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CONTENTS 21.7.1 Haemodialysis 4861 Robert Mactier 21.7.2 Peritoneal dialysis 4874 Simon Davies 21.7.3 Renal transplantation 4879 Nicholas Torpey and John D. Firth 21.7.1 Haemodialysis Robert Mactier ESSENTIALS Maintenance haemodialysis (HD) is a highly successful treatment for patients with established renal failure and is the default therapy when other renal replacement therapy options are not available. In the developed world, the HD population continues to increase and is becoming more elderly and dependent. Principles—HD uses the countercurrent flow of blood and di- alysate through a hollow fibre dialyser to maximize the concentra- tion gradient for diffusive transport of solutes. A hydrostatic gradient across the dialyser membrane induces ultrafiltration (UF) of water and convective transport of solutes by solvent drag. Dialysers and types of dialysis—high-flux membranes are standard in most HD centres and are needed to achieve significant re- moval of middle molecules, of which β2-microglobulin (the cause of dialysis-related amyloid) is the prime example. The technique of haemodiafiltration (HDF) contributes additional convective removal of fluid and better clearance of middle molecules. Vascular access—the need to secure and maintain reliable vas- cular access is fundamental to achieving adequate dialysis and maintaining health. An arteriovenous fistula is the preferred option, with fewer complications and longer survival than other access op- tions. Dependence on tunnelled central venous access lines con- tributes to morbidity and excess mortality, mainly from line-related sepsis, and often represents a failure in access provision. Dialysis adequacy—for historical and pragmatic reasons, HD is normally provided three times per week. Working definitions of adequacy are based on small-solute—typically urea—removal. The optimal dialysis dose has not been well defined, but minimum tar- gets of delivered dose measured by urea reduction ratio (URR) and normalized urea clearance

(Kt/V) have been established. Current guidelines recommend targeting a URR of 65% or normalized urea clearance (Kt/V) in excess of 1.2 per session for thrice-weekly treat- ment. Higher doses of dialysis delivered thrice weekly (as judged by Kt/V) do not produce a significant improvement in outcomes, but a longer duration of dialysis delivered thrice weekly does, as do short daily HD or nocturnal daily HD treatments. The technique of HDF provides a survival benefit over HD. Complications—the main acute complication of HD is intradialytic hypotension, resulting from an imbalance between the UF rate and the rate of vascular refill. Underlying cardiovascular disease, antihypertensive drugs, autonomic dysfunction, shortened dialysis times, large interdialytic fluid gains, and inaccurate dry-weight as- sessment all predispose. Other acute complications include dialysis- related haemorrhage, acute haemolysis, air embolism, dialyser reactions, and dialysis disequilibrium. In the longer term, dialysis- related amyloidosis is a disabling, progressive condition caused by the polymerization of β2-microglobulin within tendons, synovium, and other tissues. The incidence and prevalence of a wide range of comorbid medical conditions is increased in HD patients, including ischaemic heart disease, cerebrovascular disease, and peripheral vas- cular disease. Introduction An ever increasing number of patients with established renal failure are dependent on haemodialysis (HD) to sustain their lives. HD has very few absolute contraindications and so is the default therapy of all forms of renal replacement therapy (RRT). Ninety days after commencing RRT 65% of incident patients in the United Kingdom in 2017 were receiving HD, compared with 19% on peritoneal dialysis (PD) and 10% with a functioning kidney transplant (6% had died or stopped treatment). Kidney transplantation is recognized as the best mode of RRT, and 55% of the prevalent patients at the end of 2017 in the United Kingdom had a functioning kidney transplant while 37% were on centre HD and 7% were on home dialysis modalities (5% PD and 2%


 home HD). There has been a dramatic expansion in the number of prevalent patients receiving these different forms of RRT in all de- veloped countries over the past four decades, which is exemplified by Fig. 21.7.1.1 which shows the RRT modality of all established renal failure patients in Scotland from 1973 to 2013. Long-term patient survival in incident HD patients of all age groups has increased gradually during the past 20 years along with progressive improvements in delivered dialysis dose and supportive medical care. There also has been progressive expansion in the number of satellite HD units to make centre HD available more lo- cally. The small rise in home HD observed in the United Kingdom and North America has been prompted by recognition of the ad- vantages of home HD, particularly if this provides more frequent HD sessions than the traditional three sessions per week provided in HD units. Nevertheless, HD provision faces many ongoing challenges. Reliable vascular access is the cornerstone of adequate HD and most renal units fail to achieve the audit measure of 80% of preva- lent HD patients using a functioning arteriovenous fistula or graft for vascular access. Within the UK 14–18% of patients each year still present to the local renal service within 3 months of needing to commence RRT and so have little opportunity for arteriovenous fistula creation and its maturation for use for vascular access prior to starting HD. The prevalent HD population is ageing and has major comorbidity, particularly from coexisting vascular disease, diabetes, depression, and cognitive impairment. Concomitant comorbidity has led to optimum medical conservative care being considered a better option than RRT for an increasing proprotion of patients with progressive stage 5 chronic kidney disease (see Chapter 21.6). Worsening quality of life associated with progressive coexisting or new comorbidity may lead to some patients wishing to withdraw from ongoing HD in the knowledge that without HD they will not survive for long. Consequently, the

prevalent HD population within the United Kingdom is growing very slowly, whereas the kidney transplant population continues to expand every year (Fig. 21.7.1.1). This chapter outlines the main issues required for delivering high- quality HD and maintaining patient safety on HD and highlights the randomized clinical trials that have influenced current medical practice. Principles of haemodialysis HD requires an integrated machine with the following essential components (Fig. 21.7.1.2): • A pump to deliver blood from the vascular access to the dialyser • A dialysate concentrate proportionating system to prepare dialysis fluid from treated water and then deliver the dialysis fluid to the dialyser • Volumetric control of fluid removal (ultrafiltration (UF)) • A range of patient safety monitors and alarms HD uses the countercurrent flow of the blood and dialysate path- ways in the dialyser to maximize the concentration gradient for diffusive transport. Diffusive transport is greater for smaller and uncharged solutes. HD also uses a hydrostatic gradient across the dialyser membrane to induce UF of water and convective trans- port of solutes by solvent drag. The diffusive and convective trans- port of solutes leads to net removal of urea, creatinine, potassium, and phosphate in the dialysate and uptake of bicarbonate from the dialysate (Fig. 21.7.1.3). The permeability of the membrane to larger solutes, such as vitamin B12 or β2-microglobulin, is used to

218 343 545 1006 1441 384 438 351 426 774 1132 1406 1724 0 500 1000 1500 2000 2500 3000 3500 4000 4500 1973 1978 1983 1988 1993 1998 2003 Number of patients Year 1773 1810 2044 2505 2008 2013 Transplant APD CAPD Home HD Hospital HD Fig. 21.7.1.1 Renal replacement therapy modality of all established (chronic) renal failure patients in Scotland from 1973 to 2013. APD, automated peritoneal dialysis; CAPD, continuous ambulatory peritoneal dialysis; HD, haemodialysis. Reproduced from Scottish Renal Registry Report 2013. © NHS National Services Scotland/Crown Copyright 2014.

