ELSEVIER

The First Lung Transplant in Man (1963) and the First Heart Transplant in Man (1964)

J.D. Hardy

MODERATOR Felix Rapaport, other members of this distinguished panel, and members of the audience, I will use my allotted 4 minutes to present briefly the first lung transplant in man and the first heart transplant in man.

THE FIRST LUNG TRANSPLANT IN MAN

We began experimental lung transplantation in animals in the second half of the 1950s. A wide variety of studies were performed that involved several hundred animals, largely dogs. These investigations included operative techniques, function of the reimplanted lung, regeneration of lymphatics, regeneration of nerves (histologically and as reflected in return of the Hering–Breuer reflex), the effect on respiration of differential division of the structures of the hilum, allotransplantation (including relief of induced pulmonary hypertension), and growth of the reimplanted lung in puppies. Most of these investigations were published. Dr Fikri Alican participated importantly.

In late 1962, Dr Watts R. Webb and I obtained permission from the administration of the University of Mississippi Medical Center to perform a lung transplant in man if a patient should present who fulfilled the appropriate clinical and ethical considerations.

On April 15, 1963 a dyspneic 58-year-old white man with carcinoma of the left main-stem bronchus was admitted to our University Hospital. Most of the left lung was collapsed distal to the occluding bronchial malignancy, and the right lung exhibited extensive emphysematous changes. He agreed to accept a left lung transplant if clinically feasible at the time of operation. He exhibited borderline renal insufficiency, but his marginal renal function was considered sufficient to permit the mandatory operation to manage the infection distal to the occluded left main stem bronchus.

The operation (Fig 1) was begun on the evening of June 11, 1963, and completed during the early hours of June 12. The patient recovered from the operation (Fig 2) promptly and the transplanted lung functioned immediately, as attested by the intraoperative blood gas samples from its pulmonary artery and pulmonary veins, and from other lung function studies performed postoperatively. At his death 18 days later, caused by renal failure and his general debility from his extensive left lung and thoracic wall malignancy, the transplanted lung exhibited only minor evidence of rejection.[1] The immunosuppressive regimen had consisted of azathioprine, prednisone, and cobalt therapy directed to the mediastinum.

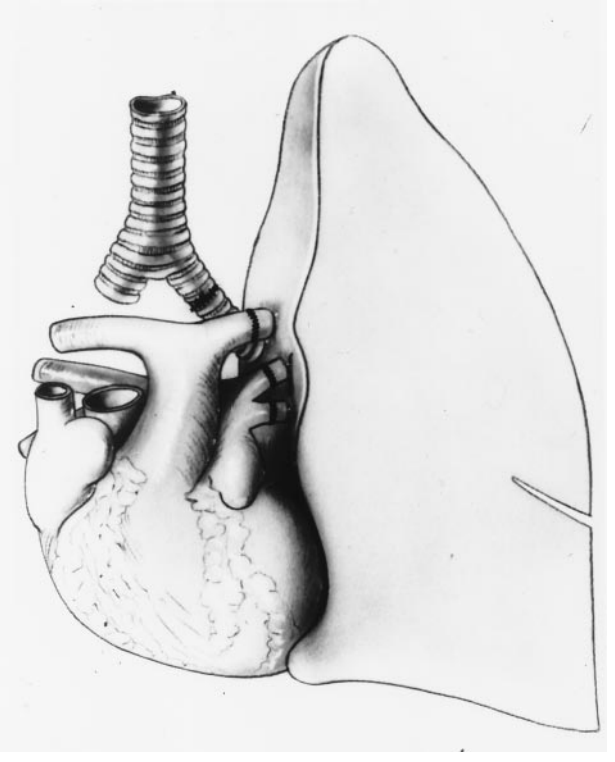

Fig 1. Operative technique used in the first lung transplant in man. The donor lung was ventilated intermittently with pure oxygen until its bronchus had to be closed.

We concluded that clinical lung transplantation was technically feasible, and that this new therapeutic modality could and would ultimately prove to be a successful replacement for pulmonary insufficiency.

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Fig 2. J.R., the first human lung transplant recipient following the operation.

THE FIRST HEART TRANSPLANT IN MAN

The investigation of heart and heart–lung transplantation was begun in our laboratory by Watts R. Webb in 1956, and he was able to exhibit limited survival of dogs by 1957.[2,3] We had not yet set up the pump-oxygenator, and he achieved these transplantations through the use of rapidly inserted vascular coupling devices for anastomosis of the cavae, the pulmonary artery and the aorta. Hypothermia was also employed.

