Guest Editorial: Deirdre Fetherstonhaugh

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In this issue of the RSA Journal many 'renal pioneers' from around Australia have provided their own personal recollections of renal replacement therapy in the early days of the treatment. This article will provide a potted version of the history of dialysis from some parts of the English speaking world derived from the published literature in journals and books. This article is an edited excerpt from my doctoral thesis. (Fetherstonhaugh, 2007)

The historical evolution of dialysis, as successful treatment for saving lives, has occurred on an international level. The underlying chemical understanding of the processes that make clinical dialysis possible, however, has been attributed to a Thomas Graham, a Scot from Glasgow, in the nineteenth century. He investigated the nature of osmotic force and the separation of substances across a membrane using the word dialysis to describe this process (Cameron, 2002 p. 26-27). As with many technologies, clinical dialysis techniques have developed through trial and error, with knowledge and expertise being built upon incrementally. For the early clinicians and patients it was a frightening experiment but as the alternative for those with acute or chronic renal failure was a certain death, there was no shortage of volunteers. A large amount of research is currently being undertaken to evaluate the clinical outcomes of long-term dialysis and the emphasis in the developed world now is on increasing long term survival and improving quality of life (Kher, 2002). Clinicians now have the advantage of experiential hindsight when they inform and advise their patients. The knowledge that death is almost certain without treatment has given impetus to the development of dialysis and is still an extremely co-ercive factor which impacts on treatment decision-making.

History Of Haemodialysis

The first attempted trial of haemodialysis on a human is understood to have occurred in 1924 in Germany and was performed by Dr Georg Haas assisted by the surgeon Dr von der Hulten using a venovenous circuit (Cameron, 2002 p. 63; Konner, 2005 p. 2629). There were no details of this procedure but in 1925 Haas dialysed a young boy for 30 minutes, who was dying of uraemia. The following year he performed dialysis on four more patients. While the procedure may have been technically successful its effect on the patients was negligible (Cameron, 2002). There were many 'dialysis' pioneers. One of the most well known was Willem Johan Kolff, who in 1942 performed haemodialysis on two patients. He used a pumpless, rotating drum kidney with 20 metres of cellophane dialysis tubing wound round the wooden drum which sat in an open enamel dialysis tank. It had a coupling based on a Ford car water pump which allowed blood access to the rotating cellophane tubing (Cameron, 2002). It wasn't until 1945, however, that Kolff felt that the life of one of his patients may actually have been saved by undergoing dialysis.

Other early dialysis pioneers included Gordon Murray who dialysed patients between 1946 and 1949, with five survivors out of 11 (Cameron, 2002) and Bywaters and Joekes (1948) who successfully dialysed patients from 1946. Yet another person who has been credited with the early performance of haemodialysis, was Nils Alwall who first used a static vertical coil kidney of cellophane tubing to dialyse a patient with acute reversible renal failure in 1946. His second patient survived long term (Cameron, 2002). The first haemodialysis were undertaken in Australia in 1956 using an Alwall artificial kidney (Edwards & Whyte, 1959). Haemodialysis in these times was not easy to perform. The equipment was clumsy, huge and powerful and there could be rapid changes in the composition of the patient's body fluids (Cameron, 2002 p. 115). Patients often experienced huge drops in their circulating blood volume and blood pressure. They also experienced rigors (Cameron, 2002 p. 115) and other problems. If haemodialysis had been subjected to the same scrupulous evaluation that occurs with current emerging health care technologies, it may not have been seen as successful or emerged as it has. According to Cameron (2002 p. 115), by 1950 haemodialysis had been used in 110 patients in 13 different centres in seven countries but only 37 patients (34%) had survived. Referrals for dialysis treatment were only made for patients who were seriously ill (Cameron, 2002 p. 83) as there was no alternative treatment. However, given that in many situations acute kidney failure resolves with time, evaluating the effect of dialysis on patient outcomes would have been difficult.