21.7.1 Haemodialysis 4863 categorize dialyser membranes into low, mid, or high flux. Dialyser membranes have widely different capacity to permit flow of water across the membrane and the UF coefficient of dialysers range from 3 to greater than 60 ml/min per hour per mmHg transmembrane hydrostatic pressure. Prescription of haemodialysis Small solute clearance rates The urea clearance rate will depend on whichever of the following prescription variables is the lowest (Fig. 21.7.1.3): • blood flow rate (250–500 ml/min) • dialyser urea mass transfer coefficient (300–1100 ml/min) • dialysate flow rate (500–800 ml/min) There has been a trend to prescribe higher blood flow rates (300– 450 ml/min) and to use dialysers with higher urea mass transfer co-efficients to provide higher efficiency HD than in the past. The blood flow rate that can be achieved from the patient’s vascular access is the commonest rate-limiting factor of urea clearance rates. The di- alysate flow rate should be at least 50% greater than the blood flow rate in single pass countercurrent flow HD. Increasing the dialysate flow rate to greater than 150% of the blood flow rate results in a rela- tively small increase in urea clearance rates, for example, a 60% rise in dialysate flow rates from 500 ml/min to 800 ml/min increases the rate of urea clearance by only 5 to 10% when the blood flow rate is 350 ml/min. Choice of dialyser Hollow fibre dialysers are the only type of dialysers now being used. This type of dialyser permits blood flow within fibres made from a variety of membrane materials with countercurrent flow of the dia- lysis fluid enclosed within a rigid casing. Artery Vein Pressure monitor Pressure monitor Pump Anticoagulant Dialyser Air trap and detector Fig. 21.7.1.2 Schematic representation of the key components of the haemodialysis system. Direction of solute concentration gradient Direction of hydrostatic pressure gradient Semipermeable membrane Frequently used dialysate concentrations (mmol/L) Urea

Potassium 1–2 135–140 1.25–1.50 35–40 Phosphate Sodium Blood flow rate 250–400 ml/min Dialysate flow rate 500–800 ml/min Calcium Bicarbonate Plasma water Fig. 21.7.1.3 Schematic representation of transmembrane solute and water transport in a haemodialyser.

section 21 Disorders of the kidney and urinary tract 4864 Biocompatible dialysis membranes Synthetic and modified cellulose membranes have been shown to be more biocompatible than unmodified cellulose membranes (Box 21.7.1.1). A systematic Cochrane review found no reduction in either mortality or dialysis-related adverse symptoms when synthetic membranes were compared with cellulose/modified cellulose mem- branes. Nevertheless, the use of biocompatible instead of unmodi- fied cellulose dialysers has been justified on the basis of the former dialysers' biological benefits and equivalent costs. High- or low-flux biocompatible dialysers The key decision when using more biocompatible, modified cel- lulose or synthetic membranes is whether to prescribe a low-, mid-, or high-flux dialyser. A multicentre, randomized con- trolled trial failed to show improvement of anaemia in stable HD patients treated over a 12-week study period with high-flux bio- compatible membranes instead of conventional cellulose mem- branes. One small prospective randomized study showed better preservation of residual renal function when using high-flux membranes combined with ultrapure water. The proven benefits of high-flux membranes in randomized trials are limited to ad- vantages arising from improved biocompatibility and enhanced removal of middle molecules, such as β2-microglobulin, rather than better survival rates in patient groups. Evidence of improved patient survival with the use of high-flux membranes is restricted to prevalent patients in the HEMO study who had been on HD for more than 3.7 years and incident patients in the Membrane Permeability Outcome (MPO) study who had lower serum albumin concentrations (<40 g/litre) or had diabetes mellitus (Table 21.7.1.1). High-flux dialysers are now used as standard in most HD centres. Risk of hypersensitivity reactions Dialysers sterilized with ethylene oxide have been associated with hypersensitivity or hypersensitivity-like reactions. This risk can be avoided by using dialysers that have been sterilized using steam or gamma radiation. Treatment time on haemodialysis per week Weekly solute removal rates may be increased by either increasing the frequency and/or duration of HD sessions per week. Frequency of haemodialysis HD frequency is a more powerful determinant of weekly solute re- moval than the duration of each session. Twice per week HD is not regarded as an adequate long-term form of chronic RRT and should be avoided, although it may be acceptable provided: • the patient has a significant level of residual renal function (e.g. a mean of combined urinary urea and creatinine clearance above 5 ml/min per 1.73 m2) • the patient's residual renal function is monitored at least every 3 months • the frequency of dialysis is increased when renal function decreases The routine use of a three times per week HD schedule evolved from empirical considerations in the belief that it reconciled adequate treatment with adequate breaks between treatments to provide the patient with a reasonable quality of life within a 7-day treatment cycle. It is common practice to prescribe daily HD in the short term when patients with chronic renal failure develop an acute intercur- rent illness or (rarely) pericarditis. Two forms of more frequent, long-term HD have been advocated recently: • Short daily HD is usually prescribed as six 'daily' sessions of dia- lysis of 2 to 3 h duration with one rest day per week Box 21.7.1.1 Beneficial effects of biocompatible haemodialysis membranes • Lower activation of complement and leucocytes • Greater adsorption of cytokines • Greater adsorption of β2-microglobulin • Higher flux and removal of middle molecules (e.g. β2-microglobulin) Table 21.7.1.1 Randomized controlled trials of mortality rates with high- and low-flux dialysers Study HEMO study MPO study Study design Prospective, multicentre, randomized controlled trial 1846 prevalent patients on HD for a median of 3.7 years 2

× 2 factorial study design: high- vs low-flux and high- vs standard-dialysis dose 10-fold increase in β2-microglobulin clearances in the high-flux vs low-flux groups Dialyser reuse permitted Prospective, multicentre, randomized controlled trial 738 incident HD patients Comparison of high- and low-flux HD Stratified into two groups with serum albumin < or >40 g/litre Few exclusion criteria No dialyser reuse Outcomes No differences were observed in all-cause mortality between the high- and low-flux groups or the high- and standard dialysis dose groups No difference was observed in all-cause mortality in the high- and low-flux groups Secondary analysis In the patient subgroup which had been on HD for longer than a median of 3.7 years before enrolment: a) use of high-flux dialysis membranes was associated with a 32% reduction in all-cause mortality (P = 0.001) b) use of high-flux dialysis membranes was associated with a 37% reduction in cardiac death (P = 0.016) Survival rates in women randomized to the higher-dose group were higher than women in the lower-dose group (relative risk 0.81; P = 0.02) after adjusting for different indices of body size In the patient subgroup with serum albumin <40 g/litre on enrolment: a) use of high-flux dialysis membranes was associated with a reduction in all-cause mortality (P = 0.032)