Following the limited but gratifying success of our first human lung transplant and our experience with several hundred experimental heart transplants in the laboratory, Dr Webb and I obtained University permission to explore the feasibility of a heart transplant in man. Numerous possible recipients were evaluated, but it became increasingly apparent that to have an acceptable human donor heart available at the instant the prospective recipient was dying would be highly unlikely.

Meanwhile, Dr Webb had accepted the chair of cardiothoracic surgery at the Southwestern Medical School in Dallas, and Dr Carlos M. Chavez moved up as his replacement.

I had visited Tulane University where Reemtsma and his associates[4] had transplanted several chimpanzee kidneys with a surprising degree of success. And I had bought four large chimpanzees to use as kidney donors when no human organs were available.

The Operation

In brief, on January 23, 1964, a potential recipient patient (Fig 3) became terminal from years of hypertensive cardiac failure. No human donor heart was available, and so the heart of our largest chimpanzee was transplanted (Figs 4 and 5). The donor heart was preserved by the retrograde gravity flow of cold, oxygenated blood through the coronary sinus (Fig 6). The operative technique was that described by Lower, Stofer, and Shumway[5] (Fig 7 and 8). The transplanted heart (Fig 9) functioned immediately, after being rewarmed and defibrillated, and it maintained a host blood

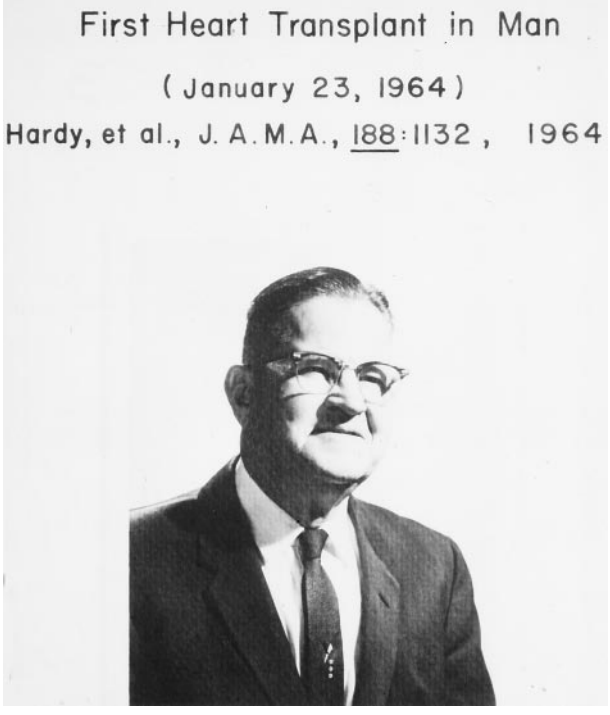

Fig 3. B.R., the first heart transplant recipient. This photograph was taken several years before his terminal heart failure developed.

OPERATIVE PERMIT

I hereby give full permission for left leg amputation and heart surgery on Boyd Rush. I understand that any clots present will be removed from the heart to stop them from going to still more arteries of his body. I further understand that his heart is in extremely poor condition. If for any unanticipated reason the heart should fail completely during either operation and it should be impossible to start it, I agree to the insertion of a suitable heart transplant if such should be available at the time. I further understand that hundreds of heart transplants have been performed in laboratories throughout the world but that any heart transplant would represent the initial transplant in man.

Signed (for family) Mrs J. H. Thompson (sister)

Witnessed Maurice C. Lucas

Witnessed Phyllis Ann Ward R.N.

January 23, 1964

Fig 4. The operative permit for transplantation of the first heart in man.

Fig 5. The operation: The first heart transplantation in man.

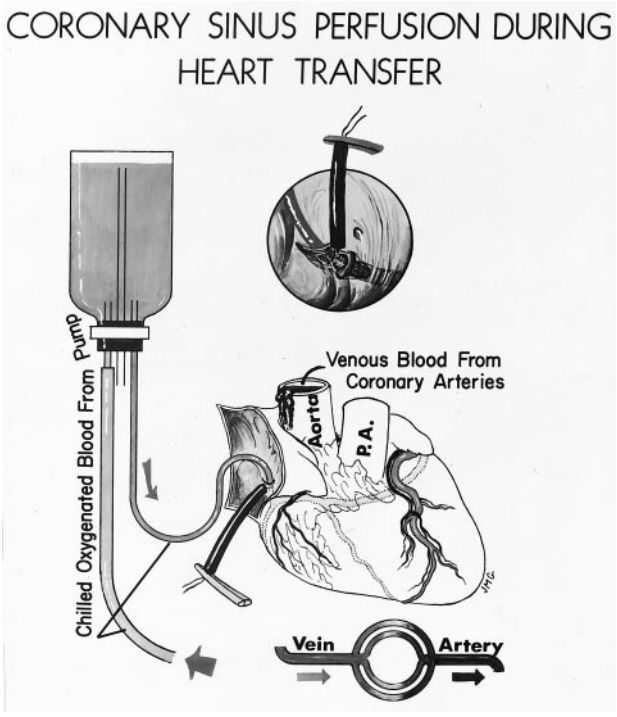

Fig 6. Heart preservation during transfer. Retrograde gravity flow of cold oxygenated blood through the coronary sinus.

