Seminar

Haemodialysis

N P Mallick, R Gokal

This paper charts the development of haemodialysis, the cornerstone of renal replacement therapy (RRT). It has enabled patients with end-stage renal failure to survive for years, in many cases with a surprisingly good quality of life. Through technological advances, RRT can be offered to patients who are older and more frail. Many have intercurrent comorbid illness. Such patients can have good quality of life, but their survival is shorter since they are likely to succumb early to comorbid illnesses. The challenge to nephrologists is to provide treatment based on exacting standards for all those patients who can benefit, yet to maintain cost-effectiveness. There is increasing recognition that, however good the technology underpinning dialysis, what justifies the cost and commitment that dialysis entails is the provision for the patient of a satisfactory quality of life.

End-stage renal failure (ESRF) occurs when nephrons are lost to the extent that the retention of non-volatile, metabolic waste products, salt, and water is potentially fatal. ESRF is less common than such disorders as ischaemic heart disease, malignant disorders, and chronic obstructive airways disease, but when it occurs it leads rapidly to death unless renal replacement therapy (RRT) is started. The treatments available are life-long, complex, and costly.

Renal failure develops gradually in most cases and the end-stage is reached when the glomerular filtration rate (GFR) approaches 5 mL/min. Even before that stage, there are effects on metabolic processes—patients become anorexic and lose body mass; salt, water, and phosphate are retained; production of renal hormones (renin, calcitriol, erythropoietin) is perturbed; and production of endogenous vasodilator compounds such as nitric oxide and kinins is reduced. Over time, uraemia impairs the function of nearly every organ of the body. The aim of RRT is to correct these disturbances. An essential action of RRT is the removal of retained waste products and excess fluid. Treatment must also restore the hormones that are not produced and provide as good a quality of life as possible for each patient.

ESRF can be treated by extracorporeal blood purification (haemodialysis, haemofiltration), or by kidney transplantation. A successful transplant restores renal function sufficiently for the patient to return to a normal life, with few restrictions, albeit with the need to take drugs for immunosuppression and for complications such as hypertension. Transplantation remains the treatment of choice for suitable patients. This seminar describes management by haemodialysis and next week's seminar describes peritoneal dialysis. Haemofiltration, which uses a highly porous membrane to remove plasma fluids in bulk, is not discussed.

Incidence and causes of ESRF

Renal failure is the result either of primary renal disease or of renal damage in a multisystem disorder (figure 1). The

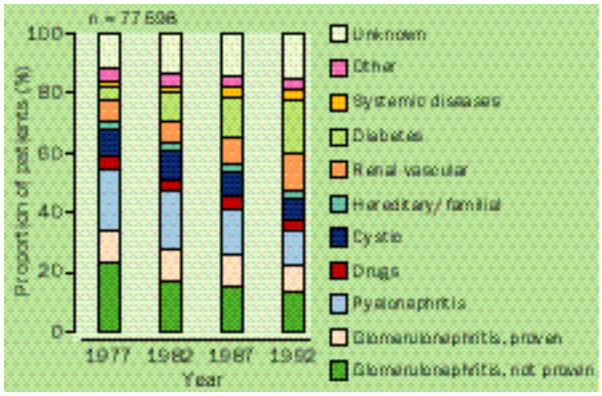

Figure 1: **Causes of ESRF as reported to European Dialysis and Transplant Association Registry**
Patients of all ages.

underlying causes and the incidence vary among countries. Generally, the incidence is higher in less-developed countries. Different diseases are common at different ages and the proportion of patients who progress to ESRF also varies among underlying disorders. Together these features determine the population that requires RRT. In the UK and urban USA, about 30% of patients who need dialysis present for the first time with terminal uraemia,[1] which makes diagnosis and management very difficult. Strategies for early recognition of renal impairment are needed, especially in high-risk groups.

In the UK, two prospective studies[2,3] concluded that each year 80–90 white patients per 10^6 population below the age of 80 years will need treatment for the first time. The incidence of ESRF is three times greater for people of Afro-Caribbean or Indian origin.[4] The incidence of ESRF increases with age; in the UK, the incidence increases six-fold to ten-fold from age 30–50 to age 70–90.