21.7.1 Haemodialysis 4865 • Nocturnal daily HD is usually prescribed as slow overnight treat- ment for 5 to 7 nights per week while the patient is sleeping Both forms of daily HD have been shown to provide a number of medical advantages compared with standard-duration, thrice- weekly HD (Box 21.7.1.2). Short daily HD offers the additional benefit of higher weekly re- moval of small and large molecular weight solutes for the same total time on HD per week, while daily nocturnal daily HD provides: • very large doses of dialysis • greatly reduced need for phosphate binders • reduction in sleep disturbance and sleep apnoea The Frequent Haemodialysis Network daily study showed that the composite endpoints of death and change in left ventricular mass or death and change in physical health in 245 patients were im- proved on HD six days per week compared with thrice-weekly HD. However, both the Frequent Haemodialysis Network daily and nocturnal trials showed that there was an increased risk of a first access event in the groups receiving HD on 6 days per week, presumed related to more frequent cannulation of the vascular access. Duration of haemodialysis It is difficult to separate the influence of dialysis duration and dose on patient outcomes. The National Co-operative Dialysis Study (NCDS), an historical randomized trial in the United States of America when cellulose membranes and acetate dialysate were used, is the only randomized study so far to address the issue of optimal dialysis time. This two-by-two factorial design study randomized nondiabetic patients into one of four dialysis regimens: • Two with short (2.5–3.5 h) dialysis times • Two with longer (4.5–5.0 h) dialysis times • Two with different time-averaged urea concentrations Longer dialysis times gave better but statistically insignificant sur vival rates. However, several observational studies have shown an association between risk of death and shorter dialysis duration (Box 21.7.1.3). These observations suggest that the duration of thrice-weekly HD should not be reduced below 4 h unless the patient has significant residual renal function. A randomized controlled study of longer dialysis sessions in thrice-weekly HD is needed. Dialysate composition Bicarbonate should be used as the buffer base. The concentration of components of dialysate may be altered, and an example of the components of a standard dialysis fluid is shown in Table 21.7.1.2. The potential for developing dialysis-induced hypoglycaemia can be avoided if the dialysate contains glucose. Individualization of di- alysate potassium concentrations may be required in patients with a tendency to hypokalaemia, and adjustment of the dialysate sodium concentrations during HD (sodium profiling) may be beneficial in patients with haemodynamic instability. Ultrafiltration on haemodialysis The interdialytic fluid (weight) gain is removed under volumetric control by the HD machine making adjustments to the transmem- brane

pressure to achieve the prescribed UF rate. Treatment time and UF rates are related inversely in HD. Higher rates of UF may be poorly tolerated and were associated with a greater risk of death in the Dialysis Outcomes and Practice Patterns Study (Table 21.7.1.3). Long-term observational data from Tassin, France, have dem- onstrated that target ‘dry’ body weight and good control of blood pressure without antihypertensive medication are more likely to be achieved with long duration HD sessions and lower rates of UF. It is recommended that the UF rate should not exceed 10 ml/kg body weight per hour. Box 21.7.1.2 Medical advantages of daily HD versus standard duration thrice-weekly HD • Improved well-being and better quality of life • Improved fluid balance and blood pressure control • Regression of left ventricular hypertrophy • Higher dietary protein intake and better nutritional status • Lower hospital admission rate • Reduced need for erythropoietin Box 21.7.1.3 Observational studies showing better patient outcomes with longer-duration HD • Very low mortality rates were observed in patients treated with long- duration thrice-weekly HD with mean Kt/V of 1.67 ± 0.41 in Tassin, France. • Increments in dialysis duration up to 5.5 h were associated with im- proved patient survival rates in a large Japanese population after adjusting for dialysis dose. • Patients in the United States of America who received dialysis for less than 3.5 h per session three times per week had approximately twice the risk of death of patients on HD for more than 4 h three times per week. • The Dialysis Outcomes and Practice Patterns Study (DOPPS) has shown that patient survival, independent of dialysis dose, was greater in patients with treatment times above 4 h. • The Australian and New Zealand Dialysis and Transplant Registry has shown that patient survival, independent of dialysis dose, was greater in patients with treatment times above 4.5 h. Table 21.7.1.2 Representative concentrations of components of bicarbonate dialysis fluid Dialysate component Concentration in dialysis fluid (mmol/litre) Chloride 108 Bicarbonate 35 Acetate 3 Sodium 138 Potassium 2 Calcium 1.25 Magnesium 0.5 Glucose 1

 Planning and initiating haemodialysis for established renal failure Patient education and patient choice are important aspects of predialysis care to ensure that patients are well prepared to start the RRT modality that is most suited to them in a timely fashion. United Kingdom Renal Registry data demonstrate that the mean estimated glomerular filtration rate (eGFR) at dialysis initiation increased linearly from 6.2 to 8.7 ml/min per 1.73 m2 between 1997 and 2009, but this trend reversed after the publication in 2010 of the IDEAL (Initiation of Dialysis Early and Late) study, which randomized 828 incident adult patients commencing dialysis in 32 centres in Australia and New Zealand to receive dialysis early (eGFR 10–12 ml/min per 1.73 m2 based on the Cockcroft and Gault formula) or late (eGFR 5–7 ml/min per 1.73 m2) and showed no survival benefit from starting dialysis early before the onset of symptoms. Previous studies from Scotland and the Netherlands had suggested that any survival advan- tage from commencing dialysis earlier may be attributed to lead time bias. HD and other forms of RRT are usually now commenced when patients with progressive chronic kidney disease stage 5 (eGFR <15 ml/min per 1.73 m2) develop persistent fluid overload despite diur- etics, persistent hyperkalaemia despite dietary potassium restriction, acidosis despite bicarbonate supplementation, or symptoms sug- gestive of uraemia such as poor appetite and gastrointestinal symp- toms. Progressive decreases in dietary protein intake and nutritional status as residual renal function declines may also be an indication to initiate dialysis. Based on this rationale the United Kingdom Renal Association Clinical Practice Guidelines recommend that the deci- sion to start RRT in patients with chronic kidney disease stage 5 (eGFR <15 ml/min per 1.73 m2) should be based on ‘a careful discussion with the patient of the risks and benefits of RRT, taking into account the patient’s symptoms and signs of renal failure, nutritional status, comorbidity, functional status, and

