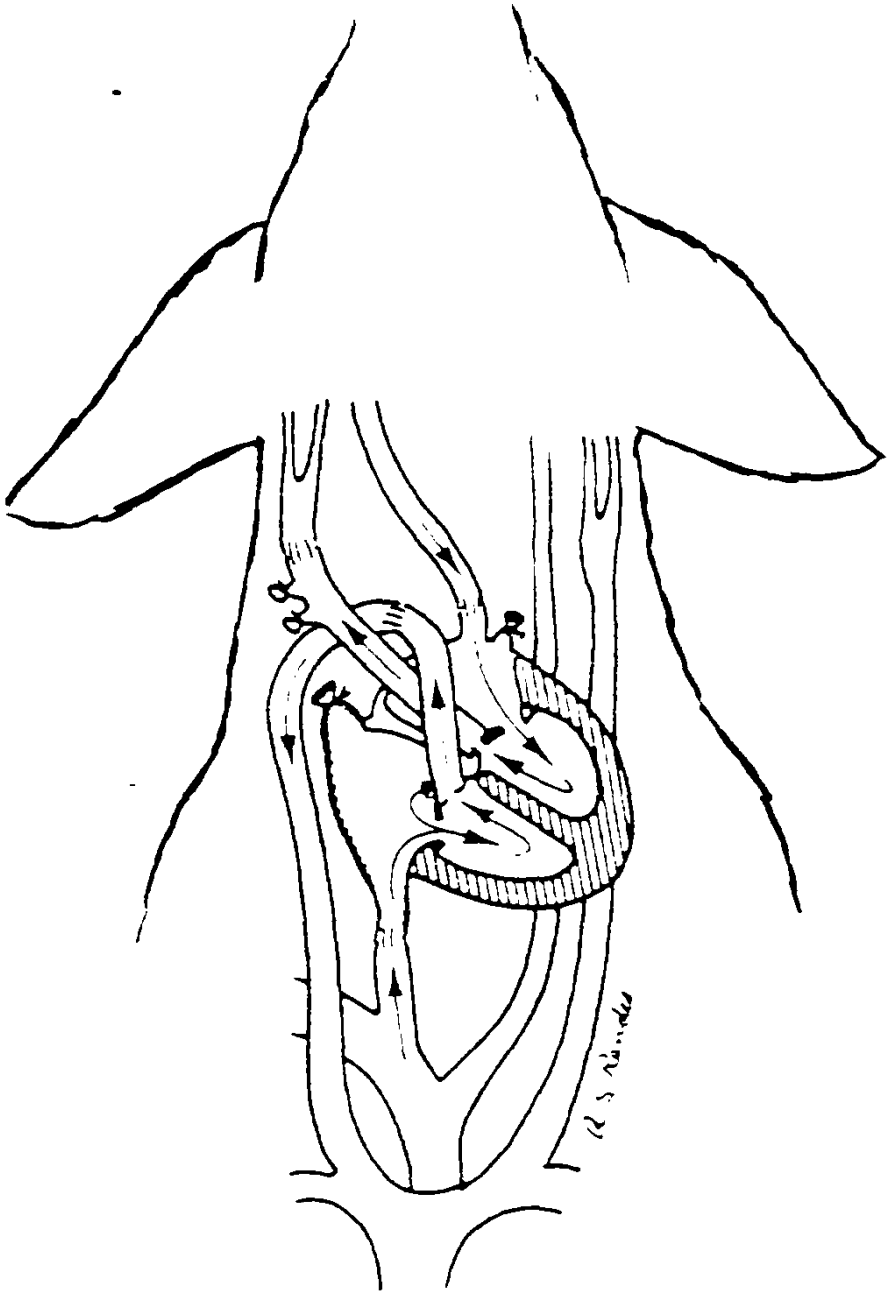

Figure (1): Possible anastomotic arrangement used by Carrel and Guthrie in 1905. *(After Greipp and Ergin, 1984).*

from its blood supply, sutured into the circulation of a second animal, and recover sufficiently so that organised contractions will reappear. (Baumgartner,et al,1984.).

