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Dialysis and transplantation: problems for the future

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HAEMODIALYSIS

The effective treatment for renal failure dates from the invention during World War II of the first workable artificial kidney by Dr Wilhelm Kolff in Klampen in occupied Holland. He demonstrated that it is possible to remove waste products of metabolism from the bloodstream, thereby cleansing the body when the kidneys have failed. Moreover, he showed that clinical improvement followed rapidly. By repeated use of this treatment, some patients could be kept alive long enough for their own kidneys to regain normal function. As far as I am aware, he provided the first evidence that acute renal failure need not be irreversible. While the idea of removing toxic substances from the bloodstream was not new, Kolff was the first to devise practical equipment for this purpose (Fig 1). The patient's blood was passed from a cannula in the radial artery into a long tube of cellophane sausage-skin which was wound around a supporting drum-shaped framework. The frame rotated on a spindle so that the blood-filled tubing was bathed in a tank containing dialysis fluid. The cleansed blood was returned by another cannula inserted into a convenient large vein and the process repeated until the biochemical abnormalities were considerably ameliorated. The blood was prevented from clotting by repeated injection of heparin into the blood circuit.

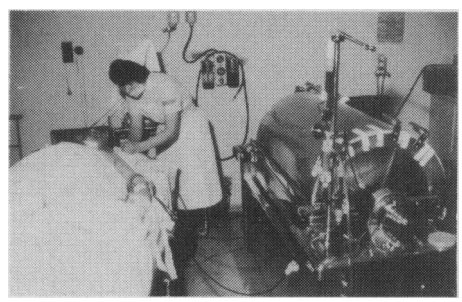

Fig 1. One of Kolff's rotating drum artificial kidneys, first developed about 1948.

Kolff went on to devise an improved artificial kidney in which the cellophane tubing is contained within a compact coil, the necessary large surface area provided by two tubes, the bloodstream being divided into two to supply each tube. This design was capable of being manufactured and sterilized ready for use — the first disposable kidney. In all coil dialysers the dialysis fluid is pumped around the blood-filled dialysis membrane, rather than the tubing itself being rotated through a stationary bath of dialysis fluid. The coil is supported in a container and the dialysis fluid is pumped through the coil and splashes back into the bath to be recirculated again. Fig 2 shows the twin-coil kidney with which we began our service for renal failure in Belfast in 1959.

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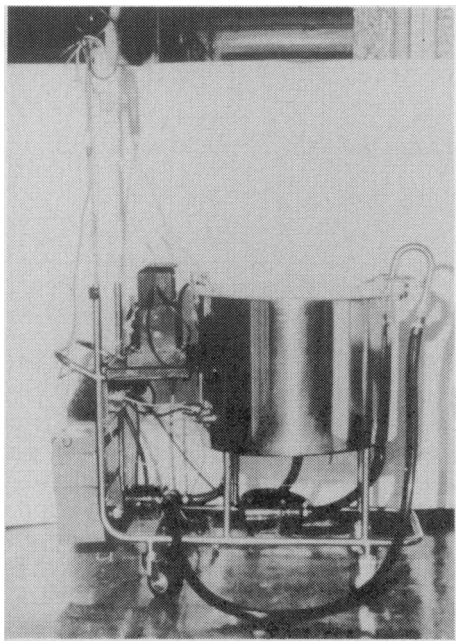

Fig 2. Kolff's twin coil kidney, Belfast, 1959.

Several other forms of artificial kidney have been devised. These include flat plate dialysers in which two sheets of dialysis membrane are sandwiched between plates of polypropylene which are engraved with grooves, along which the dialysis fluid is pumped and passed to waste. The prototype of this was designed by Kiil in 1960 and uses two such sandwiches. The artificial kidney now most widely used is the capillary kidney in which the blood is passed through enormous numbers of capillary tubes made of dialysis membrane, around which the dialysis fluid is pumped.

After the War, Kolff gave artificial kidneys to Hammersmith Hospital in London, Mount Sinai Hospital in New York, and the Royal Victoria Hospital in Montreal, all of whom reported successful treatments. Sadly the kidney which he gave to Amsterdam was never used. The artificial kidney stimulated interest in the kidney, its functions and its diseases. At Hammersmith Hospital there was very active interest in the kidney when Dr Graham Bull came as a Research Fellow from Cape Town in 1948. He was involved, with Milne, Borst and others, in the early use of the artificial kidney. By his accounts the original Kolff with its wooden tank and framework was difficult to set up and patients developed convulsions and rigors during treatment. He became more interested in water and electrolyte balance and the dietary management of renal failure, and published seminal papers with Borst and Milne.[1,2] They developed the subsequently famous Bull-Borst diet, a protein-free regimen which provided energy as pure carbohydrate and oil. The aim was to provide enough energy to prevent wasting of body tissues, thus sparing nitrogen production, without giving sodium and potassium. The diet was difficult to take, the patients became nauseated by the mixture of glucose or lactose and oil, and developed sore mouths. Equally important was the concept of fluid restriction, because patients with uraemia become thirsty, and, if allowed to drink freely, develop oedema and then heart failure. Graham Bull was appointed the first full-time Professor of Medicine in Queen's University in 1952, bringing to Belfast the new expertise in management of kidney diseases. I had the good fortune to join his Department as an MRC Research Fellow in 1953.

