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Haemodialysis – clinical standards and targets

Introduction

3.1 Haemodialysis (HD) remains the default therapy for all end stage renal disease (ESRD). Despite the success of transplantation and peritoneal dialysis (PD), HD continues to have the highest rate of growth of all treatment modalities.¹ Many patients are maintained by HD after rejecting transplants or because they have had to abandon PD. Furthermore, a number of PD patients transfer to HD during the last few months of their lives.¹ About 40% of patients starting renal replacement therapy (RRT) are referred as late uraemic emergencies with no time for the planning of, or counselling on, the options for dialysis,² and such patients are more likely to remain on HD.³ These factors combine to increase the co-morbidity burden of the HD population. It is obvious that to improve survival on RRT requires that HD be delivered to a high standard.

3.2 HD treatment has evolved rapidly since its introduction, and continues to do so. Changes have seldom been underpinned by sufficiently large randomised trials. Nevertheless, day-to-day clinical decisions on appropriate treatments have to be made, and standards have to be set on the best available evidence.^{4,5} HD may be performed in a variety of settings, including hospital-based units, free-standing units, and in the home. Not all UK units provide home HD. Where this option is available, the choice should be largely determined by patient preference rather than on economic grounds. Recently there has been an increase in some areas in the provision of home HD driven by the lack of space in hospital dialysis units. The standards set in this chapter apply equally to each of these settings.

Dialysis equipment and disposables*

Standards

- ▶ All equipment used in the delivery and monitoring of therapy should comply with the relevant standards for medical electrical equipment (BS-EN 60601-2-16:1998, BS 5724-2-16:1998, IEC 60601-2-16:1998. Medical electrical equipment. Particular requirements for safety. Particular requirements for the safety of haemodialysis, haemodiafiltration and haemofiltration equipment). **(Good practice)**
- ▶ Disposables such as dialysers and associated devices are classified as medical devices and should display the CE mark. The presence of such a mark signifies compliance with the national and international standards: haemodialysers, haemodiafilters, haemofilters, haemoconcentrators and their extra corporeal circuits (BS-EN 1283:1996). Plasma filters (BS/150 13960).

Recommendation

- ▶ Machines should be considered for replacement after seven years service or after completing 50,000 hours operation, whichever is first. **(Good practice)**

*See Appendix D for details of standards abbreviations used in this chapter.

RATIONALE

3.3 Equipment used in renal units represents a substantial asset which must be carefully maintained. The selection of equipment should be in accordance with a policy that conforms to the recommendations of the Medical Devices Agency (MDA) (Device Bulletin DB 9801, 1998, *Medical device and equipment management for hospital and community based organisations*) and National Audit Office (*The management of medical equipment in NHS acute trusts in England*, National Audit Office, 1999).

3.4 Renal units should endeavour to adopt a programme of phased replacement of older HD machines. Although it is possible to keep a dialysis machine operating safely for many years, practical considerations of obsolescence and maintenance costs require a more structured approach. When a particular model of a machine becomes obsolete, companies generally only undertake to supply replacement parts for seven years. We accept that there is no firm evidence that replacement, as suggested above, is the most cost-effective strategy.

Concentrates and water for dialysis

Standards

- ▶ Concentrates used, either purchased ready-made or manufactured 'in house', must meet the requirements of prEN 13867: 2002 (concentrates for HD and related therapies). **(Good practice)**
- ▶ Water used in preparation of dialysis fluid must meet the requirements of BS ISO 13959 2001 (water for HD and related therapies) for bacterial and chemical contaminants. If routine monitoring demonstrates continuous excess contamination, a phased programme to improve this should ensue. When alternatives to conventional HD with low flux membranes are used, such as haemodiafiltration and haemofiltration, more stringent limits in respect of bacterial contamination are mandatory. For such alternative applications microbial count should not exceed 0 Colony Forming Units (CFU)/ml and endotoxin level should be less than 0.015 IU/ml. **(Good practice)**
- ▶ A routine testing procedure for product and feed water should form part of the renal unit policy. Samples should be cultured on Tryptone Glucose Extract Agar or Reasoner's 2A and, for fungi and yeast, on malt extract agar or Sabourad's Dextrose Agar (all incubations at room temperature, ie 20–22°C). The frequency for testing should not fall below monthly and should be sufficiently frequent to detect trends. **(Good practice)**