the physical, psychological and social consequences of starting dialysis in that individual'. The 2018 NICE guideline on renal replacement therapy and conservative man- agement recommends considering starting dialysis 'when indicated by the impact of symptoms of uraemia on daily living, or biochemical measures or uncontrollable fluid overload, or at an estimated eGFR of around 5 to 7 ml/min/1.73 m2 if there are no symptoms'. Vascular access for haemodialysis Reliable and safe vascular access is a prerequisite for adequate HD. A native arteriovenous fistula is the preferred access in the great majority of HD patients as it provides the highest blood flow rates, minimizes the risk of sepsis, and has the greatest longevity. An ar- teriovenous graft is the second-best option for long-term vascular access. Tunnelled and nontunnelled central venous access are in- ferior options. The rate of vascular access-related infection was 2.5 per 1000 dialysis sessions for patients with native fistulae or grafts, 13.6 per 1000 dialysis sessions for tunnelled central venous catheters, and 18.4 per 1000 dialysis sessions with temporary cen- tral venous catheters. The CHOICE study of 616 incident patients showed that the adjusted relative risk of death was 1.2 for an arterio- venous graft and 1.5 for a central venous catheter compared with the reference group with an arteriovenous fistula. Central venous catheters may, however, be the only option for some patients: some may have a needle phobia; others may have ves- sels unsuitable for creation of a functioning arteriovenous fistula or graft able to provide adequate blood flow rates and adequate HD. Patients may also run out of options for further fistula or graft cre- ation if the current fistula or graft fails and then need to rely upon a tunnelled central venous catheter to allow them to remain on HD or switch to PD. Many HD patients require multiple access procedures to enable them to stay on HD, hence vascular access continues to be HD's Achilles' heel. Adequacy of haemodialysis Adequacy of haemodialysis dose The molecular weights of the solutes to be cleared by dialysis range over three orders of magnitude, from small (water, urea) to large (β2-microglobulin). Adequate clearance of the whole range of mol- ecules by dialysis is important and in the future monitoring of β2-microglobulin levels may be used to assess dialysis adequacy. For practical reasons, adequacy of HD dosage thus far has been measured using small, easily measured solutes such as urea. Three methods of assessing urea removal on HD are in current use (Table 21.7.1.4): 1. The URR is the percentage fall in blood urea achieved by a dia- lysis session, is easy to perform, and is the most widely employed index of dialysis dose used in the United Kingdom. URR does not take into account solute removal via UF or residual renal function or urea generation during dialysis. However, this is un- important clinically if the main aim of measuring small solute removal by HD is to ensure that a minimum target dialysis dose is delivered consistently. A number of large observational studies in populations of HD patients have shown that variations in URR are associated with major differences in mortality and have led to recommendations that the URR should be at least 65%. 2. Kt/V urea can be predicted from several simple formulae and, if Kt/V is being used for comparative audit, it is important that the raw data are collected to allow calculation of estimated Kt/ V using a single formula. The formula validated and reported by Daugirdas is recommended (Table 21.7.1.4). 3. Urea kinetic modelling (UKM), the most complex measure, in- volves analysis of the fall in blood urea concentration during HD, the rise in blood urea in the interdialytic period, clearance of urea by residual renal function, and the total clearance pre- dicted from the dialyser clearance, blood and dialysate flow, time on dialysis, and fluid removal during dialysis. Kt/V measured by Table 21.7.1.3 Ultrafiltration rate and survival rates in the Dialysis Outcomes and Practice Patterns Study (DOPPS) Study design Observational international study of risk of death in 22 000 HD patients Outcomes adjusted for demographics, comorbidity, dialysis dose (including RRF) and body size Outcomes UFR >10 ml/h per kg was associated with higher risk of intradialytic hypotension (RR = 1.3; P = 0.045) UFR >10 ml/h per kg was associated with higher

risk of death (RR = 1.1; P = 0.02) RR, relative risk; RRF, residual renal function; UFR, ultrafiltration rate.

21.7.1 Haemodialysis 4867 formal UKM is more accurate than URR, particularly at high values of URR and Kt/V. Its use allows accurate prediction of the effects of changing one particular component of the dialysis pre- scription (e.g. dialyser size, dialysis duration, blood flow rate) on the delivered dialysis dose, although this benefit has been over- stated given the limited number of practical options for chan- ging the dialysis prescription. Most United Kingdom HD units only collect pre- and postdialysis urea concentration, and only a few perform UKM. For comparative audit, the choice therefore currently lies between calculation of URR and estimation of Kt/V urea from such data. All methods of assessing urea removal depend upon an accurate measurement of the blood urea concentrations after HD. Postdialysis rebound in blood urea concentration results from cardiopulmonary recirculation of treated blood returning from the extracorporeal cir- cuit and from continuous return of blood from poorly dialysed body 'compartments'. Accurate comparison of delivered dialysis dose therefore requires estimation of the equilibrated blood urea concen- tration, allowing calculation of URR and 'equilibrated' Kt/V (eKt/ V). Full re-equilibration takes about 30 min, but it is impractical to ask patients to wait this long for postdialysis blood sampling on a routine basis. The amount of rebound is determined by several fac- tors including the efficiency of dialysis and the size of the patient. Formulae have been validated for predicting 30-min postdialysis or 'equilibrated' blood urea from blood samples using either the stop dialysate flow method (or similar sampling methods) or the slow flow method. Utilizing one of these methods was recommended in the latest updates of the United Kingdom Renal Association and Kidney Disease Outcomes Quality Initiative (KDOQI) clinical prac- tice guidelines on HD. Doubts have been raised about Kt/V being a good index of dialysis dose since survival rates on HD are higher in patients with larger body size and better nutrition, even though this patient group tends to have lower Kt/V values. Non-normalized dialysis dose (Kt) has been proposed as an alternative and a better index of dialysis dose to Kt/V since the former index obviates the trend for smaller pa- tients with poorer nutritional status to be accorded a higher dialysis dose. In a large cross-sectional analysis using Kt as the index of dia- lysis dose, mortality risk was observed to fall if the delivered dialysis dose was a minimum Kt of 42 litres in women and 48 litres in men. A further difficulty with the use of the Kt/V index for other than thrice-weekly HD is that the significance of any weekly Kt/V value depends on the frequency of dialysis since more frequent dialysis therapies, such as daily HD, will deliver greater small solute removal at the same weekly Kt/V. Minimum and target dialysis dose The optimal dialysis dose has not been well defined, but minimum targets of delivered dose measured by URR and Kt/V have been es- tablished. Observational studies have shown a reduction in mor- tality rates with increases in dialysis dose or no further reduction in mortality above Kt/V of 1.3 or URR of 70%. These studies led to the HEMO trial (Table 21.7.1.1) which showed no difference in patient survival or secondary endpoints between the high- and standard- dose groups, even though dialysis doses were well separated with achieved eKt/V of 1.16 in the standard-dose group (URR 66.3 ± 2.5%) and eKt/V of 1.53 in the high-dose group (URR 75.2 ± 2.5%). Based upon this evidence, the minimum dialysis dose delivered thrice weekly should have a URR of 65% or an eKt/V of 1.2 (cal- culated from pre- and postdialysis urea values, duration of dialysis, and weight loss during dialysis). To achieve a URR above 65% or eKt/V above 1.2 consistently in most patients, the minimum target doses should be a URR of 70% or eKt/V of 1.4 in individual patients. An association between higher dose and lower mortality rates was observed in women but not in men in the HEMO study and was confirmed using the URR of incident patients in the United States of America and