DEVELOPMENT OF HAEMODIALYSIS IN BELFAST

Up to this time Professor Bull had maintained that most patients with acute renal failure would recover with conservative treatment and that the population of Northern Ireland was not big enough to justify an artificial kidney. In 1958, the son of one of our consultant obstetricians developed acute renal failure following a road traffic accident. Conservative treatment did not seem to be enough and he

was flown to Hammersmith, where it was found he was already producing urine again and he did not need dialysis after all. However, questions were asked in Stormont about the need for an artificial kidney for Northern Ireland, with the result that it was decided to set up a Renal Unit in the Belfast City Hospital. The choice of the City Hospital for the siting of the new service was due to the late Mr John Megaw (Fig 3). I was given the task of setting up the service, with the grade of Junior Hospital Medical Officer, in 1958, to be elevated to Senior Hospital Medical Officer in 1960.

Fig 3. John McIlroy Megaw, FRCSEd, consultant surgeon at the Belfast City Hospital, 1948-71.

The artificial kidney arrived one day in early June 1959 but the ward was not ready for occupation for another nine months. It happened that a GP refresher course was being held at the City Hospital two days later and Mr Megaw, always an enthusiast, insisted that I should set it up and demonstrate it to the GPs. By this time a technician, Mr Maurice Bingham, had been recruited from the Biochemistry Laboratory to assist me. I had seen a twin coil once; he had never seen one at all. The pair of us read the booklet, which came with the apparatus, and proceeded to set it up using red ink to mimic the blood circuit, much to the satisfaction of Mr Megaw and his class of GPs.

Meantime, Dr Eliahou from Israel, who was finishing a year's attachment with Professor Bull, learned of the arrival of our equipment and wanted to see it in action before departing for home. Professor Welbourn tied the ureters of a dog and we waited 48 hours for it to become uraemic. Our first haemodialysis was carried out in the animal theatre in the Department of Surgery. We managed to give the dog a short dialysis, enough to demonstrate a satisfactory fall in blood urea. Dr Eliahou returned to Israel where he later set up the Renal Unit in Tel Aviv, and he is now a world expert on acute renal failure.

At this point, I felt that I was ready to visit the Renal Unit at Halton to see how dialysis should really be carried out. However, the following week an elderly man was admitted in uraemia due to prostatism. He was semicomatose with a blood urea over 600 mg/100 ml. Mr Megaw demanded that I should treat him by dialysis. 'You dialysed a dog last week, you cannot let my patient die without trying'. Mr Maurice Bingham and I set up the twin coil kidney in Ava 2 theatre (which no longer exists) and Miss Eileen Martin, the Medicine Department technician, weighed out three sets of chemicals to make up three changes of the dialysis fluid. Mr Megaw inserted the cannulae in the radial artery and cephalic vein, and in fear and trepidation we treated our first patient. My stepson, John Freeland, sat in my car at the front of the Ava to act as messenger. When I wanted to send a blood sample to the laboratory, or when I needed to have an extra set of chemicals weighed out after I had stupidly spoilt one bath of dialysis fluid, I just stuck my head out of the window and hollered for him to come up. It was a very

successful treatment in that the blood urea fell from around 600 mg/100 ml to 200 mg/100 ml after about six hours, and the patient wakened up. Unfortunately he died within a week from a cerebrovascular accident.

From then on we were in business. We were still without the promised accommodation in Ward 9, and our headquarters consisted of a small room in Ward 15 formerly used as a store. The hospital van took us and the kidney to the patient, most often to the Royal Victoria Hospital where we dialysed many times in the classroom between Wards 1 and 2, and 3 and 4, in the old ward theatres and later in Ward 22 where Dr Gray was beginning to provide ventilation for patients with respiratory failure. The second patient recovered from 36 days of virtual anuria and was well when I last heard of her a few years ago, more than 20 years later. Another early recovery from acute renal failure after an incompatible blood transfusion is working in the Wakehurst Unit. Not all the patients recovered but, looking back at those early days, the recovery rate seems to have been higher than it is now. This is probably because patients with grave injuries or illness are now resuscitated and live long enough to develop renal failure but may not survive other complications, sometimes dying after renal function has returned. And so I never got to Halton to see how dialysis should be done, and was entirely taught by the book.

