HAEMODIALYSIS IN EDINBURGH 1957–1987

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ORIGINS OF RENAL MEDICINE IN EDINBURGH

Active conservative treatment of patients with severe uraemia was started in the early 1950s before dialysis was available. This was carried out in Professor Derrick Dunlop's metabolic ward in the Royal Infirmary of Edinburgh (RIE) by Drs James Robson and C.P. Stewart. Patients were given a low protein, low salt, low potassium and high calorie diet as proposed by Giovannetti.[1] Professor Dunlop, Dr Robson and Dr Anne Lambie, from the Department of Therapeutics at the RIE, had interests in endocrine disease and metabolic medicine. The renal unit in Edinburgh gradually evolved from the Department of Therapeutics and Clinical Medicine.

HAEMODIALYSIS IN EDINBURGH: HOW IT ALL BEGAN (1958)

The first practical human haemodialysis machine was developed by W.J. Kolff and H. Berk from the Netherlands in 1943.[2] The Royal Postgraduate Medical School at Hammersmith Hospital in London received one of the rotating drum artificial kidneys that Kolff gave away after World War II and reported its use in a series of patients in 1948.[3] However, haemodialysis was a difficult, time consuming and dangerous procedure at the time, and in the UK, more rigid protocols for fluid and dietary management were strongly believed to be better.[4] Although dialysis techniques and experience improved in the 1950s, it was against some resistance that it was reintroduced to the UK by Dr Frank Parsons at Leeds General Infirmary in 1956.[5]

In 1958 Dr Rae Gilchrist, consultant cardiologist at the RIE, was impressed by Professor Nils Alwall's work on artificial kidneys while attending a conference in Sweden, and suggested that an artificial kidney should be installed in the RIE. Doctor James Robson and Dr Hugh Dudley, who were both senior registrars at the time, were asked to visit the three places in UK where the use of artificial kidneys was established by this time – The Royal Air Force Renal Unit at Halton, Hammersmith Postgraduate Medical School in London (which had obtained a new machine, the French Usifroid version of the rotating drum dialyser) and Leeds General Infirmary (which possessed a 'Kolff-Brigham'-modified Kolff dialysing machine from Boston) – to obtain information about the design and operation of artificial kidneys used in this country. However, it was the newer Kolff-Travenol twin coil artificial kidney in use at Halton that impressed the visitors the most. Group-Captain Ralph Jackson, medical specialist at Halton, spent two days demonstrating how haemodialysis worked and its exciting results. It was reported by Professor Robson and Professor Dudley that:

> . . . the Kolff-Travenol pressure-dialyser possesses material advantages over the other two (dialysers) in respect of ease in sterilisation (i.e. disposable coil), ease of setting up and running, adaptation to ultra filtration and dialysis and, in our opinion, safety in the method and accuracy of the control of the blood volume in the machine . . . The Kolff-Travenol machine is more compactly made and more easily maintained . . . It is considerably cheaper in the capital cost, though more expense is involved in each dialysis . . . The Kolff-Travenol Artificial Kidney with disposable coils and incorporating ultra filtration and dialysis is the machine which combines the most advantages. Its simplicity of preparation and operation and its intrinsic safety are outstanding. It has the additional advantage of relative cheapness.[6]

THE FIRST ARTIFICIAL KIDNEY IN EDINBURGH (1959)

The first artificial kidney unit in the RIE was set up in a small room converted from three clinical laboratories and became known as the Artificial Kidney Unit (AKU). The AKU was opened on 20 May 1959 by the Earl of Wemyss, then Lord High Commissioner to the General Assembly of the Church of Scotland, accompanied by a member of his Bodyguard of Archers. He regretted that it was not possible to fill the 100 litre tank of the artificial kidney with champagne to mark the occasion! The first patient was dialysed two days after the opening of the AKU. A young man presented with biliary sepsis, *Escherichia coli* septicaemia, oliguria and uraemia, who was unfit for the necessary surgery.[7] He was dialysed (see Figure 1) and biliary drainage was subsequently performed. He made an excellent recovery.

Nine patients were dialysed in the first six weeks after the AKU opened, and many more thereafter. The AKU received patients referred from many parts of Scotland, even from as far away as the Orkney Islands. Haemodialysis in those days was lengthy, often taking up to six hours in patients with acute renal failure (ARF) and eight hours in some patients who had been poisoned.