Many patients present with ESRF but no indicative history. Occult, atheromatous, renovascular disease may be the cause of ESRF in up to 20% of patients aged over 70. In younger patients, particularly those of Indian origin, the only finding may be small, smooth kidneys, with the cause of the damage remaining obscure. Both diabetes and hypertension are common causes of ESRF in older patients, especially for selected ethnic groups. For example, diabetes is more common in people of Indian origin than in

Lancet 1999; **353:** 737–42

Department of Renal Medicine, Manchester Royal Infirmary, Manchester M13 9WL, UK (Prof N P Mallick FRCP, R Gokal FRCP)

Correspondence to: Prof N P Mallick

white people. In the UK and the USA, hypertension is commonly the attributed cause of ESRF in Afro-Caribbeans.[4,5] In this population there is evidence that hypertension may be associated with progressive renal failure due to intrarenal vascular changes.[6]

Process of haemodialysis

The acceptance of patients onto RRT forms a contract between the patient and the doctor, with both parties accepting the responsibilities involved in RRT.[7] In itself, age is not a barrier to successful treatment; some older patients do extremely well on dialysis.[8] However, many are frail and have medical complications that must be taken into account.

The management of ESRF has changed from being a restricted and specialised field to a front-line activity in medicine. Eventually it is likely to support 750–800 patients per 10^6 population at any time and to take at least 2% of the national budget for health care.

Technical features

Haemodialysis requires an extracorporeal filter or dialyser, consisting of a semipermeable membrane to which blood is taken and returned through sterile tubing. Dialysis fluid, which has an electrolyte composition similar to that of the extracellular fluid, is passed in the opposite direction across the outside of the membrane channels of the dialyser through which the blood is circulating. Electrolytes and non-volatile waste products diffuse into this dialysis fluid from the blood, which is then returned to the body. At the same time alkali can be restored to the body by diffusion from dialysis fluid to blood across the membrane. If negative pressure is applied to the filter, fluid will be removed from the blood circulating through it by convection at the same time as solutes are passing across it.

Vascular access

Initially, repeated access to the circulation was achieved by the insertion of rigid Teflon tubes into an adjacent forearm vein and artery; the tubes were connected on the forearm surface by flexible tubes that could be separated and connected to the filter at each dialysis (Quinton-Scribner shunt). This arrangement was superseded by an arteriovenous fistula (Cimino-Brescia fistula) created in the forearm, into which needles are inserted for access at each dialysis. When this fistula cannot be formed, several options are available, including the placement of synthetic grafts subcutaneously, or of a long central line into a great vein.

Dialysers

The first commercial dialysers were in the form of coiled cellulose tubing. Later developments were of large, flat polypropylene plates sandwiching a blood compartment of copper-cellulose sheets (which had to be changed manually), then compact, factory-made, flat-plate filters. Nowadays, they consist of small units made up of bundles of finely extruded hollow fibres. During haemodialysis, membranes based on cellulose become variably coated by platelet aggregates and leucocytes. Complement activation and cytokine release have been documented. Another option is to use biocompatible synthetic membranes that do not attract cell aggregates.

High-flux dialysis membranes with larger pore size can be constructed. Since such membranes inevitably allow the transfer of much larger volumes of plasma water and electrolytes, the dialysis technique is altered radically. Fluid transfer must be controlled carefully by automated ultrafiltration. Substantial fluid replacement is needed as dialysis proceeds. Even with these membranes, molecules such as β_2-microglobulin (1200 kDa) are retained and form troublesome amyloid deposits in patients on long-term dialysis.

Modern dialysers are disposable, but to keep costs to a minimum, they are commonly reused several times. Reuse is less common in Europe than in the USA, except for expensive, high-flux dialysers, and European regulations are likely to render the practice obsolete. Although reuse saves money, the safety is disputed. Some researchers have attributed increased mortality in patients on chronic dialysis to reuse.[9] Others have reported that there is increased cytokine production and that fever and symptomatic hypotension are more common when cellulose dialysers are reused.[9] The available evidence is not conclusive,[10,11] but reuse is likely to be phased out.

Dialyser surface area for adults varies from 1·0 m^2 to more than 1·8 m^2. At a blood flow rate of 300 mL/min, the largest dialysers may produce such rapid shifts in solute and fluid that intolerable symptoms develop. With automated ultrafiltration control, these symptoms can be limited in many cases. Large dialysers have clear advantages for large patients or those who have a low blood-flow rate because of difficulties with access.

If any part of the dialysis circuit is not sterile, direct bacterial infection occurs readily. Meticulous attention must be paid to ensuring that the machine and circuit are sterilised. Most modern equipment is self-sterilising and disposable components are used wherever possible.