eKt/V of patients in the DOPPS data from seven countries. Aiming for these target doses also addresses the concerns raised by recent data that suggest that women and patients of low body weight may have improved survival rates if the URR is main- tained above 70% or eKt/V is at least 1.4. Definition of adequacy of dialysis In addition to measurement of dialytic clearance of urea, global as- sessment of the adequacy of all aspects of the HD treatment is re- quired to optimize patient outcomes. This should include a clinical assessment of the patient's general well-being, nutritional status, monitoring of biochemical and haematological parameters, quality of life, blood pressure, and fluid status. Large observational studies have shown that patient survival in patients on thrice-weekly HD is highest when predialysis biochem- ical and haematological measurements are maintained within the Table 21.7.1.4 Methods of measuring urea removal on haemodialysis to assess adequacy of dialysis Method Required input data Calculations Urea reduction ratio (URR) Pre-HD urea concentration Post-HD urea concentration (Pre-HD urea − post-HD urea) /pre-HD urea × 100% Kt/V urea Pre-HD urea concentration Post-HD urea concentration Duration of HD Weight loss during HD See: Daugirdas JT (1993). Second generation logarithmic estimates of single-pool variable volume Kt/V; an analysis of error. J Am Soc Nephrol, 4, 1205–13 Urea kinetic modelling (UKM) Pre-HD urea concentration Post-HD urea concentration Duration of HD Weight loss during HD Dialyser clearance Interdialytic urine collection for measurement of urea concentration and volume Pre-HD urea concentration in the subsequent dialysis Data are uploaded on a computer programme which, assuming steady state, calculates Kt/V urea and normalized protein catabolic rate

 target ranges shown in Table 21.7.1.5, and these parameters are audited routinely by local renal units and nationally by the United Kingdom Renal Registry in ongoing efforts to improve the quality of delivered HD. Observational studies have shown an association between ex- cessive interdialytic fluid gains and reduced survival rates. The im- pact of blood pressure control on HD patient survival is uncertain as patients with hypotension have lower life expectancy than pa- tients with uncontrolled hypertension. In particular, the frequency of dialysis-related hypotension, defined as an acute symptomatic fall in blood pressure during dialysis requiring immediate inter- vention to prevent syncope, is an indicator of poor prognosis for survival in HD patients. This may reflect underlying overt or occult cardiac disease in patients with dialysis-related hypotension. The achievement of clinical practice guidelines is dependent on patients' concordance with treatment. Increasing patients' under-standing of the benefits of delivering all aspects of optimal dialysis, including adequate dialysis dose and creation of native vascular ac- cess, may help to improve outcomes. Patients are often reluctant to increase HD duration if the delivered dialysis dose is inadequate des- pite increasing the dialyser blood flow rate, dialysate flow rate, and dialyser performance to the maximum that can be achieved, and pa- tients with a central venous catheter may be unwilling to have an ar-teriovenous fistula created. Data from the DOPPS have evaluated the relative risk of death of HD patients who fail to meet clinical practice guidelines for five modifiable clinical variables (Table 21.7.1.6). This observational data suggests that the use of central venous catheters for vascular access and nutrition/inflammation are at least as im- portant as adequate dialysis dose or control of hyperphosphataemia in influencing patient survival rates. Factors affecting patient safety on haemodialysis Haemodialysis machine monitors and alarms HD machines must be serviced and maintained in full working order at all times to ensure that all of the safety monitors and alarms shown in Box 21.7.1.4 are functional. Table 21.7.1.5 United Kingdom Renal Association clinical practice guidelines for haemodialysis Audit variable Recommendation Nondialytic measures Urea

clearance by HD Minimum target URR 70% or minimum target eKt/V 1.3 Fluid removal rate by HD Less than 10 ml/kg/h Dietary fluid and sodium restriction Pre-HD serum potassium concentration Less than 6 mmol/litre Dietary restriction Pre-HD haemoglobin concentration in patients receiving erythropoietin stimulating agents 10–12 g/dl Erythropoietin, iron supplementation Pre-HD serum phosphate concentration 1.1–1.7 mmol/litre Dietary restriction, phosphate binders, calcimimetic medication Pre-HD serum calcium concentration (adjusted for serum albumin) 2.2–2.5 mmol/litre Alfacalcidol, calcimimetic medication Serum parathyroid hormone 2–9 times the upper limit of the normal range of the assay Control of serum phosphate and calcium, parathyroidectomy Pre-HD serum bicarbonate concentration 20–26 mmol/litre Vascular access in incident HD patients 60% should have functioning arteriovenous accessa Vascular access in prevalent HD patients 80% should have functioning arteriovenous accessa a Arteriovenous fistula or arteriovenous graft. Table 21.7.1.6 Adjusted relative risk of mortality of patients who fail to achieve clinical practice guidelines (DOPPS I and DOPPS II; international) and percentage of British patients outside each guideline or practice pattern (United Kingdom DOPPS II data only) Modifiable practice pattern Level at which clinical practice guideline parameter was achieved Mortality relative risk (RR) Patients outside range (%) RR P-value Dialysis dose Single pool Kt/V <1.2 1.13 0.0023 17.8 Anaemia management Haemoglobin <10 g/dL 1.21 <0.0001 21.5 Mineral metabolism PO4 >1.8 mmol/litre 1.11 0.001 41.6 Nutrition/inflammation Albumin <35 g/litre 1.48 <0.0001 36.6 Vascular access Facility catheter use >10% 1.20 <0.0001 76.8

21.7.1 Haemodialysis 4869 Vascular access Integrity of the extracorporeal blood circuit is paramount for patient safety on HD. Dislodgement of vascular access needles or catheters and disconnection of the HD lines should be very uncommon com- plications of HD and should be detected promptly if they do occur. Patients are at risk of exsanguination following dislodgement of the venous needle or line as the patient will continue to lose blood at the rate of the blood pump speed unless the HD venous pressure alarm or blood detect device is activated. Anticoagulation during haemodialysis Extracorporeal anticoagulation is usually required to prevent thrombosis of the dialyser and extracorporeal circuit (Box 21.7.1.5). Reuse of dialysers Dialysers are generally marked for ‘single use only’, although some are designed for multiple use in an individual patient. Reprocessing of dialysers for reuse is a combination of cleaning, disinfection, and sterilization processes. Changing from multiple to single use of dialysers has been reported to result in a reduction in the mor- tality rate in a large population in the United States of America, and the cost of high-flux dialysers has fallen gradually such that the use of high-flux biocompatible dialysers is now cost-effective without reuse. Water quality for haemodialysis Quality assurance of the water used in the preparation of dialysis fluid is of paramount importance as HD exposes the blood of the pa- tient to more than 300 litres of water per week through a nonselective dialyser membrane, in contrast to an average of 12 litres per week through a highly selective membrane (intestinal tract) in healthy in- dividuals. Intact dialyser membranes have been shown to be perme- able to bacterial contaminants as well as permitting backdiffusion and backfiltration of chemical contaminants from the dialysate. Table 21.7.1.7 summarizes the quality standards for testing for chemical and microbiological contaminants in the water used in the preparation of dialysate that have been endorsed by the Association of Renal Technologists and United Kingdom Renal Association. Achieving this standard of treated water purity usually requires soft- ening, carbon filtration, reverse osmosis, and an effective disinfec- tion programme for all pipework between the treatment plant and dialysis machines. Sodium is included in the ‘mandatory’ group be- cause, although the drinking water limit is 200 mg/litre, additional sodium is introduced by softening. Ultrapure water