THE KOLFF-TRAVENOL TWIN COIL ARTIFICIAL KIDNEY: TECHNICAL ASPECTS

Dialysis with the Kolff-Travenol twin coil artificial kidney was a labour-intensive procedure. The dialysis machine

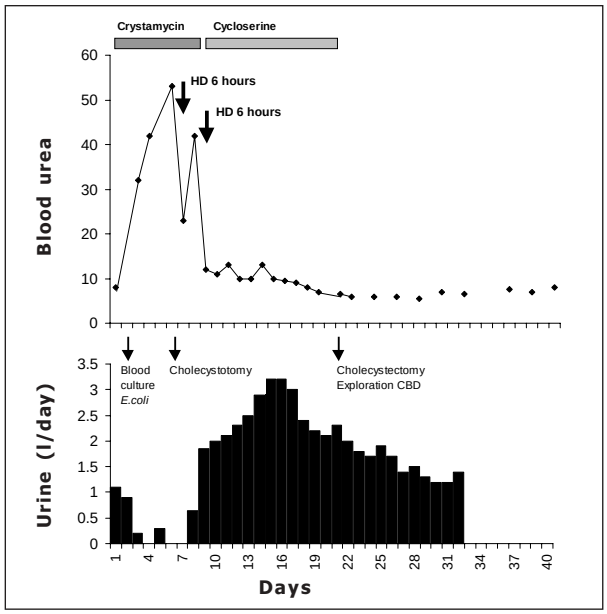

FIGURE 1

Graph showing the urine output and the blood urea level of the first patient dialysed at the AKU in Edinburgh in May 1959.

consisted of a twin coil seated in a big cylindrical steel tank that could hold about 100 litres of water (see Figures 2A & B). Hot and cold water were mixed to the correct temperature, as the heater was only able to maintain a given temperature. Solutes including sodium chloride, calcium acetate, potassium acetate, sodium bicarbonate, glucose and lactic acid were weighed individually and added to the water to make up the dialysate (called the 'bath' at the time). The potassium concentration was altered according to each patient's requirements, and as the physicians became more experienced the concentration of bicarbonate was also modified appropriately. The dialysate bath was emptied and changed every two hours. The patients were weighed continually during dialysis using a weigh-bed, but it often proved difficult to get to the desired weight accurately.

The safety features for the Kolff-Travenol artificial kidney were also limited: there were no alarms, temperature or pressure monitors, full function checks, blood leak detectors, ultra-filtration pumps or air embolism detectors. The machine also had no mechanism to record changes in pressure. The Kolff-Travenol twin coil artificial kidney was kept in use in Edinburgh until the late 1980s despite being a labour intensive operation, since the bicarbonate buffer was more suitable than a lactate buffer for patients with ARF and its use was associated with less circulatory disturbance.

HAEMODIALYSIS OUTCOME FOR PATIENTS WITH ARF

Haemodialysis gave rise to very exciting prospects, as the mortality from severe ARF had previously been almost 100%. As it was a relatively new procedure at first, patients were initially dialysed only if their chance of death due to uraemia was greater than the possible risks of haemodialysis. The results were very exciting; patients who would otherwise have died recovered with dialysis.

FIGURES 2 A & B

The Kolff-Travenol twin coil artificial kidney with its dialysate tank (the 'Kolff bath') (provided by Dr A. Cumming and Dr P. Gibson).

TABLE 1

Percentage survival rate for patients with ARF who were dialysed in Edinburgh between 1959 and 1987. The percentage survival rate improved despite the increasing complexity and severity of the causal illness.

Year	Total number of patients dialysed	Number of patients alive	% survival
1959–1960	29	15	52
1960–1961	25	14	56
1961–1962	26	13	50
1962–1963	29	15	52
1963–1964	29	15	52
1964–1965	25	14	56
1965–1966	42	24	57
1966–1967	37	19	51
1967–1968	38	24	63
1968–1969	38	15	39
1969–1970	42	22	53
1970–1971	42	20	48
1971–1972	36	17	47
1972–1973	38	16	42
1973–1974	51	26	51
1974–1975	52	24	46
1975–1976	43	22	51
1976–1977	40	23	57
1977–1978	41	16	39
1978–1979	52	35	67
1979–1980	61	36	59
1980–1981	33	26	79
1981–1982	52	34	65
1982–1983	53	31	58
1983–1984	69	43	62
1984–1985	58	43	74
1985–1986	69	48	69
1986–1987	93	64	69

As a result, the morale and team spirit among the doctors in the AKU were optimal.