RATIONALE

3.5 HD exposes the blood of the patient to in excess of 300 litres of water per week through a non-selective membrane, in contrast to an average 12 litres per week through a highly selective membrane (intestinal tract) in healthy individuals. Patient related applications require the production of water of appropriate chemical, bacteriological and microbiological purity. The combination of devices required to achieve this will be determined by the quality of the incoming water and how it is used in the renal unit or patient's home. Knowledge of the potentially harmful effects of trace elements and chemicals is still growing, and techniques of water treatment are continuously being developed. The Association for the Advancement of Medical Instrumentation (AAMI) in the USA has taken a useful lead in these areas over a number of years. These

recommendations reflect the AAMI Standards and those of the European Dialysis and Transplant Nurses Association/European Renal Care Association (www.edtna-erca.org) (Appendix 1).

3.6 The dialysis membrane has long been regarded as an effective barrier against the passage of bacteria and endotoxin (potent pyrogenic materials arising from the outer layers of bacterial cells) from dialysis fluid to blood. This produced a complacent attitude towards the purity of dialysis fluid. About 10 years ago, several *in vitro* studies showed that intact membranes used in dialysers are permeable to bacterial contaminants.⁶⁻⁸ The pore size of the membrane appears to be less important than the thickness and the capacity of the membrane to adsorb bacterial products. Consequently low flux (standard) dialysis does not necessarily translate into higher microbiological safety than high flux dialysis or HDF. Patients receiving standard dialysis treatment with low flux cellulose-based membranes (thickness 6–8 microns), may therefore be at greater risk of pyrogenic reactions (see below) than those treated using thicker synthetic membranes which have the capacity to adsorb endotoxins and endotoxin fragments. This increased adsorptive capacity arises from the hypophobic domains in the membrane structure, which bind such fragments by Van der Waals forces. In patients treated with high flux membranes, a risk of pyrogen transfer due to back filtration (a movement of dialysis fluid into the blood pathway of the device due to a pressure gradient rather than the diffusion gradient discussed above) may exist. Lonneman *et al*,⁶ however, concluded that diffusion rather than convection is the predominant mechanism of trans-membrane transport of pyrogens, and back-filtration across pyrogen adsorbing membranes does not necessarily increase their passage. It should be emphasised that the adsorption capacity of the synthetic membranes is not infinite and that a breakthrough of pyrogenic substances can occur in the event of excessive water contamination.

3.7 Because a raised C-reactive protein (a sensitive marker of activation of the acute phase response) is associated with a significantly increased risk of death,⁹⁻¹¹ this has led to speculation that impure dialysate may contribute to an increased risk of death in dialysis patients. Impure dialysate has also been implicated in the pathogenesis of dialysis-related amyloidosis.¹²⁻¹⁴ While this suggestion has not been tested in clinical practice, it would seem prudent to ensure that water is as pure as reasonably possible. A range of standards exist world wide in respect of microbiological purity of water used in RRT. Within the UK the current draft International Standard (ISO/DIS 13959) will be adopted as a British Standard (BS-EN 13959) and any water used in the preparation of dialysis fluid should meet the requirements of this standard as a *minimum*. The standard stipulates that the product water used in the preparation of dialysis fluid should have a total viable microbial count not exceeding 10^2 CFU/ml and an endotoxin content not exceeding 1 IU/ml (~0.25 ng/ml for the limulus amoebocyte lysate (LAL) test). Ultrapure water is readily achievable using modern water treatment techniques and should be regarded as the standard for all newly installed water treatment plants.¹⁵

Standard

- ▶ The dialysate should contain bicarbonate as the buffer. (A)

RATIONALE

3.8 One of the critical functions of dialysis is the correction of the metabolic acidosis caused by the diseased kidney's failure to excrete non-volatile acids and to regenerate bicarbonate. Bicarbonate is the natural buffer normally regenerated by the kidneys and was the initial choice as dialysate buffer. If, however, sodium bicarbonate is added to a calcium- or magnesium-containing dialysate, their respective carbonate salts will precipitate unless the dialysate is maintained at a low pH level. Since it does not precipitate calcium or magnesium, acetate was used as an alternative buffer¹⁶ because of its rapid conversion to bicarbonate in the liver. In the late 1970s and early 1980s, a number of studies suggested that some of the morbidity associated with HD could be attributed to the acetate component of the dialysate.^{17,18} This appears to have been unmasked by the introduction of high-efficiency and short-duration dialysis, using membranes with large surface areas. Acetate intolerance led to the reappraisal of bicarbonate as a dialysis buffer in the early 1980s and, following the solving of the issue of precipitation, to its reintroduction. A recent systematic review of 18 randomised trials indicated a reduction in the number of treatments complicated by headaches, nausea/ vomiting and symptomatic hypotension when bicarbonate was used.¹⁹ Economic evaluations showed the cost of self-mix bicarbonate buffer to be similar to that of acetate. It should be noted, however, that even 'bicarbonate' dialysate contains moderate amounts of acetate.²⁰

