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The dark early years of heart transplantation: Some lessons learned

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Christiaan Barnard's first human heart transplant in Cape Town on December 3, 1967, stunned the world and surprised the medical profession.[1] This was followed 3 days later by Kantrowitz in New York who transplanted a 2-day-old donor heart in a 17-day-old baby. The infant died 6 hours later. Barnard's first transplant recipient, Washkansky, died after 18 days, but on January 2, 1968, he performed a second transplant on Philip Blaiberg, a 58-year-old dentist, who lived for 20 months. During this time Blaiberg, published an interesting account of his experiences with the title "Looking at my Heart."[2]

These first 3 operations heralded a wave of misplaced enthusiasm and 150 transplants were done worldwide during 1968 and 1969 performed by 50 different teams (Table 1). Many of these had their reputation tarnished by embarking on heart transplantation without a proper understanding of the complex issues involved. At the same time, the publicity given to some of the personalities and events surrounding these operations had an adverse effect on many members of the public and the medical profession. A combination of this and the generally poor survival rates soon resulted in the work being abandoned in all but a few centers, so that by the beginning of 1978, there were only 4 centers in the world where heart transplantation was still being practiced.

Methods and results

The data to illustrate these poor early results have been taken from the book "Hearts," written by Thomas Thompson in 1971.[3] This is largely about the feud between Denton Cooley and Michael DeBakey, both of whom were early into heart transplants. However, it contains an Appendix that lists the 168 transplants performed from Barnard's first until October 23, 1970, when the book was sent to the publisher. This gives the date of each transplant, the name and age of the recipient, the age of the donor, the length of survival in days, and the cause of death, which is given in all cases but 2. From this material I have used data from the first 60 transplants—30 from the United States and 30 from the rest of the world—to illustrate just how poor survival was in these early cases.

Table 2 provides the United States experience with the name of the surgeon who did the operations. You will see that 3 surgeons, Cooley, Shumway, and DeBakey were responsible for more than 66% of the total, with Cooley accounting for the largest number. Kantrowitz and Lower did 2, and 5 other surgeons, Lillehei, Webb, Bahnson, Effler, and Starzl did 1 each.

By contrast Table 3 gives the 30 transplants performed during the same period in a wide variety of other countries without naming individual surgeons. In 5 countries, only 2 operations were performed and 6 others accounted for a single transplant.

Table 4 provides information on the survival of these transplants and compares results in the United States with the rest of the world. No fewer than 11 of the 60 recipients, 5 in the United States and 6 elsewhere, died within 1 day, and 19 died between 1 day and 1 month, 7 in the United States and 12 elsewhere, so that by the end of 1 month, half of the total had died. By the end of 1 year, only 11 were still alive, 4 of whom survived more than 2 years. Comparing survival between the United States and the rest of the world, it would seem that results, although still very poor, were marginally better in the United States

I suspect that details of the causes of death given in the Appendix may not be entirely accurate. However, I have divided them into broad categories of rejection (acute and chronic), infection (at all sites and from all causes), cardiac (both recipient and donor related), and "others," which comprise a variety of causes, including 2 patients for whom no cause of death was given. The information for countries other than the United States is given in Table 5. Other causes (14) and the one surviving at the time of publication accounted for half the deaths, with infection,[5] rejection, (6) and cardiac (4) causes responsible for the remainder.

Table 6 provides the causes of death ascribed to those surgeons in the United States who did more than 2 transplants and to the unnamed 5 others who only did 1. There is little remarkable about these findings except perhaps that 66% of Cooley's 12 transplant recipients died of rejection.

Comment

The Appendix in Thomas's book continues to provide data on the number and outcome of transplants worldwide until October 1970 and there was little improvement during this

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Table 1 Number of Heart Transplants per Year Worldwide

Year	Transplants, No.
1967	2
1968	102
1969	48
1970	16 (to Oct 23, 1970)
Total	168

time. With the exception of Shumway in Stanford, who continued to approach the problem professionally and methodically, and Barnard in Cape Town, results after 1970 remained generally poor, and interest in cardiac transplantation elsewhere began to wane. This was exemplified in Britain where, in February 1973, the Department of Health issued a moratorium on further heart transplants in the United Kingdom.