Water purity and buffers

Water purification is important. The passage of endotoxin from dialysis fluid into the blood has always been a potential source of morbidity in haemodialysis. At first, the dialysis fluid was made from an appropriate electrolyte concentrate and tap water, from which calcium was removed by "softening", and the dialysis membrane was expected to exclude endotoxin. In the 1970s, evidence accumulated that aluminium, added at source to clarify mains water, accumulated in blood stem cells, brain, and bone, and caused anaemia, various movement disorders, and fracturing bone disease. A cohort of patients had acquired an aluminium load that was difficult to remove.

Deionisation and reverse-osmosis filters were therefore introduced, resulting in water free of chemical contaminants. The need for even more rigorous purification to obtain ultra-pure water with no chemical additives and a negligible endotoxin concentration (negative in a test that detects 0·125 U endotoxin per mL) has become pressing. Some modern dialysis membranes (high flux) are designed to permit larger solutes to pass through them, so facilitating endotoxin passage from dialysis fluid into the blood. For many years, the buffer used in dialysis fluid has been acetate, which passes into blood at the dialyser and is metabolised in the liver, providing hydroxyl radicals. At the much faster flow rates needed for modern, short-duration dialysis, acetate is absorbed rapidly and the residual blood concentration is high enough to cause nausea or vasodilation. Therefore, bicarbonate, rather than acetate, is now the buffer of choice in the dialysis fluid. It must be produced close to the dialysis filter, and pure water is needed.

Panel 1: **Assessment of dialysis adequacy**

Urea reduction ratio (URR)

$$URR = \frac{\text{Predialysis urea} - \text{Postdialysis urea}}{\text{Predialysis urea}} \times 100$$

Plasma clearance

Kt/V is a measure of the amount of plasma cleared of urea (K [urea clearance]×t [time]) divided by the urea distribution volume (V), which is roughly equal to total body water. Many formulae have been proposed to calculate Kt/V, which is mathematically linked to URR. Complex formulae are logarithmic and include volume of ultrafiltration and patient's bodyweight.

Urea kinetic modelling

The dialysis dose is regularly adjusted to take account of the measured, as against prescribed, Kt/V.

Computer management

The dialysis technique itself has been dramatically influenced—and made safer—by information technology. Modern dialysis equipment not only monitors the blood flow rate and the temperature and content of the dialysate, but also adjusts the rate of fluid removal and is able to assess electrolyte and urea concentrations during the procedure. The use of a computer database allows regular updating of records of the "adequacy" of dialysis, for which several formulae have been proposed (panel 1).

Optimum dialysis

The combination of biocompatible membranes, bicarbonate dialysis with ultra-clean water, and computer recording with feedback to the length of dialysis sessions of key variables are thought to ensure optimum and economic dialysis for all patients. However, large trials with long follow-up times are needed for any advantage to be shown. Such trials are difficult to do because of imperfect randomisation and high withdrawal rates.[12] Since there is agreement that biocompatible membranes are superior to cellulose ones in management of very ill patients in acute renal failure, their use for regular haemodialysis may be more important in these patients. Studies in progress, carefully designed to measure removal of various impurities and fluid with different dialysis membranes,[13] should help to resolve this issue.

Dialysis and management of the patient

Dialysis regimen

The basic requirement is that haemodialysis removes retained solutes and water. Most patients undergo dialysis three times weekly, thereby avoiding large swings in biochemical variables between dialysis sessions. Such intermittent treatment cannot fully replace normal renal function. For a person aged 40 who weighs 70 kg, a normal GFR is about 120 mL/min; at a blood flow rate of 300 mL/min and with three 6 h dialysis sessions per week, the GFR equivalent achieved by haemodialysis will not exceed 20 mL/min when averaged over the whole week. Standard or low-flux dialysis membranes are not as efficient as the native kidney at clearing molecules of middle-range molecular weight (500–25 000 kDa), some of which are thought to be toxic. High-flux membranes are better at clearing these molecules, but some of the toxic substances retained in ESRF are lipophilic and some are protein bound; these are not cleared efficiently by dialysis.