There were many problems for our travelling dialysis service. Plugs never fitted and there always seemed to be a problem about the water supply. The team consisted of Maurice, replaced in the spring of 1960 by Mr Jack Lyness, and myself. About two hours were needed to prepare the apparatus; the treatment lasted six hours, with another hour or more to clear up. It never seemed possible to complete the procedure in less than 10 hours.

Things became easier when we moved into the new unit in Ward 9. Thereafter the patients were brought to us, except for the very seriously ill on respirators. I was still the only doctor; there was no question of a rota. Eventually, in 1963, I was able to persuade Matron that we needed our own nurse and Staff Nurse Kay Maguire was appointed. She has contributed enormously to the development of the service and as Senior Nursing Officer leads the now large nursing team. From this point the work increased greatly and patients with undiagnosed renal failure began to be admitted. Many of these had chronic renal failure. At that time the artificial kidney was not used for treatment of chronic renal failure because all available superficial blood vessels were soon used up. This situation was changed in 1960 by the invention by Scribner[3] of an external shunt between artery and vein, which could be opened for treatment, then reunited as a shunt. This could be repeated many times allowing treatment to be continued almost indefinitely.

Our first arteriovenous shunt was inserted by Mr Will Hanna, then a senior registrar, in 1964. The first patient died from septicaemia after a short time. This occurred because we attempted to make the treatment less expensive, re-using the twin coil by washing it free from blood with saline and storing it in the refrigerator between treatments. His brother was to become our first transplant later on. Both brothers had renal failure from polycystic disease.

The second patient commenced treatment in January 1965, and soon became well enough to live at home, returning twice a week for treatment; thus we were able to keep her well but were prevented from accepting any new patient. She had a transplant in St Mary's Hospital, London, in 1965, which functioned well for seven years, eventually being lost due to a deep venous thrombosis which

followed an aeroplane journey. This transplant led to a partnership with Professor Peart's unit and a regular small trickle of patients was sent to London for the transplant operation, returning to Belfast for long-term supervision of the immunosuppressive treatment necessary to prevent rejection of the graft. I will return to the transplant story later.

By this time the flat plate kidney had appeared. This had several advantages for treatment of patients requiring regular haemodialysis, the most important of which was that the volume of the complete blood circuit was much less than that of the twin coil kidney. This meant that the kidney could be primed with saline instead of blood which was needed for the larger volume coils. Moreover the cost of the cupraphane membrane sheets was very little compared with coils costing £22.00 in 1965 money. An engineer in London called Heppel made a copy of the original Swedish model for treatment of his wife in the Royal Free Hospital. He later set up a small business to manufacture Kiil kidneys. He was kind enough to let me have two sets on the understanding that I would pay for them some time. We set to and taught ourselves how to build the brutes, by sweat and tears. Professor Love may remember finding me one Saturday literally in tears because the wretched kidney developed a leak every time it was tested. There were many new tricks to that trade which had to be learnt.

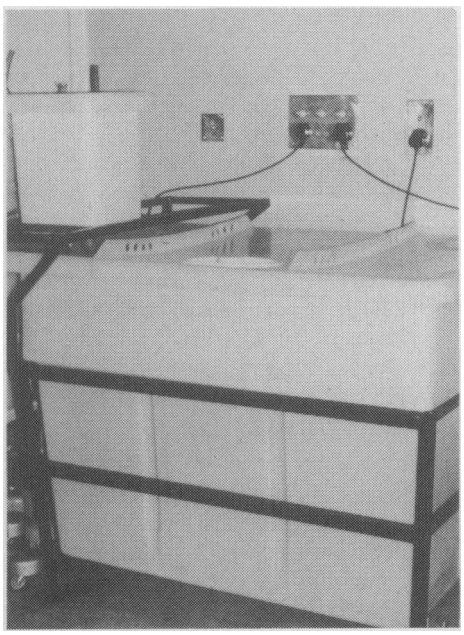

Fig 4. Four hundred litre tank for dialysis fluid, installed 1965.