In the first year of haemodialysis, survival was about 52% (see Table 1). Patients usually died of non-dialysis-related problems such as the underlying condition, severe shock or severe infection. They no longer died from the biochemical disturbances associated with renal dysfunction.

Patients with ARF were very susceptible to cross-infection, so nursing in isolation was thought to be beneficial. Initially this was carried out in a room in the Clinical Laboratory that had previously been used to see out-patients. Subsequently, the Renal Isolation Unit was constructed.

THE RENAL ISOLATION UNIT FOR PATIENTS WITH ARF (1962)

A suite of rooms in Ward 23 of the RIE was designed in collaboration with Dr John Bowie, the hospital bacteriologist, to protect against infection. Dialysis for patients with ARF was carried out in this Renal Isolation Unit from 1962 (see Table 2). Four Kolff-Travenol twin coil artificial kidneys were acquired. To prevent cross-infection, reverse-barrier nursing was practised: there was also positive pressure ventilation, designed to prevent air-borne spread of infection from one room to another, and staff working in the unit wore theatre gowns and masks.

The work of the unit increased steadily, and by the end of 1960 65 dialyses had been performed on 50 patients with ARF, and more than 800 were treated by 1981.

HAEMODIALYSIS FOR PATIENTS WITH CHRONIC RENAL FAILURE (CRF) IN EDINBURGH

Although resources would later become an issue, it was

TABLE 2
Important historical data for the Renal Unit at the RIE.

Date	Acute Renal Failure
20 May 1959	First artificial kidney unit established
1962–1993	Renal Isolation Unit: four Kolff-Travenol twin coil dialysers, later replaced by Cobe proportional pumping machines
1964	Opening of the Assisted Ventilation Unit (Ward 19); many of these patients needed dialysis
1993	Renal High Dependency Unit (Ward 43) opened
Date	**Chronic Renal Failure**
Early 1960s	Renal Isolation Unit: a few patients with chronic renal failure dialysed alongside those with acute renal failure
1964	Artificial Kidney Unit: three refrigerated machines with Kiil boards
1966	Ward 21: three proportional pumping machines installed
1969	Medical Renal Unit building opened with ten dialysis stations
1980s	Continuous Ambulatory Peritoneal Dialysis (CAPD) for patients with chronic renal failure began
1982	Ward 44 opened for CAPD training
1994	General nephrology wards (Wards 41 & 42) opened
2001	Currently 17 dialysis stations at the Medical Renal Unit building

vascular access that prevented the immediate application of haemodialysis to end-stage renal failure. Early methods of gaining access to the circulation involved puncturing major arteries or the sacrifice of smaller vessels. Eventually, a technical improvement made repeated access possible; in 1960, workers in Seattle reported the development of an exteriorised Teflon arteriovenous shunt – the Scribner shunt.[8]

At the International Congress of Nephrology in Prague in 1963, there was evidence that dialysis of patients with CRF was beneficial. Subsequently in Edinburgh, a few patients with CRF were dialysed alongside patients with ARF using the Kolff-Travenol twin coil dialysers. The first patient with CRF was dialysed in Edinburgh in the early 1960s. It was not certain at the time whether she was suffering from ARF or CRF, apparently precipitated by influenza. She was dialysed and the outcome was good, although her renal function remained very poor. She was subsequently dialysed at fairly long intervals.

The original AKU was used to dialyse patients with CRF for some time after 1964. Kiil board dialysers were used. To begin with, the dialysis bath was made up in the large refrigerated tank of the dialysis machine. It was thought that refrigeration would reduce bacterial growth in the dialysate during dialysis, which might take up to nine hours. After a short period, this machine was abandoned and the dialysate was made up in a huge plastic tank sited in the laboratory next to the AKU. The fluid in this tank, maintained at room temperature, supplied three Kiil dialysers. Kiil board dialysers are made up in layers like sandwiches: layers of cellophane (the dialysis membrane) between layers of plastic. Theses layers were clamped together tightly. It was often called the 'Kiil sandwich', and it required a fair amount of skill and experience to construct. The AKU worked two shifts per day. The beds were placed in the corridor while the machines were being cleaned in the room. Three patients were dialysed each night at the AKU. Each patient was dialysed twice a week. A summary of the haemodialysis machines used in Edinburgh can be found in Table 3.