Fluid removal and dry weight

Excess fluid must be removed to restore normal circulatory volume and blood pressure. This aim is very difficult to achieve in patients who do not simultaneously restrict their fluid intake yet whose circulation is vulnerable to rapid fluid removal during dialysis. The amount of fluid removed by dialysis is 6 L per week, if there are three sessions per week. Insensible water loss in a temperate climate is about 4 L per week. If fluid balance is to be maintained, intake cannot exceed the sum of this loss and that removed by dialysis (10 L per week, or about 1400 mL per day). 800 mL water is produced by metabolism during the average day, and food itself provides at least 600 mL water. The patient on haemodialysis therefore should not drink at all. Needless to say, patients cannot do this and many find even modest fluid restriction difficult to accept. There is no precise way to measure the body's sodium and water content daily, although several methods, including ultrasonographic measurement of the diameter of the superior vena cava, have been proposed. The so-called dry weight of a patient, at which no excess sodium and water are retained, is therefore difficult to achieve. At haemodialysis, retained sodium is removed along with excess water, but if this removal happens too quickly, hypotension results. Patients with cardiac compromise may be very sensitive to plasma-volume fluctuations. The risk of hypotension on dialysis can be counteracted by use of slower dialysis or by sodium profiling. In the latter process, the dialysis sodium concentration can be changed as dialysis proceeds. If the concentration is initially set for 146 mmol/L, for example, and programmed to fall to 140 mmol/L during the session, water can be removed by convection while plasma sodium is stabilised. In some patients this process prevents hypotension, but this disorder remains troublesome in many patients, reducing the efficacy of the procedure, since ultra-filtration flow rates cannot be maintained.

Phosphate

Phosphate concentrations depend on dietary intake, prevention of absorption by phosphate binders, and removal from plasma by dialysis. On a carefully monitored diet, a protein intake of 1 g/kg bodyweight provides an obligatory phosphate intake of about 1000 mg daily. Dialysis removes around 700 mg phosphate per session, so to achieve a neutral phosphate balance, gastrointestinal elimination of phosphate needs to be around 700 mg daily, compared with a normal amount of 400 mg. Thus oral phosphate binders are needed. Suitable substances include calcium carbonate, calcium acetate, magnesium carbonate, calcium ketovalin, and polyuronic acids. Calcium salts are the most widely used binders, but may result in hypercalcaemia, especially when used in conjunction with 1,25 dihydroxycholecalciferol (calcitriol). Aluminium salts are best avoided because they contribute to aluminium poisoning.

Nitrogen

Haemodialysis patients lose some nitrogen at dialysis and are in positive hydrion balance for much of the week. These influences militate against efficient nitrogen anabolism.[14,15] Studies consistently show that, overall, haemodialysis patients are in negative nitrogen balance. Dietary protein intake should be adequate to avoid negative nitrogen balance, but discipline is necessary to limit retention of toxic waste products. A reasonable intake is 1 g protein per kg bodyweight, with emphasis on foods of high biological value. For each 1 g protein, the patient should eat 146 kJ (35 kcal) from non-protein foods to achieve optimum anabolism.

Hormone replacement

Anaemia aggravates the cardiac dysfunction that accompanies uraemia.[16] The use of synthetic erythropoietin has enabled increases in haemoglobin concentration to above 10 g/dL in more than 70% of dialysis patients. This value of haemoglobin is likely to be cardioprotective. Patients with haemoglobin concentrations of less than 9 g/dL or symptoms of anaemia at higher haemoglobin concentrations should receive erythropoietin. The Renal Association of Great Britain and Ireland recommends maintenance of haemoglobin concentration between 10 g/dL and 12 g/dL. 50–75% of ESRF patients need erythropoietin at an average cost at present of about UK £3000 annually. Nearly all need iron supplements, and iron increasingly has to be given as an intravenous preparation.

Concentrations of calcitriol, the active metabolite of vitamin D, are generally low once creatinine clearance falls below 30 mL/min, because the enzyme that converts 25-hydroxycholecalciferol to 1,25-dihydroxycholecalciferol (1α-hydroxylase) is located in the mitochondria of the proximal tubule of the kidney. Decreased renal mass, increased serum phosphate concentrations, acidosis, and uraemia probably all contribute to inhibition of synthesis of 1,25-dihydroxycholecalciferol, and an increase in serum parathyroid hormone. Calcitriol has direct inhibitory effects on the parathyroid gland, in addition to an indirect effect mediated by increased gastrointestinal calcium absorption and increased serum calcium. Calcitriol directly affects osteoblasts in bone where it influences bone formation and mineralisation. Consequently, treatment with vitamin D analogues is commonly required for optimum management of secondary hyperparathyroidism and the resulting osteodystrophy. Such analogues can be administered according to various regimens (panel 2).