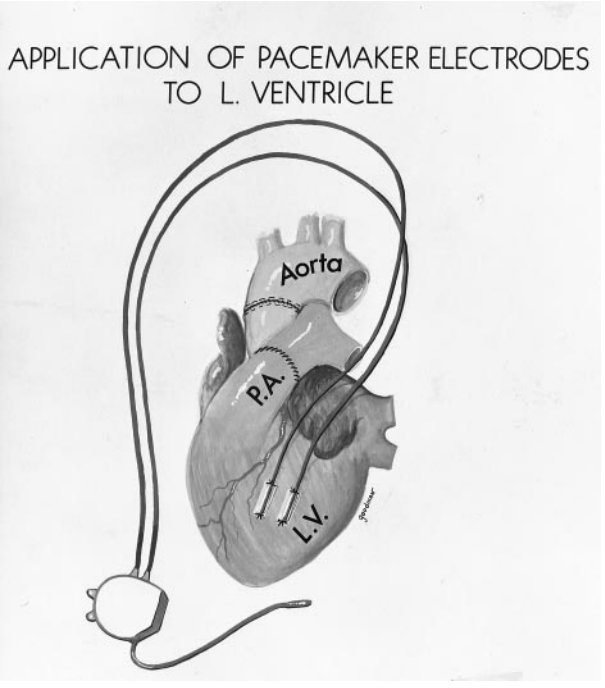

Fig 8. Completed transplantation with pacemaker applied.

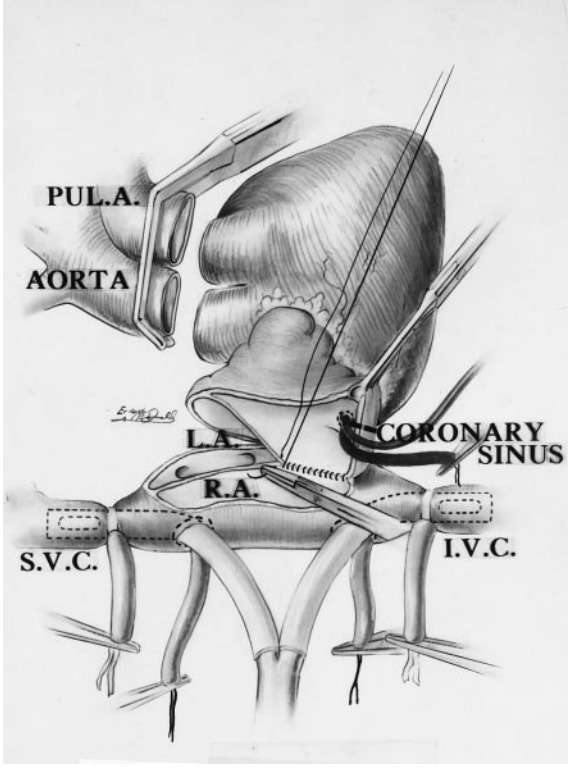

Fig 7. Operative technique for heart transplantation.

Fig 9. Transplanted heart in situ.

Mario S. Barnard
(S. Afr. Med. J. 41, 1967):

"Hardy and co-workers had in 1964 transplanted a chimpanzee heart into a man . . . a regular forceful beat was restored . . . the feasibility of cardiac transplantation was now irrefutable."

Fig 10. "It is often enough to know that a thing may be possible."

pressure of 90 to 100 mm Hg for approximately 90 minutes.[6] The donor (chimpanzee) heart proved to be too small for the large male recipient, and the metabolic deterioration of the recipient in his state of intermittent shock over several days was doubtless a major factor.

We concluded that heart transplantation in man was technically feasible by the laboratory methods in current use and that, given a donor organ of appropriate size and a recipient in metabolic balance, heart transplantation in man could eventually provide a useful replacement for the failed heart in man. This perception was endorsed by the group in South Africa at the time of their successful human heart transplant in 1967 (Fig 10).

Thank you.

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