Several of the pioneers of haemodialysis started their work with the intention of treating people with chronic irreversible kidney failure but ended up treating a different group of people – those with acute reversible kidney failure. By the

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end of the 1950s dialysis was perceived as necessary treatment to be performed in any major hospital in every developed country for selected patients with acute reversible renal failure (Cameron, 2002 p. 147). According to McBride, (1987 cited by Cameron 2002 p. 135), by 1959 in the United States there were 110 hospital units capable of performing dialysis and by 1962 there were over 250. In Australia up to March 1959 haemodialysis had been used on 44 occasions in 31 patients (Edwards & Whyte, 1959 p. 418).

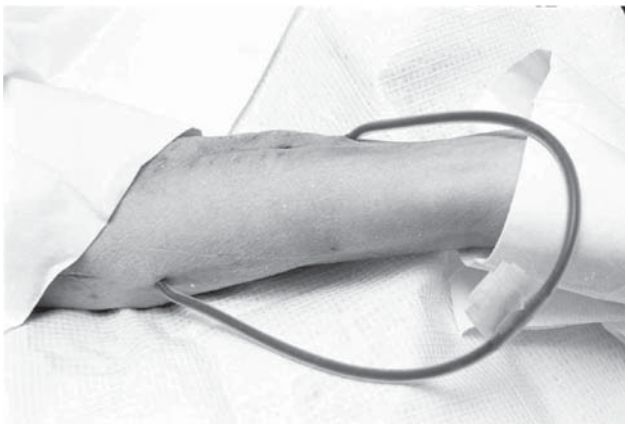
Haemodialysis was used to treat American soldiers who went into renal failure as a result of their injuries during the Korean War (1950-1953). Its success, in dramatically reducing the soldiers' mortality rates, contributed to the growing acceptance of haemodialysis as an effective treatment for acute reversible renal failure (Cameron, 2002 p. 139-140). In 1959 an article in the Medical Journal of Australia (Edwards & Whyte, 1959 p. 418) concluded that if dialysis was used 'judiciously' in the patient with acute renal failure then

> 'intravenous and intragastric tubes are rarely necessary, nursing is simplified and there is less likelihood of complications such as bed sores, bronchopneumonia and thrombo-embolism'.

However, despite this expansion of dialysis for the treatment of acute reversible renal failure, including those people who had overdosed on salicylates and hypnotics, no progress had been made in caring for those patients who had chronic irreversible renal failure.

Chronic irreversible kidney failure

One of the main problems with providing ongoing dialysis for end stage kidney failure (ESKF) was the absence of a permanent form of vascular access as each natural blood vessel could be used for only one dialysis treatment (Fox & Swazey, 1974; Herman, 2003). In 1960 Belding Scribner developed the first prototype of the 'shunt', made of polytetrafluoroethylene (PTFE), which enabled the joining of venous and arterial blood vessels together on the outside of the skin to ensure continuously flowing blood access (Fox & Swazey, 1974). This shunt was implanted surgically (Quinton, Dillard, & Scribner, 1960) and the first two patients who commenced maintenance haemodialysis survived for many years. It has been suggested that the treatment of one of these patients, Clyde Shields, represents 'one of the few instances in medicine where a single success was all that was required to validate a new therapy' (Scribner, 1990 p. 513).



Arm shunt in the 1970s, courtesy of Prince Henry's Hospital, Victoria

Dialysis effectiveness did not need to be assessed statistically or with the use of randomised clinical trials, as it was known that people with failed kidneys died quickly and dialysis, as a dramatic intervention, could save lives (Briggs, 2004 p.136). This was the beginning of haemodialysis for ESKD (Blagg, 2005).

The early 'kidney' doctors rapidly published the results of their first treatments for ESKD and were likely to choose patients most likely to survive as they would help establish the credentials of the new treatment (Stanton, 2005). According to de Wardener (1966 p. 106) doctors followed the reasoning that

> 'when a new technique is having to establish itself it is justifiable to choose first those patients who will do best. It is imperative for the survival of the technique, that in the beginning it should be shown to work'.