3.9 It is not possible to set evidence-based standards for other components of the dialysate. There is recent evidence, however, that dialysis of non-diabetic patients against glucose-free dialysate is associated with a surprisingly high rate of asymptomatic hypoglycaemia without an associated counter-regulatory response.^{21,22} The long-term effects of repeated dialysis-induced hypoglycaemia are uncertain. Hypoglycaemia is not seen if the dialysate contains glucose, but glucose-containing dialysate is slightly more expensive.

Standards

- ▶ Patients whose estimated life expectancy is more than seven years and who are unlikely to receive a transplant as a result of human major histocompatibility complex (HLA) sensitisation, high risk of recurrent disease, rare tissue type or other contra-indications (including personal choice), are at high risk of dialysis-related amyloidosis. Such patients, and those with symptoms of dialysis-related amyloidosis should, where possible, receive a dialysis regimen with better clearance of beta 2-microglobulin, and ultrapure dialysate. Such treatments include HD with high flux synthetic membranes and haemodiafiltration. (B)
- ▶ For other patients the balance of evidence favours the use of low flux synthetic and modified cellulose membranes over unmodified cellulose membranes. (A)
- ▶ Those reusing dialysers marked 'for single use only' should have read the MDA Device Bulletin DB 2000(04) *Single-use medical devices: implications and consequences of reuse*. (Good practice)

RATIONALE

3.10 The use of synthetic membranes which can have more porous characteristics (high flux) than standard cellulose membranes started in the mid-1980s with a view to increasing the depurative capacity of HD. Interest was heightened by the subsequent discovery that a number of these membranes (eg polysulphone, polyamide, polyacrylonitrile) had markedly less ability to activate complement and other cellular elements than standard cellulose, and hence decrease the inflammatory response, ie they were more bio-compatible.

3.11 Cellulose membranes have been modified to make them both more bio-compatible and of slightly higher flux (semi-synthetic membranes), and synthetic membranes with lower flux properties have also been produced. The cost of the latter two types of membrane is now approaching that of cellulose membranes although currently the high flux synthetic membranes cost about three times as much.

3.12 Dialysis-related amyloidosis is a disabling, progressive condition caused by the polymerisation within tendons, synovium, and other tissues, of β -2-microglobulin, a large (molecular weight (MW) 11,600) molecule which is released into the circulation as a result of normal cell turnover but is not excreted in renal failure and is not removed by cellulosic membranes. Exposure to bio-incompatible membranes may increase β -2-microglobulin generation.¹⁵ Symptoms are typically first reported 7–10 years after commencing HD. A systematic review²³ of 27 randomised trials comparing cellulose, modified cellulose and synthetic membranes, showed a significant reduction in end of study β -2-microglobulin values when high flux synthetic membranes were used; one small study showed amyloid occurred less frequently with this treatment. High flux HD membranes remove β -2-microglobulin by a combination of diffusive clearance and adsorption; HDF removes substantially more as a result of convective clearance. Both treatments are thought to reduce the risk of developing dialysis-related amyloid.

3.13 Whether bio-compatible membranes have other advantages, as a result of the reduced activation of the inflammatory response during dialysis, is less certain. The systematic review showed no evidence of benefit when synthetic membranes were used compared with cellulose/modified cellulose membranes, in terms of reduced mortality or reduction in dialysis-related adverse symptoms.²³ Comparison of unmodified cellulose and modified cellulose membranes was not undertaken. Despite the relatively large number of randomised controlled trials (RCTs) undertaken in this area, none of the studies that were included in the review reported any measures of quality of life. Plasma triglyceride values were also lower with synthetic membranes in the single study that measured this outcome. Differences in these outcomes may have reflected the high flux of the synthetic membrane. Serum albumin was slightly higher at certain time points in some studies when synthetic membranes of both high and low flux were used. Given the adverse prognostic impact of hypoalbuminaemia in dialysis patients, this may be an important finding.^{11,22,24–28} Further trials are needed, and several are in progress.

