

Early days in renal transplantation at Sydney Hospital 1967 – 1983

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Abstract

Kidney transplantation remains the treatment of choice for end-stage renal failure. The Sydney Hospital and Royal Prince Alfred Hospital transplant programme were an integral part of national and international transplant developments. Improvements in immunosuppression, antivirals and other drugs have dramatically improved graft survival rates so that early graft loss is now a rare event. These improvements are the consequence of the sacrifices and commitment of patients, donor families and staff in the early days of transplantation.

Based on a presentation at Royal North Shore Hospital on the occasion of renal donors being recognised (2006).

Recollection:

In 1967 I completed my membership of the Royal Australasian College of Physicians, deciding upon a specialist career in Renal Medicine. I was then at St Vincent's Hospital in Sydney. Fortunately the Sydney University Renal Transplant Group decided to embark on a community based cadaveric renal transplant program for NSW (Sheil, Stewart, Johnson et al. 1969). Renal transplants had been performed in NSW at Prince Henry Hospital at least two years earlier and other NSW patients with living donors had also been referred to Adelaide where an Australian surgeon Peter Knight was performing living renal donor transplants. The Sydney University group was headed by Dr John Stewart from Sydney Hospital, Dr John Sands and Professor Ross Sheil from Royal Prince Alfred Hospital with transplant operations taking place at both hospitals from potential donors referred from all major NSW hospitals. Professor Sheil is a Queensland graduate who had trained in Boston after a sojourn in England. His appointment to Sydney Hospital in March 1967 provided political clout

within the Sydney University group as well as surgical and clinical expertise. Dr John Stewart is a New Zealand graduate who had trained at Hammersmith Post-graduate Hospital in London as well as other UK centres before his appointment to Sydney Hospital in the mid-sixties. He had a particular interest in the bleeding disorders of uraemia. Collaboration between teaching hospitals in Sydney in those days was a rare event so this was a new and exciting venture for all involved. The Sydney University Group needed the co-operation of other interested parties to find and provide the cadaveric donors across NSW to make it viable. Accordingly I was invited as a St Vincent's Hospital representative to a series of evening meetings to discuss the mechanics of organ donation. In the event, in late 1967 a kidney donor was identified at St Vincent's Hospital; I was heavily involved in the organisation and my colleague the late Dr Michael Donnellan organised the operating suite for the visiting surgical team. Unfortunately there had been no approval at any level in the hospital for such procedures and Michael and I were summoned next day to a meeting with

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Mother Rectress, Monsignor Connolly from the seminary at Manly and other significant figures to explain ourselves. After due consideration the programme was then approved.

The state-wide programme was arranged so that a neutral party, the Red Cross Transfusion Service in Sydney did the tissue typing under the direction of Dr Helen Bashir and allocated the kidneys according to the best HLA match, with the ABO blood groups being compatible. Unfortunately there was no infrastructure so the Red Cross technician rang the doctor at the donor hospital about the possible recipients and that doctor became responsible for contacting the other hospitals involved. As most donor operations were done at the end of the day's operating list, and tissue typing took 8 hours, most of these phone calls were made in the wee small hours. Moreover renal physicians across Sydney were usually involved directly in requesting approval for organ donation from distressed families of suitable donors. Brain death legislation introduced in about 1972 was a boon to more certain identification of suitable donors. Prior to that legislation only non-beating heart donors were used for transplantation. The subsequent appointment of the transplant co-ordinators in about 1972 was very much appreciated by the senior medical staff as they took over all these roles related to identification of suitable donors, obtaining consent, and the organisation of donor surgery.

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As it happened the operations were shared reasonably equally between the two hospitals. The first renal transplant at Sydney Hospital was performed in August 1967. At Sydney Hospital, Dr Brian Storey, a urologist appointed as staff surgeon specialising in urology, renal transplantation and vascular access surgery did most of the donor nephrectomies and transplant operations. As most nephrectomies for transplantation were done after-hours, the burden of the transplant surgery largely fell on Brian during the night shift. The renal physicians were also involved in perfusing the donor kidneys and their transport, eg picking up from the RAAF base at Richmond, until co-ordinators were appointed.