The Kiil kidney is flushed by fresh dialysis fluid at the rate of half-a-litre per minute, and, as the treatments then lasted 14 hours, a large volume of dialysis fluid was required (Fig 4). The necessary salts had to be weighed out and the fluid mix prepared in a huge plastic fish tank, containing 400 litres. We ordered our tank but it was not to be ready for several months so we set about treating two patients in a make-shift way using the 100-litre tank of the original coil kidney. The patients were treated at night so that the coil kidney could be used during the day for the acute service. Mr Megaw kindly lent us one of his two cystoscopy theatres for this purpose. The tank of fluid had to be replenished four times during the night. The service was possible only because Mr Jack Lyness volunteered to sleep on a couch in the surgeons' room four nights a week, to be awakened by the night nurse when the fluid level went down to a critical point. Mr Lyness did this in addition to his daytime duties for about six months until the new tanks arrived. The cleansing of the Kiil kidneys presented a problem. It is horrifying now to think that, oblivious to the perils of hepatitis B, the bloodstained Kiils were carried the length of Ward 9 to the bathroom at the far end where they were scrubbed in the patients' bath. The dialysis tanks had to be scrubbed and sterilised with hypochlorite and, on occasions, our washings leaked through to Casualty situated just beneath us. At

one stage, patients frequently developed rigors during dialysis, but the cause eluded us for some time. Eventually we discovered pigeon droppings in the water tank which supplied the Unit. The rigors disappeared when we installed a direct supply from the water main.

In 1964 it was envisaged that there would be a haemodialysis unit in the new Tower Block, and in that year I drew a sketch plan, with the enthusiastic help of Mr Paddy Semple, of what I thought was required. In 1965 it became clear that some provision for the growing needs of the Renal Unit would be necessary long before the most optimistic estimate for the opening of the Tower Block. The only way this could be provided was by a new building behind Ava, as there was no space available in the main hospital. The successful treatment of our second patient by regular haemodialysis, followed by transplantation, determined us to develop a service for the treatment of chronic renal failure, which would include transplantation. There was still no other doctor assigned to the Unit though some of Professor Bull's British Council Research Fellows worked with us from time to time to gain practical experience in the management of renal failure. From 1960 onwards a succession of British Council Fellows came to Belfast for the specific purpose of working in the Renal Unit, a number of whom stayed long enough to acquire a PhD. They were Doctors P Metaxis, A Billis, N Papadoyannakis, D G Oreopoulos (all from Greece), R Gupta, J Jindal (India), H Goetz (Hamburg), I Taraba (Hungary), and M A O Soyannwo (Nigeria).

The first phase of the building, now known as Renal I, was ready in July 1968. It contains six single-patient rooms, a theatre and a two-bed dialysis room, later to become the transplant theatre, plus the usual offices. The patient rooms are situated between 'clean' and 'dirty' corridors, communicating with each. The staff enter the Unit through changing rooms, as to a theatre suite. All medical and nursing care is provided from the 'clean' corridor. Disposal of used items is via pass-through cupboards to the 'dirty' corridor. Each area has its own air supply and differential pressure ventilation ensures that air flows from 'clean' towards 'dirty' areas. The system provides good quality reverse barrier nursing, without need of airlocks, provided that the discipline of usage is carried out meticulously. The design of the Unit makes it possible to nurse patients with low white cell counts due to immunosuppression, who are very susceptible to infection, in rooms adjacent to patients with acute renal failure who are often infected.

The expansion of the service has depended on a series of technical advances. When several patients are treated simultaneously a very large volume of dialysis fluid is required, and it is no longer feasible to make up batches of fluid in large tanks. This problem was solved by the introduction of concentrated dialysis fluid made commercially at 35 times the working concentration, which is diluted automatically by a proportioning system of pumps controlled by conductivity meters. The dialysis fluid is no longer recirculated, as it was in coil kidneys, but is a single pass to waste, so that the blood is always dialysed against fresh fluid. Enormous quantities of water are required to dilute the commercial concentrate to working strength. The water must be purified by filtration to remove suspended 'gunk', then passed through a de-ionizer to remove calcium and aluminium, both of which are injurious if continuously absorbed during the many hours of treatment. Ideally the water should have a final purification by reverse osmosis but we have been able to dispense with this due to the good quality of Belfast water.

During the late 1970s, several systems were developed permitting dialysis by single needle. The bloodstream is immediately divided by a Y-junction into two

streams, one entering and one leaving the artificial kidney. The best of these systems uses two blood pumps, the return one being set to return the blood very rapidly to prevent mixing with the blood about to pass into the dialyser, as mixing would obviously reduce efficiency. This extra equipment is expensive but has obvious advantages to the patient. Thanks to the Northern Ireland Kidney Research Fund we were able to change to single needle haemodialysis as early as 1978.