3.14 Adequate solute clearance can be achieved using higher blood and dialysis fluid flows, and higher surface area membranes, than in the past. Since small MW solute (eg urea) removal can be formally quantified by validated techniques, dialysis times can

be reduced while maintaining 'equivalence' in the degree of blood purification. Since so-called 'middle molecules' (MW 200–20,000) diffuse only slowly into dialysis fluid, shortened treatment times have a proportionately greater deleterious effect on their clearance which may have implications for the long-term health of dialysis patients. Theoretically, reductions in sessional dialysis time can be more safely pursued if there is a concomitant improvement in middle molecular (MM) clearance, a goal which cannot be achieved by high blood flow rate or dialysis fluid flow rate and large surface areas of membranes impermeable to middle molecules. While the use of high flux membranes can increase this, a more effective way of promoting MM clearance is to superimpose convection upon standard diffusive blood purification technique using HDF. In this technique approximately 20 litres of 'extra' fluid, over and above the patients' interdialytic fluid gain, is removed through the dialyser and an equal volume of physiological 'replacement' fluid is returned to the blood downstream of the dialyser. HDF can be carried out safely and has been adopted as standard treatment in at least two UK centres.²⁹

Re-using membranes

3.15 Haemodialysers and their extracorporeal circuits contain sterile non-pyrogenic pathways. Such items are generally marked for single use only, although some are now designed for multiple use in an individual patient. Reprocessing is a combination of processes aimed at cleaning, disinfection and sterilisation of the item. Within the UK, reprocessing of items marked 'for single use' is discussed in the Medical Devices Agency Device Bulletin DB 2000(04) *Single-use medical devices: implications and consequences of reuse*. This is obtainable from the Medical Devices Agency, Hannibal House, Elephant and Castle, London SE1 6TQ.

3.16 Re-use has been shown to be safe in a number of studies^{30,31} and to have benefits, specifically the reduction in β -2-microglobulin. Some studies report an overall reduction in mortality among patients treated with re-used dialysers,³² although this may depend on the type of membrane used and on the agent used for re-processing, the use of bleach being associated with lower mortality than use of formalin.^{33,34} In this way high flux bio-compatible membranes can be used more cost effectively. In recognition of this, recently an agreement was reached between the Food and Drug Administration (FDA) in the USA and the manufacturers, requiring that some dialysers should be labelled 'for multiple use' and that manufacturers should issue protocols for the safe reprocessing of their devices. Currently, manufacturers have different marketing strategies in different countries and the main suppliers in the UK do not currently supply 'for multiple use' labels with the same devices which are so labelled in the USA. Eventually it is hoped that mass production will result in lower prices for high flux bio-compatible dialysers making them cost-effective without re-use.

Dialysis frequency and dose

Standards

► HD should take place at least three times per week in nearly all patients. Reduction of dialysis frequency to twice per week because of insufficient dialysis facilities is unacceptable. (Good practice)

- ▶ Every patient receiving thrice weekly HD should show:
 - either* urea reduction ratio (URR) consistently >65%
 - or* equilibrated Kt/V of >1.2 (calculated from pre- and post-dialysis urea values, duration of dialysis and weight loss during dialysis). (B)
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Recommendations

- ▶ Patients receiving twice weekly dialysis for reasons of geography should receive a higher sessional dose of dialysis, with a total Kt/V urea (combined residual renal and haemodialysis) of >1.8. If this cannot be achieved, then it should be recognised that there is a compromise between the practicalities of dialysis and the patient's long-term health. (Good practice)
 - ▶ Measurement of the 'dose' or 'adequacy' of HD should be performed monthly in all patients. All dialysis units should collect, and report to the Registry, data on pre- and post-dialysis urea values, duration of dialysis, and weight loss during dialysis. (Good practice)
 - ▶ Post-dialysis blood samples should be collected either by the slow-flow method, the simplified stop-flow method, or the stop-dialysate-flow method (Appendix 2). The method used should remain consistent within renal units and should be reported to the Registry. (B)
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RATIONALE

Frequency and duration

3.17 The most powerful determinant of solute removal is dialysis frequency rather than duration. The thrice weekly dialysis schedule has evolved from empirical considerations in the belief that it reconciles adequate treatment with adequate breaks between treatments to provide the patient with a reasonable quality of life, although there is no hard evidence for its superiority. Furthermore, all outcomes data have been derived from patient groups undergoing such dialysis schedules. The frequency of twice weekly dialysis has decreased world wide, including in the USA³⁵ where it fell from 12.9% to 3.6% of new patients between 1990 and 1996.