I went overseas for nearly 2 ½ years from mid 1968 and returned in late 1970 as Staff Physician at Sydney Hospital. By that time Dr John Stewart had accrued some 75 transplant patients, was running the hospital haemodialysis unit, and had initiated a home haemodialysis unit based on the Seattle experience. Peter Morris, an Australian businessman had developed end stage renal failure while in Seattle in 1966, returned to Melbourne in 1967 where he was trained in home dialysis by Dr John Dawborn (who had trained in Seattle) at Royal Melbourne Hospital where I first met both of them, and moved back to Sydney subsequently. Peter was a major force in The Lions Clubs in NSW which provided the first haemodialysis machines for home patients and eventually embarrassed the State government into providing them.

The patients from the first renal transplant cohort at Sydney from August 1967 were a very eclectic and interesting group of people who insisted on taking the senior medical staff to dinner annually, and contributing to a research fund. At least two of those patients have now survived 40 years from the time of renal transplant, each with their first graft. Another, recently deceased, survived a record 35 years with her third

kidney transplant. In retrospect this group of patients seems to have done well because they had been frequently transfused while on dialysis and despite such provocation had negative cross matches with their donors so that the then available immunosuppression proved adequate for most. Professor Peter Morris, then a Melbourne transplant surgeon, described the paradoxical effect of blood transfusion whereby multiply transfused patients did well with transplantation while the prevailing theory held that transfusion provoked antibodies which should initiate early rejection (Morris et al. *Med J Aust* 1968, 2;1088-1090). Transfusion is a two-edged sword in that those who don't react and develop antibodies are likely to accept grafts whereas those who react strongly develop antibodies to most white cell antigens, i.e most of the donor pool, and are likely to reject grafts. This issue has only been resolved with the development of Erythropoietin some 30 years later, the most significant dialysis advance in the last 40 years. Erythropoietin has significantly reduced transfusion needs in the dialysis population and the number of highly sensitised potential recipients.

Until 1970, the only immunosuppression available was prednisolone and azathioprine. Professor Sheil had been involved with the development of antilymphocyte globulin while in Boston and had initiated programmes at Sydney University to produce such globulins from a horse, with the assistance of Doug Meares who continues in renal transplantation to this day. The clinical trial of antilymphocyte globulins conducted by the Sydney University group in the early 1970s proved beneficial (Antilymphocyte globulin in patients with renal allografts from cadaveric donors. Late results of a controlled trial (Sheil et al. *Lancet* 1973,2; 227-228). Those three drugs provided the immunosuppression protocol for the next 10 years until cyclosporine became available in the early 1980's. Because of the broad

immunosuppression (not directed at the specific pathways of transplant rejection especially by T cell activation) opportunistic infections were common. We saw our share of Pneumocystis, Cryptococcus, Mucormycosis, atypical M. tuberculosis of the skin, Listeriosis and Cytomegalovirus, the last being a real problem until the advent of effective antiviral therapy and prophylaxis in the mid 1980s. It soon became apparent that there were also major skin complications, especially the frequency of squamous cell carcinoma, occasionally lethal, in our largely Caucasian recipients. Later studies found that these were related to pre-transplant sun exposure and were more common in fair skinned blue-eyed recipients (Kelley et al 1987).