(defined as <0.1 cfu/ml and bacterial endo- toxins <0.03 IU/ml) is readily achievable using modern water treat- ment techniques and should be regarded as the standard for all newly installed water treatment plants. The European Best Practice Guidelines recommend the use of ultrapure water for conventional as well as high-flux HD. Reinfusion fluid, used in haemofiltration (HF) and haemodiafiltration (HDF), must be sterile (<1 cfu/1000 litres) and, particularly where large exchange volumes are required, have an endotoxin level of less than 0.03 IU/ml. Even with ultrapure water, this standard of purity can only be achieved by 'online' fluid production with multiple filtration of the dialysis fluid. Machines designed to produce reinfusion fluid usually require a water supply that meets the microbiological requirements of Table 21.7.1.7. Patient safety on HD has been jeopardized when the water supply used in the preparation of dialysis fluid has been inadvertently Box 21.7.1.4 Haemodialysis machine monitors and alarms • Blood pump speed (nominal dialyser blood flow rate) • Arterial pressure monitor and alarm • Dialysate conductivity monitor and alarm • Dialysate temperature monitor and alarm • Venous air detect alarm and air trap • Venous pressure monitor and alarm • Temperature and conductivity monitor • Ultrafiltration rate and volume • Heparin infusion pump • Dialysate blood leak detector and alarm • Blood pressure monitor (optional) • Ionic dialysance or online urea clearance for dialysis dose (optional) Box 21.7.1.5 Anticoagulation used for haemodialysis • Unfractionated heparin (with a mean half-life of 1.5 h) is best admin- istered as a loading dose followed by a continuous or bolus infusion of 500–1500 units/h that is discontinued approximately 30 min before the end of the dialysis session in patients using an arteriovenous fistula or graft. • Low molecular weight heparin is a commonly used alternative agent that has been associated with less frequent episodes of hyperkalaemia and an improved lipid profile than standard heparin. • A systematic review of 11 trials comparing the use of low molecular weight heparin and unfractionated heparin in HD patients concluded that there was no difference in the incidence of bleeding complica- tions, bleeding from the vascular access after HD, or thrombosis of the extracorporeal circuit. • The dosage of heparin may need to be increased if there has been a substantive rise in the haematocrit or reduced if the patient is on war- farin or antiplatelet drugs. • For patients with heparin-induced thrombocytopenia either heparinoids (danaparoid) or hirudin should be utilized instead of heparin. Table 21.7.1.7 Maximum recommended concentration of chemical and microbial contaminants in water for dialysis for which routine testing is mandatory Contaminant Maximum recommended concentration (mg/litre = ppm) Initial test frequency Aluminium 0.01 3-monthly Calcium 2 (0.05 mmol/litre) 3-monthly Total chlorine 0.1 Not less than weekly Copper 0.1 3-monthly Fluoride 0.2 3-monthly Magnesium 2 (0.08 mmol/litre) 3-monthly Nitrate (as N) 2 (equates to 9 mg/litre $NO_3$) 3-monthly Potassium 2 (0.05 mmol/litre) 3-monthly Sodium 50 (2.2 mmol/litre) 3-monthly Bacteria (TVC) 100 cfu/ml Not less than monthly Endotoxin 0.25 IU/ml Not less than monthly

 contaminated by aluminium, fluoride, chlorine (or chloramine), or hydrogen peroxide. Haemofiltration HF is an alternative form of extracorporeal dialysis that removes solutes by convection rather than diffusion (as in HD). The highly permeable membrane in the haemofilter allows UF of large volumes of fluid that is measured gravimetrically and replaced by infusion of the substitute fluid either into the arterial line (predilutional HF) or the venous line (postdilutional HF). HF is not commonly used as a mode of chronic RRT because ad- equate intermittent HF requires large exchange volumes (40% of body weight three times per week), high blood flow rates (350–450 ml/min), and additional costs. However, continuous or daily HF is often performed instead of daily HD for management of acute kidney injury (AKI) in many critical care settings since continuous HF can maintain fluid balance

and may promote cardiovascular stability. Haemodiafiltration HDF is a hybrid of HD and HF in which a convective volume of ap- proximately 24 litres/session is removed through the haemodiafilter and physiological ‘replacement’ fluid equal to the removed volume minus the desired weight reduction (usually the interdialytic fluid gain) is returned to the blood before (predilutional) or after (postdilutional) the haemodiafilter (Fig. 21.7.1.4). HDF offers the advantage of increasing middle-molecule clearances without the need for an increase in treatment time by superimposing convective removal of middle molecules onto the diffusive removal of the HD technique. As well as removal of ‘unwanted’ larger solutes, such as β2-microglobulin, HDF removes ‘wanted’ solutes, such as amino acids and small proteins. Vitamin B12 supplements are often re- quired in patients receiving long-term HDF. Several randomized controlled trials have compared mortality rates on HD and HDF (Table 21.7.1.8). The Turkish and CONTRAST studies failed to show a beneficial effect of HDF on all-cause mor- tality and cardiovascular events, but the ESHOL study showed that high efficiency online HDF is associated with a 30% reduction in all- cause mortality compared with high-flux HD and a 46% mortality reduction for the subgroup of HDF patients removing convection volumes of greater than 25 litres/session. A post hoc analysis of these three studies suggested a dose–effect relation: the higher the con- vection volume, the lower the mortality risk. The EUDIAL working group’s systematic review of six randomized controlled trials from 1996 to 2013 concluded that current evidence suggests that online HDF provides lower all-cause and cardiovascular mortality rates than HD. At present, HDF is mainly performed in Europe and is performed infrequently in the United States of America. Renal replacement therapy for acute kidney injury and poisoning When to start RRT? HD may need to be performed as an emergency in patients with life-threatening AKI or poisoning, or in patients with chronic renal failure who present late and in extremis. The typical indications for emergency HD are severe hyperkalaemia, severe metabolic acid- osis, fluid overload refractory to diuretics, and/or symptoms of renal failure. Patients with a dialyzable poisoning (lithium, sali- cylate, methanol, ethylene glycol) who are at risk of death or ser- ious complications if treatment is limited to full supportive care and medical therapy may also require emergency HD. It is unproven if early initiation of HD offers clinical or survival benefits in pa- tients with gradually progressive chronic renal failure and so there is no specific level of residual renal function at which HD should be commenced. Which modality of RRT? Currently there is no evidence to show if continuous or intermit- tent dialysis therapies provide better survival in patients with AKI. In a randomized dose-equivalent, prospective study of continuous venovenous HD versus intermittent HD in 80 intensive care unit patients with AKI, the continuous venovenous HD group had no improvement in patient survival or recovery of renal function. Extended daily HD and postdilutional continuous venovenous HF are commonly utilized in the management of AKI. Both provide long duration therapy to help maintain adequate fluid balance and minimize adverse haemodynamic effects in this critically ill group, and the choice of modality of RRT should be based on local experi- ence and expertise in the technique and clinical needs of the indi- vidual patient. Which dialyser membrane to use? Initial randomized studies showed that the use of high-flux biocom- patible membranes was associated with improved patient survival rates in AKI, but this was not confirmed in follow-up studies. Fig. 21.7.1.4 Comparison of high-flux haemodialysis and haemodiafiltration. Flow rates indicated in red and blue are ml/min