No further reference to transplantation of the mammalian heart appears in the medical literature until 1933, when Mann, Priestley, Markowitz, and Yater, attempted at the Mayo Clinic and at the Georgetown University to establish a denervated heart model that could be used to study the direct cardiac effects of hormones. They made a systematic study of the technical aspects of transplanting the heart into the carotid-jugular circulation. They recognised the importance not only of preventing left ventricular distension prior to establishing satisfactory left ventricular contractions, but also of avoiding coronary air embolism. The arrangement of anastomosis that they found most successful is showed in figure 2. One of their heart-transplanted dogs survived 8 days. Upon examination of the heart, when contractions had ceased, these investigators found a dense infiltration of the myocardium with lymphocytes, mononuclear cells, and polymorphonuclear granulocytes, and they commented:

"It is readily seen that failure of the homotransplanted heart to survive is not due to the technique of transplantation but to some biological factors which is probably identical to that which prevents survival of other homotransplanted tissues and organs."

This was the first recognition of the phenomenon of

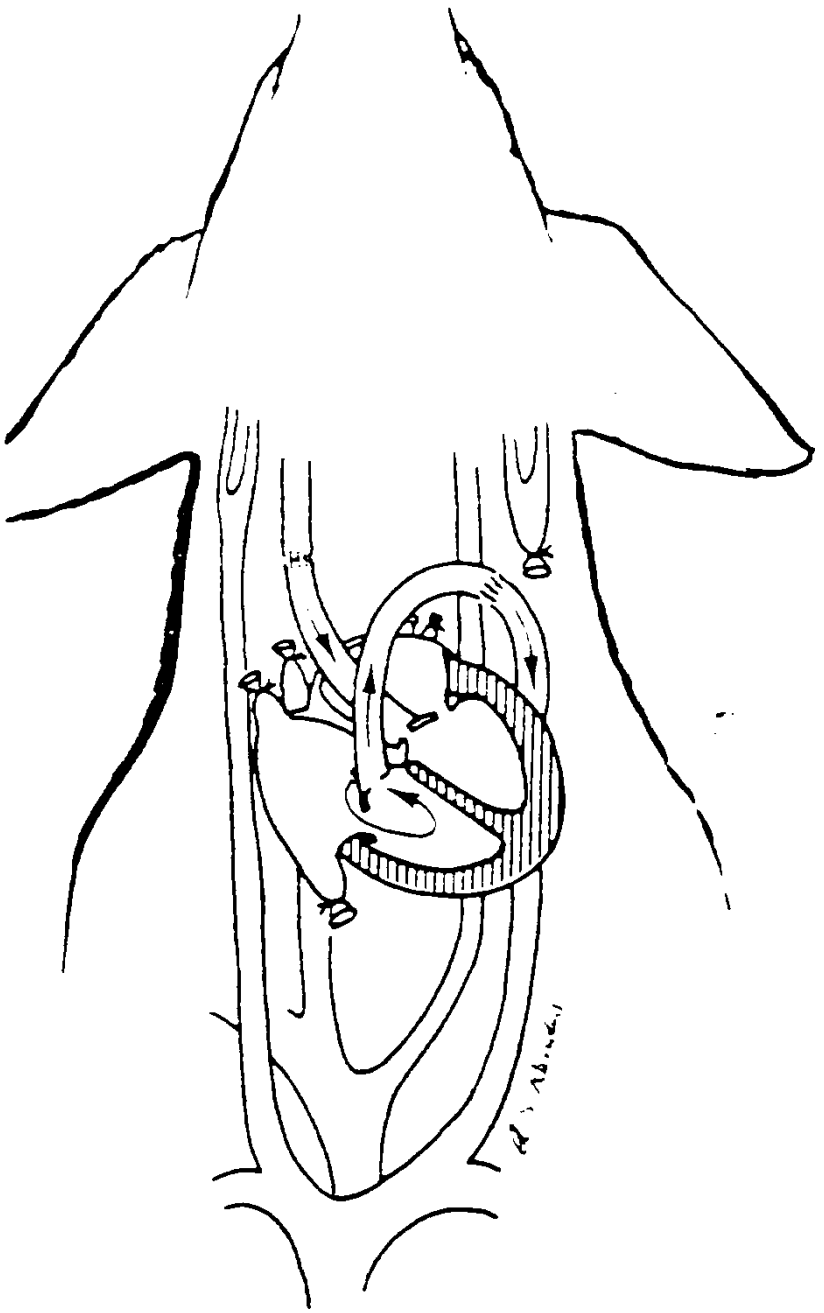

Figure (2): Anastomotic arrangement in the 1933 by Mann and Co-workers.
(After Griepp and Ergin, 1984).

allograft rejection of the heart. (Jara,et al,1980.).

In 1951, Marcus, Wong, and Luisada, working at the Chicago Medical School, reported the results of their experience with heterotopic transplantation of the canine heart. They used rather complicated techniques for their experiments and the results were disappointing. In 22 experiments, the heart was successfuly transplanted only 10 times,and the longest-living dog survived only 48 hours. This report demonstrated nicely that complicated techniques are not necessarily better than simple ones.

In 1953, Downie, working at the Ontario Veterinary College, reported his experience with cervical canine cardiac transplantation. In his series of 30 transplants performed with ischaemic times ranging from 30 to 40 minutes, 23 were successful and the longest-surviving heart beat for 10 days. No mention was made of preserving the donor heart during ischemia, either by perfusion or cooling. These experiments demonstrated that with simple techniques successful heterotopic heart transplantation could be routinely achieved. (Griepp and Ergin,1984.).

In 1962, the Russian surgeon DemiKhov succeeded in penetrating the Iron Curtain between the Soviet Union and the western world by publishing his work. He stated that in 1940, he transplanted a dog's heart into the inguinal region