In May 1973, having recently been appointed a consultant surgeon at Papworth Hospital in Cambridgeshire, I visited my friend Philip Caves, who was at the time chief resident in charge of the transplant service at Stanford. The previous year, working in the laboratory with Margaret Billingham, Philip had perfected the technique of percutaneous transvenous endomyocardial biopsy, which had a considerable effect on the management and outcome of transplant patients.[4] By being able to detect acute rejection at an earlier stage than had previously been possible using summated electrocardiogram voltages, immunosuppression could be increased earlier and more effectively and then reduced appropriately when the tissue sample showed evidence of resolution. Results at Stanford had improved, and I was impressed by seeing how well some patients were doing and by Philip's enthusiasm for the future of heart transplantation.

On my return to Cambridge and being unaware of the moratorium, I decided it was time for Britain to have its own heart transplant program, modeled on what I had seen at Stanford. Having discussed this with my senior colleague at Papworth and Sir Roy Calne, who had a busy kidney and liver transplant unit in Cambridge, I began to prepare for this, which included regular visits to Stanford, where I learned much from Shumway and his team.

In 1976 there was a significant advance when the United Kingdom Medical Royal Colleges and their Faculties first clarified and then defined the clinical diagnosis of brainstem death and equated this with death of the patient.[5] This, and our research on improving the preservation of the excised donor heart,[6] enabled us to conceive expanding the potential donor pool to all parts of the United Kingdom. By 1978 we felt ready to proceed, and I submitted our protocols to the Department of Health Transplant Advisory Panel. I received a sympathetic hearing but was informed a few weeks later that there was no money for a program and that they did not want to see any "one-off" transplants.

However, by this time we had devoted so much time and effort preparing for a program that a few months later, after gaining permission from the local Health Authority Chair to use my facilities at Papworth for 2 cases, I went ahead and we did our first transplant on January 14, 1979. To my great disappointment, this was not successful. What happened was that just after I had taken the donor heart out at another hospital, my anesthetist telephoned from Papworth to say that the recipient had suffered a cardiac arrest as he was about to undergo anesthesia. He had been rapidly resuscitated and placed on cardiopulmonary bypass, but there was uncertainty about whether he might have suffered brain damage. I decided the only chance for the patient was to go ahead with the transplant, and although the operation went smoothly, it became apparent postoperatively that a degree of brain damage had indeed occurred. He never recovered normal consciousness. The patient needed to be ventilated intermittently and died 17 days later. This inevitably resulted in some vigorous criticism, both from the public and members of the medical profession.

However, 6 months later our second case, a 52-year-old builder from London, went well, and he lived an energetic life for nearly 6 years. We thereafter obtained sporadic funding from a variety of sources, including a generous benefaction from a local Cambridge millionaire, and 4 of our first 6 patients lived between 3 and 8 years. Coincidentally with starting our program, Stanford published their cumulative results in January 1979,[7] reporting 1-year survival of 75% with a 5% annual attrition rate thereafter, and this was the target we set ourselves. We used Stanford's immunosuppressive protocol for the first 29 cases, except that I added a longer 28-day initial course of daily

Table 2 First 30 Transplants in the United States (December 6, 1967, to September 19, 1968)

Surgeon	Transplants, No.
Cooley	12
Shumway	5
DeBakey	4
Kantrowitz	2
Lower	2
Others (1 each)[a]	5
Total	30

[a]Lillehei, Webb, Bahnson, Effler, Starzl.

Table 3 First 30 Transplants: Other Countries (December 3, 1967, to October 25, 1968)

Country	Transplants, No.
Canada	8
South Africa	3
France	3
India	2
United Kingdom	2
Brazil	2
Argentina	2
Chile	2
Others (1 each)[a]	6
TOTAL	30

[a]Poland, Czechoslovakia, Japan, Spain, Venezuela, Australia.