HEPATITIS

The account of haemodialysis would be incomplete without mention of hepatitis. Hepatitis infection increased rapidly in European renal units in the late sixties. It affected staff as well as patients and some staff members died. In 1967-68 a transplant surgeon died in Edinburgh, and Manchester lost a doctor and a nurse. At that time it was customary to transfuse patients on dialysis as a matter of routine when their haemoglobin became low. It was thought that hepatitis was spread by blood transfusion and by 1968 many units began to avoid transfusion as much as possible. In 1969 laboratory tests for hepatitis B (formerly known as Australia antigen) became available and a pilot study carried out by the Public Health Laboratory Service showed that most hepatitis in renal units was hepatitis B. Attempts were made to control the outbreaks by testing sera from staff and patients regularly, dialysing infected patients in isolation and improving cross-infection precautions. Some centres trained patients with hepatitis for home dialysis but the disease sometimes spread to family members. Hepatitis B has a long incubation period, six weeks to six months, and these patients, unlike most other groups of patients receiving blood transfusion, return repeatedly to hospital, eventually becoming infective when viraemia develops. Staff and other patients become contaminated by spillage of blood or staff pricking themselves accidentally with contaminated needles.

In Belfast we were fortunate to have the help of Dr John Connolly who set up the tests very quickly, and routine testing was instituted. Renal II was opened in May 1972 and from the beginning followed the practices recommended by the Rosenheim Committee. Despite this, we experienced hepatitis for the first time in July 1972. At the beginning of June, a patient with renal failure was admitted from a peripheral hospital, and as usual on admission had the hepatitis B antigen test carried out which was reported as negative. He soon required regular haemodialysis, and was prepared for the programme. He had his first haemodialysis in Renal II on 11 July, blood being taken for a second hepatitis B test on that day as part of the routine surveillance of the Unit. On account of the 'Twelfth' holidays, it was not until 15 July that it was discovered that the test was positive. It then became known that he had received transfusion the day before he came to us, and so must have been incubating the disease. In the meantime the patient had received a second haemodialysis in the normal way. He was then isolated in a side-ward and a list of volunteers was drawn up to treat him. As the Unit was not yet fully operational there had not been any sharing of equipment with any other patient and we were optimistic that all would be well. However, three other patients developed hepatitis, the last one in October 1972. On the advice of Dr Sheila Polakoff from Colindale, we set up isolation dialysis in two mini-caravans at the back of the Unit. The Unit was closed for the admission of new patients and transplantation ceased for six months. Some patients died untreated as a result of this action. However, no further cases developed. Three patients eventually died but one survived, eventually to be declared non-infective and to have a transplant

in 1973, being well with excellent graft function over 12 years later. You can appreciate this was a very anxious time for us all, anxiety becoming acute when a patient developed a positive test shortly after one of the nurses had pricked herself while putting him in dialysis. Mercifully she did not develop jaundice but later was found to have the antibody indicating sub-clinical infection.

Hepatitis now occurs only as rare sporadic cases in the UK, but it seems to be on the increase in Europe as a whole. However, immune globulin is now available for protection of staff and patients if there is a serious risk of infection.

PERITONEAL DIALYSIS

Over the years during which these improvements were taking place in haemodialysis, other developments were occurring. It had been known from the end of the nineteenth century that water and some other substances could pass from the peritoneal cavity into the bloodstream and vice versa, the peritoneal membrane acting as semipermeable membrane. From 1920 onwards numerous experiments in animals and a few attempts in humans were made to use the peritoneum for dialysis.

Peritoneal dialysis can be carried out without special equipment other than the plastic cannula and modified Y-piece infusion sets. In theory, at any rate, it can be carried out in any hospital ward. Although the method is simple, great care is needed to prevent infection of the peritoneal cavity. Like everything else, it works better for the experienced. Since 1977 a new concept for the use of peritoneal dialysis has evolved from the work of Popovich and Nolph[4] in the USA. They showed that continuous peritoneal dialysis for six or seven days per week, changing the fluid only four times in the 24 hours, provides very effective control of uraemia. The patients experience remarkable improvement in wellbeing. The disadvantage of this method is a high incidence of peritoneal infection. Oreopoulos[5] in Toronto has introduced several improvements into this system. The most important is the use of plastic containers for the dialysis fluid which, after the fluid has run in, can be rolled up and carried in a pouch attached to a belt around the waist. The same bag is then used to collect the spent dialysis fluid. A special flexible permanent silastic cannula is used.

The CAPD method can be taught to patients of even moderate intelligence in about two weeks, compared with the two or more months' training needed for self-haemodialysis. The only equipment needed is a stand to support the bag while the fluid is flowing into the peritoneum by gravity, and a small table on which to set out a sterile towel, wipes, cleansing fluids and clamps. Storage space is required for the bags of fluid, sterile dressing packs and the necessary cleansing fluids. Oreopoulos has done a great deal to make CAPD an acceptable method of treatment and continues to investigate the long-term effects. I am proud of the fact that he received his nephrology training in Belfast and holds a PhD of Queen's University.