The possibility of permanent access to the blood circulation did not just overcome a technical hurdle but a psychological one as it destroyed 'the apparent barrier to more or less unlimited duration of dialysis' (Cameron, 2002 p. 191).

Over the years 1960-1965 there were many alternative types of shunts developed to try and minimise the need for revision and the use of anti-clotting agents. In 1965, Brescia, Cimino, Appel and Harwich created the first arteriovenous (AV) fistula which involved the connection of an artery and vein subcutaneously, thereby creating an internal shunt which had a far better success rate than the external shunt (Konner, 2005). The fistula has been improved over time and over the years some have been created using grafts with synthetic agents, natural ones or xenografts (from animals such as the carotid artery from an ox). The introduction of percutaneous subclavian lines in 1969, as a means by which to access the blood for dialysis, paved the way for the development of firstly, single lumen, and then double lumen, venous catheters in the 1970s and 1980s (Cameron, 2002).

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In the early years of maintenance haemodialysis patients were relatively well and lived at home (Peitzman, 2001). It became obvious, however, that being able to dialyse all the patients who needed it, in a hospital unit, was impossible due to lack of resources and trained personnel. Many patients were dying because of the lack of availability of haemodialysis in hospitals (Nosé, 2000 p. 13). In the 1960s the idea of self haemodialysis at home was proposed and then realised (Blagg, 2005; Bluemle, 1968; Evans, 1980). Patients then had to take responsibility for their own treatment. It was felt that this was in their best interests because it increased their self-esteem and sense of control (Shaldon, 1968) and it had the potential to empower them (Cameron, 2002 p. 196).

In the 1960s and 1970s many more patients underwent home haemodialysis than they do today. In the United States in 1972 approximately 40% of patients were undergoing home dialysis whereas by 2006 this number had dropped to approximately 0.7% (Blagg, 2005; United States Renal Data System, 2008). In Australia in 2007, approximately 9.7 % of the dialysis population were undertaking home haemodialysis compared to approximately 30% in 1978 (ANZDATA, 2008; George, 2005). Part of this decrease in the numbers of people who currently dialyse at home, at least in Australia, may be due to the gradual opening of alternative venues for dialysis such as the satellite centre in the cities and small units in country hospitals and day centres (George, 2005). The rise in popularity of continuous ambulatory peritoneal dialysis (CAPD) (discussed below) may also have been responsible for the decrease in the numbers of patients undertaking home haemodialysis (Agar, 2005; Cameron, 2002 p. 333; George, 2005). At the same time more haemodialysis equipment became available, the procedure became simpler and more reliable, and the price per unit decreased.

Another development in haemodialysis has been the introduction of slow or nocturnal dialysis usually conducted at home six or seven days a week. This regimen of haemodialysis does not necessarily require a dialysis helper as the long sessions mean that the patient is less likely to experience the fluid fluctuations and symptoms that often occur with the traditional, concentrated, thrice weekly haemodialysis regimens (Agar, 2005). It does however entail far greater patient time commitment. Not all public dialysis providers, at least in Australia, offer nocturnal dialysis as a treatment option.