3.18 Only one, now outdated, US randomised trial where cellulose membranes and acetate dialysate were used, has addressed the issue of optimal dialysis time. The National Co-operative Dialysis Study randomised non-diabetic patients to one of four dialysis regimens, two with short (2.5–3.5 hour) and two with longer (4.5–5.0 hour) dialysis times, and two different time-averaged urea concentrations in each arm. Longer dialysis gave a better outcome.^{36,37} A combination of economic constraints, better patient tolerance using improved machines and materials, and patient preference for shorter times³⁷ has resulted in a gradual reduction in the average length of dialysis sessions around the world. The mean time in the UK is 3 hours 46 minutes.

3.19 More recently, two approaches to more frequent dialysis sessions have been investigated. The first is dialysis for around two hours per day for six days, and the other a renewed interest in slow overnight treatment for 5–7 nights, which can deliver very large doses of dialysis and remove fluid such that anti-hypertensive treatment can be reduced to a minimum. Both regimes have been reported to give improved outcomes when compared with the more conventional regime of three sessions per week each of four hours.^{38–42}

Dialysis adequacy 3.20 Dialysis adequacy is a global concept which includes clinical assessment of well-being, the impact on the patient's life and measures of the molecular clearance by the dialysis process. The molecular weights of the solvent and solutes to be cleared by dialysis range over three orders of magnitude, from small (water, urea) to large (β -2-microglobulin). Adequate clearance of the whole range of molecules by dialysis is important. For practical reasons haemodialysis adequacy is calculated using small, easily measured solutes such as urea.⁴³⁻⁵

Three methods of assessing urea removal are in current use:⁴³⁻⁴

- 1 The URR⁴⁶ is the simplest. The percentage fall in blood urea effected by a dialysis session is measured as follows:
$$\frac{\{\text{pre-dialysis [urea]} - \text{post-dialysis [urea]}\}}{\text{pre-dialysis (urea)}} \times 100\%.$$
- 2 Kt/V urea can also be predicted from one of several simple formulae requiring as input data the pre- and post-dialysis urea concentrations, the duration of dialysis, and the weight loss during dialysis.
- 3 Urea kinetic modelling (UKM) involves analysis of the fall in (urea) during haemodialysis, the rise in (urea) in the interdialytic period, clearance of urea by residual renal function, and the total clearance predicted from the dialyser clearance, blood and dialysate flow, time on dialysis, and fluid removal during dialysis. These data are fed into a computer programme which, assuming steady state, calculates Kt/V urea and normalised protein catabolic rate.⁴⁷

All these methods require accurate measurement of pre-dialysis and post-dialysis urea concentrations on a mid-week dialysis session. Full urea kinetic modelling also requires:

- ▶ measurement of dialyser clearance
- ▶ measurement of weight loss during dialysis
- ▶ collection of an inter-dialytic urine for measurement of urea concentration and volume
- ▶ a pre-dialysis blood urea concentration from the subsequent dialysis session.

3.21 The URR does not take convective removal of urea into account, and therefore tends to underestimate the 'dose' of dialysis. Its accuracy is less than Kt/V measured by formal UKM, particularly at high values of URR and Kt/V .⁴⁸ URR does not take residual renal function into account, hence adjustment of dialysis dose to achieve a particular target will result in higher overall urea removal than anticipated in those with residual renal function. Despite these drawbacks, a number of observational studies in populations of dialysis patients have shown that variations in URR are associated with major differences in mortality.^{28,49-51}

3.22 Kt/V can be calculated using several formulae giving different results⁵² and hence for comparative audit it is important that the raw data are collected to allow calculation of URR and estimated Kt/V using a single formula.