Cyclosporine became available for use as immunosuppression in the early 1980's and the Sydney Hospital Group were part of the Australian multi-centre trial which determined that not only that it was effective but that stopping it after three months and continuing with azathioprine and prednisone provided better long term renal function without loss of graft or patient. (Hall et al 1988)

From the 1970's, about 40 cadaveric renal transplants were performed each year although the numbers started to fall in the late 70's. Living donor transplants were rare with the first at Sydney Hospital being performed in about 1972 and none thereafter for another five years. The preference for cadaveric renal transplantation was largely based on the early experience of the senior staff when overseas where they felt that some potential donors were coerced or remunerated or both for kidney donation. As Australia had such a good reputation for its blood transfusions, it was reasoned that cadaveric donations would also be a long term solution to renal transplantation, although this has proved not to be the case in recent years. Nevertheless, because the combined programme was so enthusiastically

pursued, the Sydney Hospital/ Sydney University programme promptly produced the largest group of successful cadaveric transplant recipients in the world. Other major centres overseas had concentrated on living donor programmes or were not as successful in their cadaveric recipients (Mahony 1989). We were able to report larger numbers of long-term cadaveric graft recipients than most world class transplant units (Mahony et al. 1995).

Between 1968 and 1970 Drs Charles George, (currently a renal physician at Concord Hospital), and Philip Clifton Bligh, (eminent Sydney endocrinologist) were registrars. In 1970 John Charlesworth (recently retired as Head of Renal Medicine at Prince of Wales Hospital) and Professor Eileen Gallery (Professor of Obstetrics and Medicine at Royal North Shore Hospital) were the renal registrars. Thereafter the Sydney Hospital Renal Unit attracted registrars for vocational training in nephrology on a regular basis, both locally and from abroad eg: Dr Dan Cattran from Toronto, Dr Paul McCarthy from Ireland, Dr Cherian Thomas from India. Other international registrars came from India, England and New Zealand. Dr Lloyd Ibels and Dr Elliott Savdie both trained in renal medicine at Sydney Hospital and Dr Savdie completed his MD thesis while there.

The transplant area at Sydney Hospital was on the 4th Floor in a purpose built area with low pathogen UV change rooms, 2 isolation beds with laminar flow, a four bedded area and 2 other beds. This low pathogen area was shared with neutropenic patients from the haematology group which made up part of the Kanematsu Research Institute, which also included renal medicine, hypertension, haematology, immunology, rheology and pathology. We were fortunate to have nurse unit managers (Sisters in Charge in those days) Mary

McGurgan, Gillian Anderson and Derani Morgan. Patients were monitored daily for at least the first month, and often up to three months if they had a rejection episode, in a formal out-patient clinic. All patients were expected to attend at least every three months even if all was well, so they could benefit from rapid advances in what was an exciting time in the development of transplantation. This arrangement allowed us to quantitate the complications of renal transplantation, and to develop methods for their prevention. (Mahony et al. 1982)

From about 1969, the Renal Unit at Sydney Hospital had run a post-graduate nursing program in nephrology and transplantation. This was initially supervised by my predecessor, Dr Krishna Mani from India who spent 1969-70 there. The course involved some nine months combined clinical and academic work. It was subsequently taken over by Sister Linda Moynahan as the supervisor, with most of the lectures given by the Renal Unit medical staff. Dr Jim Hayes from St Vincent's Hospital was regularly invited as an outside examiner for the oral examination which formed part of the requirements. Many fine nurses went through this course. These included, but are not limited to Sisters McGurgan, Anderson (both above), Lyn Richards and Liz Yuill who formed the basis of the renal unit at Westmead when it subsequently commenced in 1979; Fran Duncan and Kay Clynick who commuted daily from Blacktown with four of their fellow nurses prior to the Blacktown Dialysis Unit being established as the first satellite dialysis unit in Australia (Mahony et al. 1979). Other nurses went on to develop satellite dialysis centres, eg Chris Wilkinson in Lismore and Penny Wright at Wagga Wagga. Liz Yuill and Liz Sugar were in charge of the Sydney Dialysis Centre for over 30 years. More recently Sr Derani Morgan has been the renal transplant nurse unit manager at RNSH.