Dr Andrew Doig was a general physician with a special interest in renal diseases. One of his patients, a young child, had developed a condition that Dr Doig thought would benefit from dialysis at the RIE. Since facilities were limited, at that time dialysis was rationed. The child was not considered to be a 'high priority' case, and therefore could not be accepted for dialysis. Dr Doig suggested that the child's parents should seek lay help. After pressure from an influential person, the hospital authorities subsequently told Professor Robson that he must accept this child for dialysis. Professor Robson said he would accept the child provided that the other patients on the waiting list could also be dialysed. The hospital board agreed to purchase three more dialysis machines for the unit. In 1966, three proportional pumping machines were installed in Ward 21. Three patients with CRF were dialysed in one half of the ward. Concentrated dialysis solution was mechanically diluted with water to produce a physiological dialysis fluid. Lactate was used as the buffer. However, the machines were not very high tech. Whenever somebody flushed the nearby staff lavatory, the dialysis machines would all temporarily seize up as the water pressure dropped. All the alarms would go off for a short while! A patient who was dialysed in Ward 21 in 1966 recalled:

TABLE 3
Haemodialysis machines used in Edinburgh.

	1959–1968	1969–1979	1980s	1990s	2001
Acute renal failure	Kolff-Travenol twin coil dialysis machine	Kolff-Travenol twin coil dialysis machine	Kolff-Travenol twin coil dialysis machine, Cobe proportional pumping machine with hollow fibre dialyser, Fresenius machine with hollow fibre dialyser	Fresenius 2008C & 2008D machines with hollow fibre dialyser, Cobe proportional pumping machine with hollow fibre dialyser	Fresenius 2008C, 2008D & 4008H machines (since 1994) with hollow fibre dialyser
Chronic renal failure	1961–1963 a few CRF patients dialysed with ARF; patients using Kolff-Travenol twin coil dialyser 1964 Kiil board dialysers 1966 proportional pumping machine with Kiil board dialyser	Dylade B-machine with Kiil board dialyser, Dylade D-machine (since 1972) with hollow fibre dialyser & flat plate disposable, RSP machine with coil dialyser (since 1972)	Dylade D2 machine, Gambro 4 stack machine with machines dialysers (flat plate disposable dialyser used occasionally)	Gambro AK100 machine, Fresenius 2008C & 2008D machines, Althin 3A, 4A & 5A machines (since 1995) with hollow fibre dialyser	Fresenius 2008 & 4008 (since 1994), Althin 3A, 4A & hollow machines (since 1995), Gambro AK100 machine with hollow fibre dialyser

> I was only a wee girl when I had dialysis. Only eight years old at the time. It was terrible to be on dialysis. I was sick through the time and I vomited a lot. I felt very dizzy and there was ringing in my ears. I would go on dialysis from 8·30 in the morning till 4·30 in the afternoon.

Dialysis of patients with CRF showed a different picture from those with ARF. Dialysis kept patients with CRF alive, but it was not a cure. The public, however, thought that dialysis was a miracle because it was life saving, and those treated were very grateful. The demand for long-term dialysis grew.

THE NEW MEDICAL RENAL UNIT (MRU) BUILDING AT THE RIE (1969)

It was decided that a new unit should be purpose-built to meet the demand for dialysis for CRF and for 'maintaining the RIE's position as one of the world's pioneers in the treatment of kidney diseases', as stated in one of the press reports at the time.[9] Dr S.G.M. Francis, then Medical Superintendent, allowed his house to be demolished in 1966 to make room for the new MRU building and the new MRU building was built by the RIE and the University of Edinburgh as a joint effort. It cost about £250,000 for the building and equipment. Seventy per cent of the funding was provided by the health service, 30% by the University.[9]

In early 1969, the new MRU building was completed (see Figures 3A and 3B). The upper level provided facilities for ten dialysis stations. Staff offices, laboratories and an academic area for the University of Edinburgh were situated on the lower level. This building provided the necessary space for dialysis and for university laboratories. The University academic side was very active in the MRU. The academics included a professor (Professor Robson), a senior lecturer (Dr Anne Lambie), a lecturer and research fellows. The new facilities gave a further boost to the ongoing research on renal physiology and disease.