Panel 2: **Calcitriol treatment**

Calcitriol treatment regimen	Effect
Daily oral	Increased intestinal calcium absorption Rise in serum calcium Little direct inhibition of parathyroid-hormone secretion
Twice-weekly oral/intravenous	Direct inhibition of parathyroid hormone secretion High peak serum calcitriol concentrations Little effect on serum calcium
Thrice-weekly or alternate-day oral/intravenous	Some increase in serum calcium Some direct inhibition of parathyroid secretion

Urea

Analysis of the US National Cooperative Dialysis Study established the effect on morbidity of insufficient urea removal, whether measured as time-averaged urea concentration, or as fractional urea clearance (Kt/V). In another study,[17] a retrospective analysis of 13 473 patients on haemodialysis, a urea reduction ratio of 65–70% (Kt/V 1·3–1·6) was associated with a significantly lower risk of death. This urea reduction ratio was greater than the 50% implied to be adequate from the National Cooperative Dialysis Study; that investigation did not, however, include long-term mortality.

Adequacy of dialysis

Even though urea itself is not very toxic, measurements of the quantity of urea removed in relation to the body load are a reasonable way to detect inadequate haemodialysis. What remains controversial is whether there is a level of solute removal that constitutes adequate dialysis. The restricted capacity of haemodialysis to substitute for the normal kidneys makes the comprehensive replacement of renal function impossible. After dialysis, plasma biochemistry is improved but not normal. Indeed, there may be no upper limit to the hours of haemodialysis, in that the more dialysis the better the survival.[18]

Under-dialysis is disturbingly easy. Most patients prefer short dialysis sessions. Many units across the world have sought to limit the length of dialysis sessions so that each dialysis station can be used three or even four times per day. Although the length of dialysis itself has not been shown to affect survival, if the duration of the dialysis session is reduced to 2–3 h, blood-flow rate must be high and the dialysis surface area large for sufficient dialysis to be achieved. Also, the session must not be punctuated by periods of slower dialysis to counteract symptoms that the patient experiences.

Short-duration dialysis may be tolerated by relatively fit patients. For many patients who are less well, hypotension occurs as fluid is removed rapidly and there are incapacitating symptoms such as fatigue, anorexia, and nausea that persist for some hours after dialysis ends. In Europe, most experts advocate sessions of at least 4 h and are prepared to use 6 h sessions for patients who tolerate poorly even this rate of fluid and solute removal.

Charra and colleagues[19] have shown good survival and control of blood pressure without medication for patients dialysed for longer sessions (three 8 h sessions per week) on large, flat-plate dialysers, with cellulose membranes and acetate as the hydrion buffer. Ambulatory monitoring showed that systolic and diastolic pressure between dialyses were close to the reference values for normotensive people.[20]

Even when meticulous attention is paid to fluid control in units with dialysis sessions of 4–6 h, at least 15% of patients need to take drugs to lower blood pressure. There remains a debate about selection of patients and comorbidity, but whether 8 h of dialysis is inherently more effective than shorter periods, particularly in terms of blood-pressure control, remains unproven.

Ideally, dialysis would be continuous, with membranes selective enough to remove all toxic waste products. This ideal is impracticable. As a guide, a urea reduction ratio of at least 65 (panel 1) is judged acceptable. Beyond this value, any improvement in survival may be more subject to such confounding influences as age, cardiovascular stability, and comorbidity. Recommended standards for dialysis variables have been proposed by the Renal Association in the UK and the National Kidney Foundation in the USA.[21,22]

In an attempt to approach a continuous dialysis schedule, a few centres have adopted the technique of slow (8 h) overnight dialysis on 6 or 7 nights per week. Adequate solute and fluid removal is obtained without side-effects, and the patient has a smooth biochemical profile from day to day. Patients report a preference for this technique over a three-times weekly 4–6 h schedule, saying that they have greater well-being and few symptoms during or after dialysis.[23,24] For selected and self-caring patients, this approach could be a useful alternative. It makes use of equipment that would otherwise be unused in the dialysis