 Which dialysis dose to prescribe? There have been two large, prospective, multicentre, randomized trials comparing dialysis dose in AKI: these showed no benefit from higher dialysis doses (Table 21.7.1.9). The intensive dialysis doses used in these studies were the same as an earlier randomized study of continuous venovenous HF which had shown improved

survival in patients prescribed at least 35 ml/h per kg body weight. Centre haemodialysis versus home haemodialysis The National Institute for Health and Care Excellence (NICE) guide- line NG107 (2018) recommended that all suitable patients should be offered the choice between home and in-centre dialysis. Home HD also offers the medical advantages arising from performing home HD more frequently than three times per week Home haemodialysis versus peritoneal dialysis In most countries, patient choice of dialysis modality is limited to patients who are able to perform dialysis at home. Observational studies have shown that short-term survival rates of patients on home HD and PD are similar, but technique survival is much poorer on PD, mainly because of catheter-related infections and inadequate dialysis. Home HD has several advantages in comparison with PD tech- niques (Table 21.7.1.10). Provided the above-mentioned requirements are met, home HD may be considered more suitable for patients with large body weight or body mass index, low residual renal function, heavy pro- teinuria and/or hypoalbuminaemia, or previous major abdominal surgery. Complications of haemodialysis Access-related infections The relative risk of bacteraemia in a large prospective cohort of in- cident HD patients was 1.95 for HD with tunnelled catheters and 1.05 for HD with grafts when compared to patients with an arterio- venous fistula. Infection-related hospitalization in the HEMO study was also shown to be more frequent in patients relying on central venous catheters for vascular access, and was not reduced by the use of high-flux dialysers or a higher dialysis dose. Vascular access using central venous dialysis catheters is also associated with a higher risk of central venous stenoses and lower blood flow rates. Loss of pa- tency of central venous catheters is common. The incidence of bacteraemia in a prospective study of nontunnelled HD catheters was 5% after 3 weeks of placement in the internal jugular vein. Cuffed, tunnelled rather than nontunnelled central venous catheters are preferred if vascular access is likely to be required for more than 3 weeks since tunnelled catheters are as- sociated with a lower rate of infection and can provide higher blood flow rates. Dialysis-related symptomatic hypotension Hypotension is the most frequent complication of HD and can shorten treatment times, thus reducing the delivered dialysis dose. It is important to exclude a range of uncommon alternative

Table 21.7.1.8 Randomized controlled trials of mortality rates in HDF and HD

| Study | CONTRAST study ( J Am Soc Nephrol, 2012, 23, 1087–96) | TURKISH study (Nephrol Dial Transplant, 2013, 28, 192–202) | ESHOL study ( J Am Soc Nephrol, 2013, 24, 487–97) |
|---|---|---|---|
| Enrolled patients (N) | 714 | 782 | 906 |
| Follow-up (years) | 3 | 2 | 1.9 |
| Blood flow rate (ml/min) | 300 | 310 | 387 |
| Treatment time (min) | 226 | 236 | 236 |
| HDF convective volume (litres) | 20.7 | 20.7 | 23.7 |
| HD membrane flux | Low flux | High flux | Mainly high flux |
| All-cause mortality rate (HDF vs HD) | 12.1% vs 12.8%; n.s. | 7.0% vs 8.8%; n.s. | 6.2% vs 9.0%; P <0.05) |

Table 21.7.1.9 Randomized controlled trials of the effect of intensity of dialysis dose on mortality rates

| Study | Veterans Affairs/National Institutes of Health Acute Renal Failure Trial Network (ATN) study | Randomized Evaluation of Normal versus Augmented Level (RENAL) study |
|---|---|---|
| Study Design | 1124 patients High-dose (HD 6 days per week with Kt/V 1.2–1.4 or CRRT with effluent flow 35 ml/kg per hour vs Standard dose (HD 3 days per week with Kt/V 1.2–1.4 or CRRT with effluent flow 20 ml/kg per hour) | 1508 patients High dose (CRRT with effluent flow 35 ml/kg per hour vs Standard dose (CRRT with effluent flow 20 ml/kg per hour) |
| Outcome | 60-day mortality was the same in both groups (53.6% with high-dose and 51.5% with low-dose therapy) | 90-day mortality was the same in both groups (44.7% with high-dose and 44.7% with low-dose therapy) |

 causes whenever a patient develops hypotension on dialysis. These include cardiac disease (arrhythmias, myocardial infarction, pericardial tamponade), autonomic neuropathy, occult haemor- rhage, septicaemia, dialyser reactions, air embolism, and acute haemolysis. Dialysis-related hypotension is an independent