The renal research in the Sydney Hospital was focussed on the vascular disease in renal failure patients while on dialysis, and post transplant. This was largely because of the high rate of post transplant myocardial infarction and other vascular events earlier in the history of the programme (Ibels et al. 1974). Subsequently Dr Lloyd Ibels and Dr Elliott Savdie undertook significant research with the assistance of Georgie Crawford into the lipid abnormalities in renal failure, dialysis and transplantation (Stewart 1975). Dr Gordon Stokes from the hypertension unit at the Kanematsu Research Institute also contributed with studies into the hypertension component of renal failure. The dyslipidemia which develops during renal failure is exaggerated by time on dialysis and partially reversed by renal transplantation, although renal transplantation also contributes a higher total serum cholesterol levels in graft recipients.

The 1970's in retrospect seemed the best of times in terms of medical administration. Dr Fred Gunz was director of the Kanematsu Institute and he ran it as a benign dictatorship. We had relatively few financial concerns compared with more recent times. The weekly research meeting was a highlight with all senior members expected to contribute regularly in advancing the frontiers of science. As there was a broad spectrum of basic and clinical science from the multidisciplinary group, the Kanematsu Institute was a great training ground for all concerned, and I was fortunate to be part of it.

In 1979 Dr John Stewart took up the position as the first Head of Renal Medicine at Westmead Hospital. A number of key nursing staff left with him. Prior to his departure, Dr Elliot Savdie had been appointed as Staff Renal Physician in 1977 to assist with the burgeoning workload. In 1981, Dr Robyn Catterson was appointed as Dr

Stewart's replacement, again as a Staff Specialist in Renal Medicine. Professor Alan Alfrey, my ex-chief from the Veterans Administration Hospital in Denver, Colorado spent a 6 month sabbatical at Sydney Hospital in 1980. By this time a separate renal laboratory had been built, under Dr John Stewart's direction, with funding largely from the Isobel Menzies estate, on the 6th Level of Sydney Hospital, adjacent to the office I shared with Brian Storey. Isobel Menzies was a Brisbane woman who was a successful Sydney Hospital renal graft recipient, having been denied a transplant in Brisbane. Dr Elliott Savdie and Professor Alfrey perfected various animal models for the study of renal disease, and thyroid and parathyroid effects in renal failure.

Other staff members involved at Sydney Hospital included the pharmacist John Rothwell, Social worker Ms Julie Blyth, Sister Sylvia Martin who ran Ward 17 (the renal ward), Sisters Diane Lloyd-Jones and Di McDermott in charge of the Ward 17 verandah haemodialysis unit, and a number of local vocational registrars in nephrology including Drs Bill Chan, Paul Trevillian, Mark Thomas and Tim Furlong, all of whom have made contributions to nephrology in Australia and internationally. Ms Trish Rowan was the renal unit secretary for most of the 1970's until 1983 as described above, in an era when many manuscripts were totally rewritten and word processors were yet to be invented!

In early 1982, the State Government announced that to support the increasing population in Western Sydney and their medical needs, Sydney Hospital or parts

of it would be closed with the special units, including the Kanematsu Institute, being deployed elsewhere. Various offers and counteroffers were made but after more than 100 meetings between the Department of Health, the Renal Unit at Sydney Hospital and Royal North Shore Hospital, the renal unit from Sydney Hospital transferred to Royal North Shore Hospital in February 1983, bringing with it a renal transplant program and an in-house dialysis unit not previously available at Royal North Shore Hospital. The Sydney Dialysis Centre which had moved from Lulworth House at St Lukes Hospital in Kings Cross to "Duntrim" in Edgecliff in 1982 had always been under the control of Sydney Hospital Renal Unit and remained so after the transfer to Royal North Shore Hospital.

Conclusion

Renal transplantation remains the treatment of choice for end-stage renal failure. Its success owes much to the early patients who opted to undertake the procedure, the pioneering staff who made it possible, community support, and particularly the donor families, without whom the Sydney University combined Sydney Hospital / Royal Prince Alfred Hospital transplant programme would not have been possible. Improvements in immunosuppression, antivirals and other drugs have dramatically improved graft survival rates so that early graft loss, always tragic, is now a rare event. These improvements are the consequence of the sacrifices and commitment of patients, donor families and staff in the early days of transplantation.

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