3.23 Formal UKM, the most complex measure, requires collection of additional data on dialyser clearance, an interdialytic urine collection, and measurement of pre-dialysis urea

concentration on the subsequent dialysis. Widely available computer software is required to perform the calculations. Its major advantage is that it allows much more accurate prediction of the effects of changing one particular component of the dialysis prescription (eg dialyser size, dialysis duration, blood-flow) on the delivered dialysis dose. UKM also gives valuable information on urea generation rate and protein catabolic rate. If the patient is in a steady state nutritionally, this gives information on current protein intake, and is a useful adjunct to other methods of assessment of nutritional status.

3.24 Many UK renal units only collect pre- and post-dialysis urea concentration, and only a very few perform UKM.¹ For comparative audit, the choice therefore currently lies between calculation of URR and estimation of Kt/V urea from such data. This situation is likely to change if more units adopt formal UKM. A retrospective analysis suggested that a Kt/V of 1.0 was the watershed between 'good' dialysis (>1.0), and inadequate dialysis (<1.0). Thereafter Kt/V survived as a recognised index of dialysis adequacy.⁵³ The remaining data relating dialysis dose to outcome are observational. Early studies showed that risk of death is associated with short dialysis duration⁵⁴ and low urea reduction ratio.²⁸ More recent studies^{49-51,54-6} have shown a reduced mortality, with increasing dialysis dose measured in various ways; in some of these studies adjustment was made for co-morbidity.^{51,57}

3.25 The optimal dialysis dose has not yet been defined. One study showed no further reduction in mortality above Kt/V of 1.3 or URR of 70%.⁵⁰ Many commentators, however, believe that there is some further improvement in mortality risk with Kt/V s of up to 1.6 or even higher.⁵⁸⁻⁶¹ For the present we have retained our standard as Kt/V of 1.2 which should be regarded as a minimum requirement. The HEMO trial is a prospective randomised controlled trial in which patients have been randomised to an equilibrated Kt/V of 1.0 or 1.4 and to synthetic or semi-synthetic membranes of high or low flux.⁶² Its results are expected soon. As with all standards, achievement is dependent on patients' adherence to treatment, for instance willingness to dialyse three times a week for the requisite number of hours. Increasing understanding amongst patients of the benefits of adequate dialysis should help further to improve outcomes.

Post-dialysis sampling

3.26 All measurements of dialysis dose require measurement of the post-dialysis blood urea concentration. Contamination of the post-dialysis sample with blood returning from the dialyser or heparin, or sampling from a fistula or other access device in which there is recirculation of dialysed blood will lead to falsely low measurements, and thus to over-estimation of dialysis dose. True venous blood urea concentration rises rapidly in the first few minutes after dialysis has ceased. It continues to rise at a rate higher than that expected from urea generation for up to 30 minutes, as a consequence of continued transfer of urea from peripheral body compartments into the bloodstream;⁶³⁻⁷ the earlier the sample is drawn, the higher the apparent delivered dialysis dose. Small variations in the timing and technique with which post-dialysis blood samples are drawn can, therefore, result in clinically important errors in the estimated dose of dialysis. Such variation has been shown to be common in the USA⁶⁸ and in the UK.¹ This suggests that changes, over time, in the technique for post-dialysis sampling causing higher apparent URR, have been responsible for an apparent rise in the URR necessary for optimum survival.⁶⁹ Several methods of standardisation of post-dialysis sampling are in use in the UK. The slow-flow method and the stop-flow method (Appendix 2) were devised to give

immediate post-dialysis measurements while avoiding the effects of re-circulation within the fistula. Currently used formulae to predict 'equilibrated' blood urea have been validated using similar sampling methods. The stop-dialysate-flow method allows more re-equilibration and therefore results in systematically higher measurements of post-dialysis blood urea concentration.⁷⁰ This is currently the most widely used method in the UK.¹

3.27 A post-dialysis rebound in venous blood urea concentration results from continued return of blood from poorly dialysed body 'compartments', and is particularly marked after high efficiency dialysis. Accurate comparison of delivered dialysis dose therefore requires estimation of the equilibrated blood urea concentration, allowing calculation of 'equilibrated' Kt/V . Full re-equilibration takes about 30 minutes, but it is impractical to ask patients to wait this long for post-dialysis blood sampling on a routine basis. The amount of rebound is determined by several factors including the intensity of dialysis and the size of the patient. Several formulae, which predict the equilibrated post-dialysis urea concentration, have been validated. The three formulae in widespread use in the UK – the Smye, Daugirdas, and Tattersall equations – give very similar results.⁶⁷ All of these formulae have been validated using an immediate post-dialysis sample; prediction of equilibrated dialysis dose using the stop-dialysate-flow method requires a different formula.⁷¹