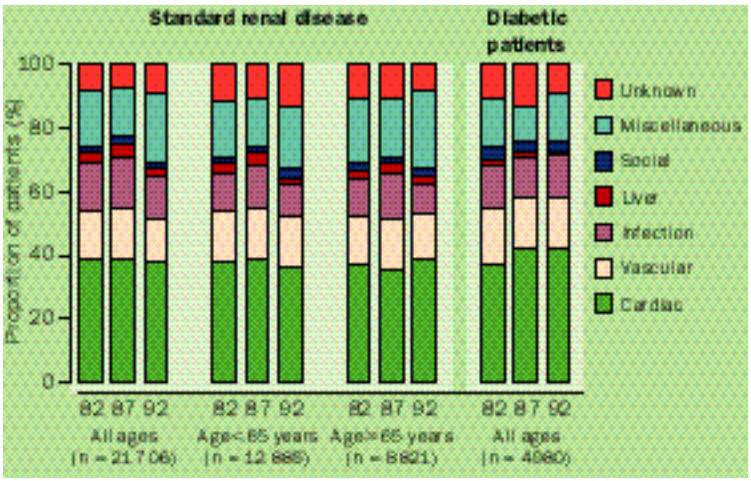

Figure 2: **Causes of death among patients with ESRF as reported to European Dialysis and Transplant Association Registry**

centre overnight. This technique has been used in the home with remote monitoring.[25]

However good the technical delivery of haemodialysis, it is insufficient in itself to achieve the best outcome for an individual patient. The management of ESRF is multi-faceted. Each patient must have regular, individual attention with regard to management of blood pressure and fluid balance, nutrition, anaemia, bone disease, and social circumstances.

Morbidity and mortality

Outlook

If haemodialysis is to be judged a successful treatment, it should control blood pressure and restore protein anabolism, well-being, and appetite. The patient should be able to resume the degree of activity that a person of that age and abilities might expect if there was no renal failure. Some patients have survived more than 20 years on haemodialysis and have had rewarding family and working lives. Hospital admission rates are highest in the first year of dialysis; thereafter, patients whose treatment is working well attend the centre only for dialysis (nowadays only a few patients dialyse at home) and for outpatient follow-up. However, not all patients fare so well and there has been much debate as to why some patients do better than others. Morbidity on haemodialysis may be related to the technique of gaining access to the circulation, to the dialyser circuit, to the uraemic state and its complications, or to coexisting illness. There must be access to the circulation for each dialysis session. Infection is always a hazard, especially if such access is by an indwelling line or by intermittent needle puncture of a subcutaneous synthetic graft, rather than of a native arteriovenous fistula. In the USA, 80% of patients older than 65 years had synthetic subcutaneous grafts for access in the years 1986 to 1990.[26] Efforts are being made to increase the proportion of fistulae in the USA.

Infection

Even with the precautions in place for a sterile dialysis procedure, infection remains one of the principal causes of hospital admission and death of haemodialysis patients (figure 2). 12% of all deaths among haemodialysis patients in the USA were due to infection.[27] Although infection is commonly a complication in patients with coexisting disorders, the procedure itself can be the source; about one in eight of the deaths in Bloembergen and Port's study[27] arose through complications of vascular access.

Chronic viral infections have been a source of concern in RRT. Patients in renal failure do not clear the hepatitis viruses efficiently. Several disastrous outbreaks of hepatitis due to blood-borne transmission have occurred in renal units; as a result, stringent precautions were introduced. Properly implemented, these precautions prevent cross-infection in renal units. The availability of blood testing for hepatitis B virus and potent immunisation against it have further limited the risk of transmission of the disease by an infected patient or staff member.

Stringent precautions must be maintained nevertheless. This need is illustrated by the emergence of hepatitis C, which was present in some European centres at a level 20–30 times that in the community. Careful reiteration of the necessary precautions greatly reduces the potential for cross-infection with this virus also.

Nutritional status

If there is inadequate dialysis, patients clear neither the fluid load nor the solute waste that has accumulated. In effect, the uraemic state persists, with anorexia, fatigue, and breathlessness. Blood pressure is higher than is necessary and many patients are malnourished.

The link between under-dialysis and malnutrition is well documented; it contributes to morbidity, as measured by inpatient days,[28] and is linked to mortality. The precise mechanisms that underlie these observations have proved elusive. The cumulative effect of retention of uraemic toxins has been assumed to prevent adequate appetite and metabolism. The search for such toxins has not, however, been successful.

Race

In the USA in 1995, the death rate for white patients aged 30–34 on haemodialysis was 46·2 per 1000 patient-years at risk (<5% per year). Death rates are lower for African-Americans, who comprise 15% of the US population but 31% of US patients with ESRF; fewer of these patients than of white patients receive RRT, but they survive longer and report a higher quality of life.[5] These differences in survival are yet to be explained.