History of peritoneal dialysis

The first 'successful' peritoneal dialysis was carried out in 1945 and was undertaken by Jacob Fine and his colleagues in the United States on a man with acute kidney failure who was dialysed for four days, after which time his kidney function returned. Two urethral catheters were used as access with a closed system and the dialysis fluid mimicked the composition of plasma (Cameron, 2002 p. 96). The main problems associated with peritoneal dialysis were the fluids used and the occurrence of infection in the peritoneum especially in the early days when antibiotics were not available. Simplification of peritoneal dialysis in 1959 meant that, after the catheter was inserted, the procedure could be managed by nurses (Cameron, 2002). The first patient was treated with maintenance peritoneal dialysis in 1959 and she survived for six months on the treatment until she developed pericarditis and then refused further therapy (Cameron, 2002 p. 201). Despite the development of a durable peritoneal catheter by Henry Tenckhoff in the late 1960s, the initial attempts at maintenance peritoneal dialysis were not very successful. Patients developed peritoneal adhesions following recurrent bouts of infections and they either died in a short time or had to be transferred onto haemodialysis. In the 1970s intermittent peritoneal dialysis was seen as a viable treatment for acute reversible renal failure but not for irreversible renal failure (Cameron, 2002). In 1970 there were only 102 patients maintained on long term intermittent peritoneal dialysis in the whole of Europe, whereas there were 5,133 people on some form of dialysis (Cameron, 2002 p. 205).

In 1975 continuous ambulatory peritoneal dialysis (CAPD) for chronic irreversible renal failure, became a possibility (Venkataraman & Nolph, 2002) and after some modifications became a viable treatment choice. CAPD was seen as a self-administered technique that could be done at home or work, the training time was generally relatively short and it relieved pressure for places in already overflowing haemodialysis units. CAPD was also seen as cheaper than in-centre haemodialysis, and, given the spiralling costs of the ESKD programs in many countries, it was thought that it might be the way forward for treating more patients at a cheaper cost per person. It is interesting to note that by the end of the 1980s and early 1990s it was the elderly, children and people with diabetes who made up a disproportionately high component of the CAPD population (Cameron, 2002 p. 277). The elderly were often put onto CAPD because they had been excluded from haemodialysis due to their age or a trial on haemodialysis had shown that their cardiovascular system did not cope with the rigours of that treatment (Cameron, 2002). For patients in countries such as Australia who were not living in a capital city, not willing or unable to re-locate and unable to undertake home haemodialysis, CAPD was often the only alternative to death. In the early 1980s intermittent cycling peritoneal dialysis machines (CCPD) were introduced often in combination with CAPD. In the 1990s (and still at the present day), automated peritoneal dialysis (APD) became popular,

sometimes in combination with CAPD, with patients having the majority of their dialysis mechanically overnight with perhaps one exchange during the day. According to Cameron (2002 p. 281) the impetus for mechanised peritoneal dialysis overnight, came mainly from patients who saw the daytime exchanges as taking up too much time.

Conclusion

Since the 1990s haemodialysis and peritoneal dialysis techniques (including the availability of vascular catheters for longer term use) have been refined and there are many different treatment regimes (frequency, duration) used around the world. More widespread use of bicarbonate dialysis and Erythropoietin treatment has improved the experience of dialysis and the health status and quality of life of ESKD patients.

However, valid and reliable comparisons of the effectiveness of treatment cannot be made between the two modalities, or the different regimes within those modalities, as the accepted gold standard of a randomised controlled trial will always now only be a 'utopian aspiration' (Foley, 2004 p. 217). Comparisons of clinical outcomes between haemodialysis and peritoneal dialysis have yielded inconsistent results due to differences in populations studied and the methods used (Collins, Weinhandl, Snyder, Chen, & Gilbertson, 2002 p. 98).

The evolution of dialysis as a successful treatment for those with ESKD has taken place over a relatively short time period. Its success has been reliant to a large extent on those clinicians and patients who were willing to take a risk and think beyond the square. John Dawborn, who was one of those early clinicians, writes in this issue about the open and enquiring minds of many of the dialysis 'pioneers'.

Just because dialysis had been successfully developed it did not mean however that everyone with ESKD had access to it. This issue of the Journal also includes a paper which discusses the rationing of dialysis. Dialysis is often used as a paradigm case in bioethics to discuss rationing and the allocation of resources. The rationing of dialysis, whether implicitly or explicitly, cannot be separated from the history of the technology as it has evolved in the way it has partly because of the fact that not everyone had, or currently has, access to it.

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