RENAL TRANSPLANTATION

As long ago as 1902, Ullman in Vienna demonstrated that a kidney could be transplanted from its normal site into the neck, and urine would be produced. A kidney from another animal, even another species, would produce urine. Carrell and others repeated this experiment and found that a dog whose own kidneys had been removed would remain well for a few days, after which the transplant ceased to function. Attempts to transplant kidneys in the human by

Voronoy in the Ukraine in 1933 were unsuccessful, as were several attempts in Boston in the early 1950s. About the same time, animal experiments in Boston showed that skin could be transplanted between litter mates, the animals not 'recognising' the transplant as foreign tissue. This led to the first successful kidney transplant operation in 1954 by Murray, also in Boston, between identical twins. Over the next five years, transplantation between identical twins was carried out in a number of centres in Europe and America. Some failed for technical reasons but in none was there evidence of rejection. An identical twin transplant carried out in Belfast in 1962 was a technical failure.

It is obvious that few patients reaching end-stage kidney failure are fortunate enough to have a twin able and willing to provide a kidney. The question was, could rejection be prevented when the graft was taken from a less closely related individual? Whole body irradiation was used to prevent rejection but the patients died from uncontrollable sepsis because of bone marrow suppression. Attempts were made to use immunosuppressive drugs and Roy Calne and others reported in 1960 that mercaptopurine prolonged survival of kidney grafts in dogs but was very toxic. Burroughs Wellcome produced a derivative of mercaptopurine, azathioprine, which proved to be a good immunosuppressive drug and much less toxic that the original. In 1962 azathioprine was used successfully when a kidney taken from a patient dying during an open heart operation was transplanted into an unrelated individual. Azathioprine thereafter became generally accepted as the main immunosuppressive drug for transplantation for almost two decades. In 1962 Goodwin reported successful treatment of several rejection episodes with steroid, in a mother-to-child transplant, although the child finally died from sepsis. After this report the combination of azathioprine and steroid was accepted as standard therapy for kidney transplantation. In 1976 cyclosporin A, a fungal metabolite, was found to be a potent immunosuppressant and is now widely used, though it too has serious drawbacks. The age of drug immunosuppression had arrived, and opened up the possibility of treating end-stage kidney failure by transplantation.

From the time of Murray and Calne's demonstration in 1962 that cadaveric transplantation was possible with the aid of azathioprine, it seemed to me that transplantation would prove to be the definitive treatment of end-stage renal failure. Good quality dialysis therapy would be needed to make the patients fit and maintain them until kidneys could be provided. If the graft fails, the patient should survive to return to dialysis therapy and have a second, even a third or fourth graft.

My first attempts to put this philosophy into practice were possible through the help of the few centres in the UK doing experimental work in transplantation. Professor Woodruff transplanted one of my patients from her father in 1962. She did not survive, but over the years 1965-68 Professor Peart at St Mary's Hospital, and later Professor Roy Calne, accepted my patients. Figure 5 shows Professor Calne, by this time Professor

Fig 5. Professor R Y Calne, FRS, FRCS, with Mr J Neill, who received a renal transplant in Cambridge in April 1966.

of Surgery in Cambridge, with his longest surviving cadaver transplant, one of my patients, who was transplanted in April 1966. The graft continues to function excellently.

Our transplantation programme began in 1968 soon after the opening of Renal I. A second consultant nephrologist was appointed and surgeons were designated to take part in the transplantation programme. (Table I). Some are no longer working with us — Dr John Hewitt, Dr Joseph McEvoy and Mr Stewart Clarke have left Northern Ireland, Dr Sam Nelson has left tissue typing. Nurse Kay Maguire who was the first renal nurse in 1963 and is now our senior nursing officer, and Mr Jack Lyness, technician since 1960, have both contributed greatly to the development of the service. I must stress that the good results we have achieved are due to the efforts of the whole team. I must also pay tribute to the great help we have received from the staff of intensive care units who have provided kidney donors. We owe a particular debt of gratitude to the Respiratory Intensive Care Unit in the Royal Victoria Hospital who have provided by far the largest number of donors, and to the others who have found kidney donors. The procurement of a donor entails a considerable amount of extra work for the doctors and nurses concerned. Our tissue typing service was set up under the leadership of Dr Sam Nelson. Following his resignation, Dr Derek Middleton has become head of the service, and indeed has contributed greatly to the development of the work over the last 13 years.

TABLE I

Renal transplantation in Belfast

Anaesthetists:	J P Alexander, C J Hewitt, J Gamble, C Gardiner.
Nephrologists:	M G McGeown, J McEvoy, J F Douglas, C C Doherty.
Surgeons:	S Clarke, J A Kennedy, W G Loughridge, R A Donaldson, R Johnston.
Tissue Typing:	S D Nelson, D Middleton.
Nursing Officer:	K Maguire (1963).
Chief Technician:	J Lyness (1960).