Age

Importantly, everywhere the population of patients on haemodialysis is now much older than formerly and in many countries the median age at the start of treatment is above 65. Survival is age related (figure 2), but age is to an extent a proxy for comorbidity; otherwise fit, elderly patients have survival similar to that of patients a decade younger who have significant comorbid illness, particularly diabetes or cardiovascular disease. Furthermore, quality-of-life studies show that older patients adapt at least as well to the discipline of RRT as younger individuals do, even where there is comorbid illness.

Quality of life

Haemodialysis is a complex life-support system, of proven efficacy. It is expensive to operate, and there are substantial extra costs for medical and nursing care, particularly for the more frail patients. To keep alive by technical means a

patient who is not deriving subjective benefit from the procedure cannot be justifiable. The moral dilemma is worse when public funds are expended. The quality of life that a patient achieves must be a key yardstick of the value of haemodialysis.

To obtain and maintain the best available quality of life on haemodialysis, careful counselling of patients and their relatives is needed. They must be encouraged to accept discipline in eating and fluid intake and to make adjustments that permit them to be socially and physically active within their natural potential. These steps are necessary complements to efficient haemodialysis if metabolic health and well-being are to be restored.

Mortality

Many deaths of patients on haemodialysis are cardiovascular. The uraemic state, anaemia, fluid overload, hypertension, and hyperlipidaemia all contribute to the cardiovascular risk, but separation of these influences has been difficult and is beyond the scope of this review. Two influences dominate—the state of the patient and the quality of the treatment. Survival decreases with increasing age, partly owing to the greater cardiovascular morbidity of older patients. Comorbidity, defined broadly as cardiovascular, respiratory, gastroenterological, and mental disability, or diabetes mellitus, is common in ESRF. In one study[29] of non-diabetic patients aged 55–74, coronary artery disease was found in 47% and peripheral vascular disease in 25%. The proportions are higher in diabetic patients who now make up about 25% of the RRT population. The presence of diabetes is equivalent to an extra decade of age in terms of survival. Results are not uniform and individual units have reported widely differing survivals for cohorts of patients with similar degrees of comorbidity.[8]

The impact of hypertension on survival has been underlined by studies showing good survival in patients with well-controlled blood pressure[19] and those showing poor survival related to left-ventricular enlargement.[16] Ischaemic heart disease in younger patients carries higher relative risks, but the absolute numbers of deaths in older RRT patients are much higher. In patients who have no evidence of ischaemic heart disease, its development during the first 5 years of RRT is unusual.[30] This observation emphasises the importance of assessment and management before the end-stage in determining the outcome of the treatment.

References

1 Hiatt RA, Friedman DG. Characteristics of patients referred for treatment of endstage renal disease in a defined population. *Am J Public Health* 1982; **72:** 829–33.

2 Feest TG, Mistry CD, Grimes DS, Mallick NP. Incidence of advanced chronic renal failure and the need for endstage replacement treatment. *BMJ* 1990; **301:** 897–900.

3 McGeown MG. Prevalence of advanced renal failure in Northern Ireland. *BMJ* 1990; **301:** 900–03.

4 Roderick P, Jones I, Raleigh VS, McGeown M, Mallick NP. Population need for renal replacement therapy in Thames regions: ethnic dimension. *BMJ* 1994; **309:** 1111–14.

5 Owen WF. Racial differences in incidence, outcome, and quality of life for African-Americans on hemodialysis. *Blood Purif* 1995; **14:** 278–85.

6 Tracey RE. Renovasculopathies of hypertension and the rise of blood pressure with age in blacks and whites. *Semin Nephrol* 1996; **16:** 126–33.

7 Mallick NP. What do we learn from the European Registry: what will be the underlying problems in the year 2000? *Nephrol Dial Transplant* 1995; **10:** 2–6.

8 Khan IH, Campbell MK, Cantarovich D, et al. Survival on renal replacement therapy in Europe: is there a "centre effect"? *Nephrol Dial Transplant* 1996; **11:** 300–07.

9 Parker TF, Wingard RL, Husni L, Ikizler TA, Parker RA, Hakim RM. Effect of the membrane biocompatibility on nutritional parameters in chronic hemodialysis patients. *Kidney Int* 1996; **49:** 551–53.

10 Valderrabano F, Moreno F, Lopez Gomez JM, Sanz-Guajardo D, Jofre R. Quality of life in dialysis patients: a Spanish multicentre study. *Nephrol Dial Transplant* 1996; **11:** 125–29.