predictor of poor patient survival and patients experiencing frequent dialysis-related hypotension are at higher risk of death, probably because dialysis- related hypotension is a marker of severe cardiac disease. The risk of dialysis-related symptomatic hypotension can be reduced by several strategies (Box 21.7.1.6). A systematic review of 22 studies concluded that a reduction in dialysate temperature is effective in decreasing the incidence of intradialytic hypotension without af- fecting dialysis adequacy. An increase in the dialysis treatment time combined with a reduction in the fluid UF rate or a decrease in the dialysate fluid temperature are the most reliable methods of redu- cing intradialytic hypotension. Dialysis-related haemorrhage Bleeding from an arteriovenous fistula or graft or from the gastro- intestinal tract is not uncommon in HD patients. Caution is required with the use of anticoagulants during HD and heparin locking solu- tions in patients with central venous catheters. Anticoagulation can be avoided or kept to a minimum by using a high blood flow rate and regular flushing of the extracorporeal circuit with saline every 15 to 30 min. Alternatively, heparin may be replaced by regional cit- rate anticoagulation, but this requires monitoring of serum calcium levels and replacement of calcium during HD, which is too complex for routine use. Thrombocytopenia is common in patients on heparin and usu- ally mild and transient (HIT-I). True heparin-induced thrombo- cytopenia (HIT-II) is a rare (1–4%) but potentially life-threatening syndrome caused by platelet-activating antibodies to complexes of platelet factor 4 (PF4) and heparin. Characteristic features are thrombocytopenia, a systemic reaction within 30 min of intravenous unfractionated heparin administration, and a hypercoagulable state with a high risk of thromboembolic complications. Severe thrombo- cytopenia and/or thrombosis in a patient on unfractionated hep- arin should raise strong suspicions. The presence of antiheparin/ PF4 antibody is confirmatory in these circumstances, in which case unfractionated heparin and low molecular weight heparin should be avoided. Danaparoid and argatroban are probably the best alternatives. Acute haemolysis This uncommon complication should be suspected if the patient develops backache, chest tightness or breathlessness, and blood in the venous line has a port-wine appearance or there is pink plasma in the venous chamber. This complication may be due to excessive dialysate temperature, kinking of the venous line, or water contam- ination with chloramines, nitrates, or copper. Air embolism This life-threatening complication should be prevented by the machine alarms if a disconnection of the arterial line or arterial access occurs. Foam is often seen in the dialysis lines and the com- monest symptoms are chest tightness if the patient is recumbent and impaired conscious level or seizures if the patient is sitting upright. If suspected, the blood pump should be stopped, the venous line clamped immediately, and the patient placed in the recumbent position on their left side and with their head tilted downwards. Dialyser reactions Chemical sterilization of dialysers and tubing with ethylene oxide has been associated with anaphylactoid reactions. This risk is now avoided by the routine use of either steam or gamma radiation- sterilized dialysers and blood lines. Dialysis disequilibrium Nausea, vomiting, restlessness, headache, confusion, drowsiness, and, more rarely, seizures may occur during or shortly after dia- lysis when patients with advanced chronic renal failure receive high-intensity dialysis. As symptoms result from cerebral oedema, presumed due to disequilibrium between cerebral water and blood water solute or hydrogen ion concentrations, this syndrome can be avoided by the use of incremental dialysis dosing when patients start HD, for example, 2 h, 3 h, and then 4 h of treatment for the first three dialysis sessions. Table 21.7.1.10 Comparison of home HD versus PD Advantages of home HD Disadvantages of home HD Higher doses of therapy per unit time Need for a designated treatment room or portacabin at home Ability to prescribe ultrafiltration volume Need for anticoagulation and risk of bleeding No need for peritoneal access Need for vascular access Quality control of the dialyser membrane as well as the dialysis fluid and

no loss of dialysis efficiency with time Training of the patient is more difficult and requires more time Lower daily protein losses Most home HD training centres require that the patient has a helper at home Box 21.7.1.6 Strategies to reduce the risk of dialysis-related hypotension • Increase postdialysis target weight if the patient is assessed as below ‘dry’ weight • Reduce interdialytic weight gain by patient reducing interdialytic fluid and salt intake • Decrease the rate of fluid removal • Reduce food intake during dialysis • Avoid the administration of blood pressure-lowering medication be- fore dialysis • A reduction in dialysate temperature during dialysis • Increase dialysate sodium concentration (but this may increase interdialytic weight gain)

21.7.1 Haemodialysis 4873 Hyperkalaemia Performing an urgent electrocardiogram is of proven use in guiding management of patients with serum potassium concentrations greater than 6 mmol/litre and can be used to determine which pa- tients should receive emergency medical treatment and/or HD for hyperkalaemia (see Chapter 21.5). Hyperkalaemia is a common indication for emergency dia- lysis among patients already on HD and accounts for 3 to 5% of deaths among dialysis patients in general. Noncompliance with the dialysis prescription and diet are the commonest contribu- tory factors, but medications such as angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, nonsteroidal anti-inflammatory drugs, β-blockers, and potassium supplements may be implicated. HD is the most appropriate emergency treatment for hyper kalaemia in the dialysis patient. The serum potassium level usually falls by 1 mmol/litre during the first hour of treatment and by a fur- ther 1 mmol/litre during the next 2 h. The rate of potassium removal is increased by using a higher dialyser blood flow rate, higher di- alysate bicarbonate concentration, or lower dialysate potassium concentration. Dialysis-related amyloidosis Dialysis-related amyloidosis is a disabling, progressive condition caused by the polymerization of β2-microglobulin within tendons, synovium, and other tissues. β2-microglobulin is a large molecular weight molecule (molecular weight 11 600 Da) released into the cir- culation as a result of normal cell turnover and not excreted in renal failure. It is not removed by cellulose membranes and exposure to bioincompatible membranes may increase β2-microglobulin gen- eration. Symptoms are usually first reported 7–10 years after com- mencing HD, although tissue accumulation of dialysis-related amyloid in the joints and bone is demonstrable much earlier. The most common clinical presentations of dialysis-related amyloid are shown in Box 21.7.1.7. Symptoms from dialysis-related amyloidosis may occur earlier if patients have no significant residual renal function or are eld- erly at the onset of dialysis, and impure dialysis fluid has been implicated in the pathogenesis. High-flux HD membranes re- move β2-microglobulin by a combination of diffusive clearance and adsorption, and HDF removes substantially more as a result of additional convective clearance. HDF has been recommended for use in patients who are not suitable for transplantation or are predicted to remain on dialysis for at least 3.7 years. Renal trans- plantation usually results in improvement in amyloid-related symptoms. Incidence and prevalence of comorbid medical conditions The incidence and prevalence of a wide range of comorbid medical conditions is increased in HD patients. These include ischaemic heart disease, cerebrovascular disease, peripheral vascular disease, falls and fractures, infective endocarditis, and metastatic staphylo- coccal infections. The management of these medical complications is similar to standard clinical practice but needs to take account of a reduction in the dosage of renally excreted drugs and allow for drug removal by dialysis therapy. FURTHER READING Randomized controlled trials in haemodialysis Astor BC, et al. (2005). Type of vascular access and survival among incident hemodialysis patients: the Choices for Healthy Outcomes in Caring for ESRD (CHOICE) Study. J Am Soc Nephrol, 16, 1449–55. Augustine JJ, et al. (2004). A randomized controlled trial comparing intermittent with continuous dialysis in patients with acute renal failure. Am J Kidney Dis, 44,

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N Engl J Med, 359, 7–20. Meta-analyses and systematic reviews in haemodialysis Lim W, Cook DJ, Crowther MA (2004). Safety and efficacy of low molecular weight heparins for hemodialysis in patients with end- stage renal failure: a meta-analysis of randomised trials. J Am Soc Nephrol, 15, 3192–206. Box 21.7.1.7 Clinical presentations of dialysis-related amyloidosis • Carpal tunnel syndrome (usually after 7 or more years of HD) • Joint pains and stiffness especially in hands, arms, and shoulders (usually after 10 or more years of HD) • Tenosynovitis of tendons in the hands • Pathological fractures due to amyloid bone cysts • Destructive spondyloarthropathy

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