Dylade®, a British company, made the B-machines that were used with Kiil board dialysers in the MRU. It took the technicians a whole morning to clean and line these Kiil boards with cellophane. Patients would arrive at the MRU at about 4 pm, and dialysis would last all night (12–14 hours). There was only one shift each day, but each patient was dialysed twice a week. The Senior House

FIGURE 3A
The new MRU building at the RIE in 1969.

FIGURE 3B
The upper floor of the MRU building with ten dialysis stations in the 1970s (provided by Sister S. Green).

Officer went round the unit and with the nurses' assistance cannulated all the artificial a.v. fistulas. In 1972, D-machines were introduced and they were used with hollow fibre dialysers or flat plate disposable dialysers. Hollow fibre dialysers are comprised of numerous bundles of dialysis tubing contained within a plastic cylinder, and they bore a certain resemblance to the first artificial kidney produced by Abel and colleagues in 1913. Safety devices, such as venous pressure alarms to detect disconnection of lines or line blockage were introduced later; for example, air embolism detectors were introduced in 1972. Before then, patient safety depended on watching the machines. Nurses used to go round the ward at night shining torches to check for blood leakage.

By 1969, there were only two dialysis units in Scotland for patients with CRF. These were at the Glasgow Western Infirmary and the RIE. Another dialysis unit at the Glasgow Royal Infirmary opened soon after.

FUNDING FOR DIALYSIS

Funding for dialysis came from the budget of the RIE. Gifts of more than £200,000 had been received over the years to help with purchasing equipment and research, reflecting the public appreciation of the work of the unit.[9] The Midway Trust and the Kidney Patients' Association were charities set up to provide dialysis patients with equipment and other items that the NHS would not buy, such as furniture, television sets, a coffee room and holiday trips for the patients. Patients and their families raised money by selling raffle tickets and organising other fundraising activities.

HEPATITIS OUTBREAK IN EDINBURGH (JUNE 1969 – AUGUST 1970)

Between 1965 and 1971 several renal units in the UK experienced serious outbreaks of Hepatitis B (see Table 4), an experience which had a strong influence on subsequent development. Edinburgh suffered particularly

badly with 11 deaths, including three members of staff.[10]

THE INDEX CASE

In April 1969, a patient with CRF was transfused with one unit of blood that was contaminated with hepatitis virus (then known as the Australia antigen). Fifty-one days after the transfusion (June 1969), the patient developed hepatitis. Fifty-eight days after the onset of hepatitis in the first patient, a second patient developed hepatitis.[11] Two more patients developed hepatitis after an interval of 90 days. The outbreak became severe after December 1969. The MRU at the RIE and the Nuffield Transplantation Surgery Unit at the Western General Hospital in Edinburgh were seriously affected despite taking all precautions then known against risk of infection.

MECHANISM THOUGHT TO HAVE CAUSED THE HEPATITIS OUTBREAK IN EDINBURGH

The index patient was treated with dialysis. A venous pressure gauge recorded the pressure in the line returning blood to the patient, and it was thought that a small volume of the infected blood had contaminated the gauge. The gauge, being a permanent feature of the dialysis machine, was not changed with the blood lines. When the next patient was connected to the dialysis machine with new lines, the infected blood was therefore passed into the patient. Likely routes of transmission other than via dialysis machines included hypodermic needle accidents, cuts in the hand and blood contacting breached skin surfaces and mucous membranes.

CONTAINMENT AND PREVENTION

The hepatitis outbreaks led to the establishment of an advisory group (the Rosenheim Committee) to the Department of Health and Social Security, the Scottish Home and Health Department and the Welsh Office. The group produced a set of recommendations largely based on work done during the Edinburgh epidemic aimed at minimising the spread of hepatitis.[10]

For six months, new patients were not accepted into the MRU of the RIE or the Nuffield Transplantation Surgery Unit. Ward 44 was set up for haemodialysis of hepatitis patients and those who were positive for the Australia antigen. Patients who recovered from hepatitis were trained to use home haemodialysis, and if they subsequently needed temporary hospital dialysis they were treated in Ward 44. The crucial modification in Edinburgh to stop spread of hepatitis was the use of a venous pressure isolator, a 'membrane' which acted as a

TABLE 4

The 12 outbreaks of hepatitis in British dialysis and renal transplantation units by September 1971 (modified from the Rosenheim Report[10]).