Between 1968 and 1985, 347 patients have received 392 grafts, there being 38 second grafts, six third grafts and one fourth graft. Most of the grafts came from cadavers, only 36 coming from live donors. Two hundred and forty-five patients are alive with functioning grafts, and 11 others are alive, having returned to dialysis after failure of their graft. We had the good fortune to achieve outstandingly good results of patient and graft survival from the beginning of our transplantation programme, and over the years since statistics have been collected centrally, have been at the top of the 'league table'.[6]

Now after almost 17 years it is possible to identify at least some of the factors which contribute to our high success rate which has continued over all this time. The careful organisation of the team has resulted in good clinical care. The most important point in the preparation of the recipient is now known to be the giving

of blood transfusion, which we have done from the beginning of our programme, despite the fact that transfusion was then beginning to be considered a risk factor rather than helpful. The drugs we have given to prevent rejection of the kidney were those in general use but we decided to use much lower doses, particularly of prednisolone, in the hope of reducing toxic side effects. We hoped to improve the results of transplantation by avoiding infection, particularly fatal infection. This we were able to do, by isolation of the patients through the use of the specially designed building, and by using very low doses of steroid compared with other centres.

THE PROBLEMS OF RENAL REPLACEMENT THERAPY

I have described to you a truly marvellous story — the discovery of how the function of a vital organ may be replaced after failure, permitting life to continue for years. Indeed the kidney is the only organ where complete failure of function can be treated. Hard on the heels of this discovery came the development of renal transplantation. Successful transplantation restores the patient to almost complete normality. Machine treatment, dietary and fluid restriction become unnecessary and the patient merely has to take a few pills daily to prevent rejection. Normal energy is regained, indeed patients with transplants become fit, even for competitive sport. One patient starred in the recent victory of Clandeboye in the Irish Senior Cup Golf Competition. Parenthood is possible even for women. One patient has had three successful pregnancies since transplantation. Many others have had one child and several have had two.

As soon as a new service develops, the demand for it grows rapidly. By the end of 1964 we were treating one patient. It was possible to squeeze in treatment for the first patient without detriment to the acute programme. The first patient died after a short time, and other patients followed one by one during 1965. Table II shows the number of patients receiving treatment from 1964 when we began regular haemodialysis until we moved to Renal I in 1968. The number of patients transplanted each year is also shown. Thanks to Professor Vallance-Owen, and the devoted work of Sister Wallace and the nursing staff of Wards 3 and 4 RVH, two patients were regularly given twice weekly peritoneal dialysis from 1968 until 1972 when Renal II was opened. After 1968 the numbers of patients treated increased slowly year by year (Table III), but this in no way satisfied the demand.

TABLE II

Renal replacement therapy in Belfast 1964-1968

Year	**Number of patients on treatment*	*Number of patients transplanted*
1964	1	2
1965	1	2
1966	4	3
1967	4	2
1968	8**	7

*Patients on treatment at any one time.
**Includes 2 patients in Ward 3, RVH.

TABLE III

Renal replacement therapy in Belfast 1969-1985

Years	*Number of patients on treatment	Number of patients transplanted
1969-72	8	16
1972-73	20	31
1974-78	30	106
1979-80	37-39	61
1981	40	25
1982	46	46
1983	50	38
1984	55	37
1985	65	34

*Patients on treatment at any one time including PD.

Since 1978 the increased efficiency of the dialysis equipment, and technical advances in general, have allowed the duration of dialysis to be progressively reduced from 28 to 16 hours weekly for an average-sized adult. We give the weekly treatment divided into two sessions. Most other centres give it in three sessions. This is more costly, which means that fewer patients can be treated, and that the patients have to attend on three occasions. My own observations lead me to consider that two longer sessions provide adequate treatment for most patients, provided they follow the regular discipline of fluid intake and salt restriction. The fact that some of our patients have remained reasonably well for as long as seven years on twice weekly haemodialysis shows that thrice weekly dialysis is in the nature of a luxury.

The shortfall in facilities has always meant that many patients who could benefit do not receive treatment. The very success of the treatment compounds the problem, as relatively few patients die. I have used the figure of 40 patients/million/year as the annual incidence of new patients with end-stage renal disease. This figure is based on a survey carried out during 1969-71 in which many Northern Ireland doctors took part by filling in letter cards to notify their patients with renal failure. It refers to patients aged 5-55 years, medically suitable for treatment, and excludes diabetics, and some other patients who would now be considered treatable. The problem of the shortfall of facilities has been made worse because we have progressively expanded the possibilities by showing that older patients do remarkably well on dialysis therapy and can also be transplanted. We have transplanted with success up to the age of 65. Moreover, it has been shown that some diabetics, and even patients with coronary bypass or ileal conduits, can be transplanted successfully.