11 Pereira BJ, Natov S, Sundaram S, et al. Impact of single use versus reuse of cellulose dialyzers on clinical parameters and indices of biocompatibility. *J Am Soc Nephrol* 1996; **7:** 861–70.

12 Locatelli F. Influence of membranes on morbidity. *Nephrol Dial Transplant* 1996; **11:** 116–20.

13 Davfirdas JT, Depner IA, Gotch FA, Greene T, Levin NW, Schulmer J. Comparison of methods to predict equilibrated Kt/V in the HEMO Pilot study. *Kidney Int* 1997; **52:** 1345–405.

14 Hakim R, Wingard R, Husni L, Parker RA, Parker TF. The effect of membrane compatibility on plasma beta 2-microglobulin levels in chronic haemodialysis patients. *J Am Soc Nephrol* 1996; **7:** 472–78.

15 Bergstrom J. Metabolic acidosis and nutrition in dialysis patients. *Blood Purif* 1995; **13:** 361–67.

16 Parfrey S, Foley RN, Harnett JD, Kent GM, Murray DC, Barre PE. Outcome and risk factors for left ventricular disorders in chronic uraemia. *Nephrol Dial Transplant* 1996; **11:** 1277–85.

17 Owen WF, Lew NL, Liu Y, Lowrie EG. The urea reduction ratio and serum albumin concentration as predictors of mortality in patients undergoing haemodialysis. *N Engl J Med* 1993; **329:** 1001–06.

18 Charra B, Calemard E, Ruffett M, et al. Survival as an index of adequacy of dialysis. *Kidney Int* 1992; **41:** 1286–91.

19 Charra B, Laurent G, Calemaro E, et al. Survival in dialysis and blood pressure control. *Nephrology* 1994; **106:** 179–85.

20 Chazoott C, Charra B, Laurent G, et al. Interdialysis blood pressure control by long haemodialysis sessions. *Nephrol Dial Transplant* 1995; **10:** 831–37.

21 Renal Association Standards Subcommittee. Treatment of adult patients with renal failure. Recommended standards and audit measures. *J R Coll Physicians Lond* 1995; **29:** 190–91.

22 US National Kidney Foundation's dialysis outcomes quality initiative (NKF-DOQI) practice guidelines on HD. *Am J Kidney Dis* 1997; **30** (suppl 2).

23 Twardowski ZJ. Daily home hemodialysis: a hybrid of hemodialysis and peritoneal dialysis. *Adv Ren Replace Ther* 1996; **3:** 124–32.

24 Buoncristianni U, Fagugli RM, Pinciaroli MR, Kulurianu H, Ceravolo G, Bova C. Reversal of left-ventricular hypertrophy in uremic patients by treatment with daily hemodialysis. *Contrib Nephrol* 1996; **119:** 152–56.

25 Pierratos A, Ouwendyk N, Francoeur R, et al. Nocturnal haemodialysis: 3 year experience. *J Am Soc Nephrol* 1998; **5:** 859–68.

26 United States Renal Data Systems 1993 Annual Data Report. US Dept of Health and Human Services.

27 Bloembergen WE, Port FK. Epidemiological perspective on infections in chronic dialysis patients. *Adv Ren Replace Ther* 1996; **3:** 201–07.

28 Rocco MV, Soucie JM, Revboussin DM, McClellan WM. Risk factors for hospital utilization in chronic dialysis patients. *J Am Soc Nephrol* 1996; **7:** 889–96.

29 Australia and New Zealand Dialysis Transplant Registry Report 1995, Disney APS, p 135.

30 Brown JH, Hunt LP, Vites NP, Short CD, Gokal R, Mallick NP. Comparative mortality from cardiovascular disease in patients with chronic renal failure. *Nephrol Dial Transplant* 1994; **9:** 1136–42.

Further reading

Cheung AK, Leypoldt JK. The hemodialysis membranes: a historical perspective, current state and future prospect. *Semin Nephrol* 1997; **17:** 196–213.

Foley RN, Parfrey PS. Cardiac diseases in chronic uremia: clinical outcome and risk factors. *Adv Ren Replace Ther* 1997; **4:** 234–48.

Hruska KA, Teitelbaum SL. Renal osteodystrophy. *N Engl J Med* 1995; **333:** 166–74.

Kopple JD. Nutritional status as a predicator of morbidity and mortality in maintenance dialysis patients. *ASAIO-J* 1997: **43:** 246–50.