Outbreak	Date	Patient hepatitis cases	Contact hepatitis cases	Staff hepatitis cases	Total hepatitis cases	Patient deaths	Staff deaths	Total deaths
Manchester	1965/66	5	–	11	16	–	3	3
Liverpool	1966/71	15	7	33	55	–	–	–
Charing Cross I	1966/67	15	–	–	15	–	–	–
Charing Cross II	1968/71	64	–	1	65	–	–	–
Birmingham	1967/71	21	4	12	37	–	–	–
Royal Victoria Newcastle	1969/71	4	1	–	5	1	–	1
Royal Free London	1969/70	3	–	8	11	–	–	–
Hammersmith I	1969/70	6	–	1	7	3	–	3
Hammersmith II	1971	6	–	2	8	–	–	–
Edinburgh	1969/71	18	2	8	28	8	3	11
Guy's London	1969/71	33	14	42	89	–	–	–
Cardiff	1969/71	16	1	4	21	–	–	–
Total		206	29	122	357	12	6	18

protector of the venous pressure gauge, so that the patient's blood no longer went directly into the gauge but reached a filter first. The length of the tubing leading to the gauge was also doubled, minimising potential contamination.

ALUMINIUM TOXICITY IN EDINBURGH (1976)

In the 1970s, outbreaks of encephalopathy and bone disease occurred in various dialysis units, and bone disease became a major problem in Edinburgh. It often seemed that not a week went by without at least one dialysis patient sustaining a fracture. Alfrey and colleagues associated the encephalopathy in dialysis patients with aluminium toxicity.[12] Studies were performed and a geographical variation of toxicity that was associated with levels of aluminium in the water supply was found.

Water that is peaty is not pleasant for drinking; this is often dealt with by treatment of the water with aluminium hydroxide and filtering. Aluminium in the water varied enormously from one area to another. Aluminium also reached patients from Alucaps® (aluminium hydroxide tablets) that were used to bind dietary phosphate in those who were hyperphosphataemic. One of the home haemodialysis patients was becoming repeatedly confused every time she was dialysed, but each time she would improve in hospital. She also exhibited terrible fractures which were not due to hyperparathyroidism. The aluminium level from the water supply in her home (to the south of Edinburgh) was tested and was found to be very high. Water from elsewhere in the Edinburgh area was subsequently tested, and the aluminium level was also found to be high.

SOLUTIONS TO ALUMINIUM TOXICITY

Water was treated using water softeners or by reverse osmosis. For home haemodialysis, aluminium was removed from the water using a simple technique involving ion-exchange and a modified water softener.[13] Nowadays, the aluminium in water and patient plasma aluminium levels are still routinely monitored, and 'dialysis dementia' has become a thing of the past.

CONCLUSION

It has been almost 60 years since the first practical haemodialysis machine for treating humans became available. In Edinburgh, haemodialysis for patients with ARF began in 1959 at the RIE, and there is much to learn from the history of renal replacement therapy. Dedicated staff overcame difficulties, setting up haemodialysis despite many odds and provided the best possible care for dialysis patients. Their undiminished care extended through a major hepatitis outbreak and this was especially commendable. By looking back on the history of renal replacement therapy, people might learn to appreciate the hard work of many of those who came before us, which resulted in the treatment options that are available today. They might then be encouraged to continue the search for new technology and yet more cures to improve medical science.

(A fuller account of the History of Dialysis and Renal Transplantation in Edinburgh can be found on the website of the Renal Unit of the Royal Infirmary of Edinburgh at http://www.edren.org, via *Renal Unit*, under the heading of *History of Dialysis and Renal Transplantation in Edinburgh*.)

ACKNOWLEDGEMENTS

We would like to thank: Dr Michael Barfoot; Dr Claire Benton; Terry Bremner; Dr Allan Cumming; Dr Mariana Dimova; Mr John Forsythe; Dr Paddy Gibson; Sister Sylvia Green; Professor Keith James; Mr A McL Jenkins; Professor M Kaufman; Sister Susan Mann; Mr Bernard Nolan; John Ramsay; Elizabeth Sloan; Dr Steve Sturdy; Dr Charles Swainson; the renal patients; colleagues at the Renal Laboratory; and all those who have helped in making this article possible.

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