How do the facilities available measure up to the needs of our population? You must bear in mind that the figure of 40 new patients per annum does not permit us to treat anyone older than 55 years, and does not allow for diabetic or other disadvantaged patients. It is, however, the target set by the DHSS for all units to achieve by 1987. A few patients die during the first year but about 83% are alive

at the end of the year to be joined by 40 new patients appearing in the second year. In the third year 86% of the first set of patients and 93% of the second set of patients remain to be joined by the new ones. Even at the end of the third year, 80% of the first set of patients remain alive. The number of patients goes on increasing until eventually equilibrium is reached when the new patients are equalled by patients dying. The statisticians tell us that equilibrium will be reached only after 25 years, but 90% of steady state will be reached after 10 years.

The cost of regular dialysis therapy, of course, escalates year by year as the number of patients increases. If the programme is expanded to include older people, diabetics and other disadvantaged patients, more will die each year, but in the meantime they will have had more medical complications and cost more to treat. It is difficult to arrive at a true cost but several years ago the DHSS costed hospital haemodialysis at £11 – 13,000 per annum, and home dialysis at £6 – 8,250 per annum. Home haemodialysis costs less but, if the patient receives a transplant, the cost of converting the home is lost and it takes two years of home treatment to break even. Satellite dialysis is nearly as cheap as home treatment and, as it avoids the cost of converting individual homes, it is the best buy. However, it is cheaper only because of the economy of staffing that becomes possible when only fit stable patients are treated. The saving in cost in the satellite is, to some extent, offset by increased costs in the mother unit which copes with the early problems, and accepts back patients who get into difficulties. Moreover, the older and otherwise disadvantaged patients are not suitable for treatment in a satellite centre.

Transplantation is cheaper but the immunosuppressive drugs cost about £1,200 per annum or more if cyclosporin is used. The saving is illusory as the transplanted patient is replaced by a new patient. The transplant often does not cover the life of the patient, who may need dialysis treatment again. While one of our patients has had a well-functioning graft for more than 20 years, and 47 for 12-15 years, the average is less than 10 years. Six patients have had three grafts and one a fourth graft. We must, however, remember that transplantation provides much better quality of life than any form of dialysis. While it is not possible for all patients the contraindications are relatively few. The limitation to transplantation is the number of donors which can be obtained.

The United Kingdom lags far behind other European countries in its provision for dialysis treatment, particularly for patients over the age of 45, because of lack of resources. Dialysis and transplantation are paid for here by the National Health Service. There is virtually no private dialysis or transplantation, except in London, where it is used almost entirely for patients from overseas. In other European countries, the financial cost of treatment is provided by insurance, and each treatment is paid for directly. If we lag behind Europe, all Europe lags behind the United States. In 1972 laws were enacted there which effectively provided treatment for all American citizens with end-stage renal failure, without charge to themselves. This led to a phenomenal growth of haemodialysis in America, where all patients are accepted regardless of age and of other diseases present. The Medicare budget for end-stage renal failure now approaches three billion dollars. In America it was considered morally intolerable to ration treatment for financial reasons, but this rocketing cost has caused a complete re-think. The medical profession there have been very critical of British nephrologists, blaming them for accepting rationing of treatment because of limited finance. They are now having to face the same moral dilemma.

I put it to you that the very success of our treatment for end-stage renal failure has produced a moral and ethical, as well as financial, crisis of the first magnitude. All patients who could benefit cannot be treated. Who then should be treated and how do we select them? Other advancing medical fields such as heart and liver transplantation must face these issues also. When resources are limited, how to resolve the competing claims of 'high-tech' medicine and the care of the mentally handicapped or the elderly? There is no real solution to this moral dilemma. In Northern Ireland we are on the brink of further development of renal services. The opening of the Tower Block will increase facilities for renal transplantation — but only if a sufficient supply of donors becomes available. However, we can be cautiously optimistic as fewer kidneys will have to be exported because of lack of suitable recipients and of beds. The beds vacated by transplantation moving to the Tower will permit considerable expansion in CAPD, to about 30 new patients per year. The provision of a satellite dialysis centre in the northwest of the Province would provide a further small increase in patients. It should eventually become possible to accept 60 new patients/million/annum, that is 90 for the Province. Even then there will be hard decisions to be made.

Research into the causes and treatment of kidney diseases holds the prospect that some types of end-stage renal disease may be prevented, or at least delayed in onset. Let me conclude by acknowledging the enormous help which we have been given by the Northern Ireland Kidney Research Fund.

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