of another animal. His experiments were then interrupted by the war, but resumed in 1964, at which time he began studying intrathorathic heterotopic cardiac transplantation. A total of 24 anatomical variants were tried, and in his most successful experiment in 1956, an intrathoracic heterotopic graft continued to beat for 32 days after implantation.(Table 1). The heart was removed as soon as the electrocardiogram demonstrated ventricular fibrillation of the transplant. The cause of failure of the donor heart was attributed by Demikhov to an infarct of the left ventricle, presumed to be secondary to an embolus. The long survival of this animal strengthened Demikhov belief that failures of all transplanted organs were secondary to technical factors and that immunology did not play a role. (Webb,1978.).

PARALLEL HETEROTOPIC HEART TRANSPLANTATION:

Once it had been firmly established that transplanted hearts could function for at least several days in the recipients, a number of investigators deviced techniques to place a graft heterotopically in the thorax, in such a way that it would assume a portion of the circulatory load. The transplanted heart could now be used as a temprory support for a diseased and failing heart. This model further allowed the heart transplant to be done without interrupting the circulation of the recipient, and has a potential, in some

models, to allow removal of the recipient heart should the total circulatory load be assumed by the donor heart. (Jara,et al,1980.).

Between 1951 and 1955, Demikhov performed 22 such intrathorathic patallel heart transplants. The venae cavae, the pulmonary artery, and the aorta of the donor organ were anastomosed end-to-side to the corresponding vessels in the recipient, and the two left atria were connected. At completion of the operation, when satisfactory contractions were re-estabilished in the donor heart, the recipient vessels were ligated between the anastomosis and the recipient heart and purse-string suture was passed around its mitral valve and tightened, thus totally excluding the recipient's heart from the circulation. In 1955, in Demikhov's most successful reported experiment, the animal awoke from aneasthesia and was able to stand and drink. After surviving for 15 hours, the animal died suddenly, death attributed to thrombosis of the superior vena cava. This animal was the first in which the circulation was completely supported for significant period of time by a transplanted heart. (Griepp and Ergin,1984.).

In 1964 and 1966, Reemtsma and his co-workers at Tulane University reported their experiences with the auxiliary intrathorathic graft. The donor's inferior vena cava was ligated, the superior vena cava was anastomosed to the