Dialysis-related hypotension

Recommendation

► Data on the frequency of dialysis-related hypotension, defined as an acute symptomatic fall in blood pressure during dialysis requiring immediate intervention to prevent syncope, should be collected and reported to the Renal Registry. **(Good practice)**

RATIONALE

3.28 Dialysis-related hypotension is the most frequent symptom to complicate dialysis and can be extremely unpleasant, as well as reducing the efficiency of dialysis.⁷² The frequency of this event is, therefore, an important indicator of the quality of dialysis from the patient's perspective. It is caused by a reflex withdrawal of sympathetic tone resulting from decreased left ventricular filling, and is therefore dependent on the rate of fluid removal from the vascular space, the rate of re-filling from the interstitial space, venous tone, and many other variables.⁷³ Patients experiencing frequent dialysis-related hypotension are at higher risk of death,⁷⁴ although this may be because dialysis-related hypotension is a marker for severe cardiac disease⁷⁵. Adjustment of the rate of fluid removal, dialysate sodium concentration, and dialysate temperature during dialysis, can reduce the incidence of this complication,^{72,76} but incurs an increased cost due to the need for on-line monitoring of changes in relative blood volume (by measurement of changes in optical density of blood).

Recommendations

- ▶ At least 67% of patients presenting within three months of dialysis should start HD with a usable native arteriovenous fistula. **(Good practice)**
- ▶ At least 80% of prevalent HD patients should be dialysed using a native arteriovenous fistula. **(Good practice)**
- ▶ No patient already requiring dialysis should wait more than four weeks for fistula construction including those who present late. **(Good practice)**
- ▶ All dialysis units should collect data on infections related to dialysis catheters and polytetrafluoroethylene (PTFE) grafts to allow internal audit. **(Good practice)**

RATIONALE

3.29 The preferred access in the great majority of HD patients is a native arteriovenous fistula (AVF) which produces the highest flows, minimises sepsis and has the greatest longevity. Although most AVFs are created at the wrist, not all are successful and, while some patients go on to have AVFs created at the elbow, about 20% will be dependent upon intravenous plastic cannulae tunnelled under the skin or grafts made of synthetic tubing inserted under the skin. In a small number, severe cardiac dysfunction is seen as a contraindication to fistula construction, as a high flow AVF can contribute to high output cardiac failure.

3.30 In practice, fewer patients have AVFs for two main reasons. Firstly, up to 45% of patients starting HD do so as uraemic emergencies where there has been no time to create permanent access.⁷⁷ Secondly, most renal units in the UK have insufficient access to surgical support including theatre sessions dedicated to renal failure surgery. Temporary and semi-permanent tunnelled catheters are unfortunate necessities for many patients awaiting creation of a natural AVF; once established on dialysis via a catheter, some patients may, despite counselling, refuse to have an AVF constructed.⁷⁸ The high numbers of patients with temporary and tunnelled lines generally indicate congestion in a service with inadequate surgical support. Use of dialysis catheters and PTFE grafts for dialysis is associated with a greatly increased risk of hospitalisation and sepsis than use of AVFs.^{79,80}

3.31 The UK is therefore lagging behind most of the larger countries with regard to the proportion of HD patients using natural AVFs. Data from the Dialysis Outcomes and Practice Patterns Study (DOPPS) show that 67% of prevalent patients in the UK have functioning AVFs, compared with the European average of 80%. This study includes data from the UK, France, Germany, Italy and Spain. Only 47% of UK patients start with a functioning AVF, compared with a European average of 66%.⁸¹

Paediatric section

3.32 Pre-emptive transplantation is usually considered for children in whom there is a predictable decline in renal function to ESRD. When dialysis is required, PD is the first choice in most paediatric units, with a ratio of PD to HD of 2:1 in the UK⁸² and North America,^{83,84} although this proportion becomes equal by adolescence. There is no evidence that PD is superior to HD, but in most instances HD is more disruptive to family life and schooling. It is usually reserved for children who are unable, for physical or social reasons, to be managed by PD at home.⁸⁴ However, experience dictates that a paediatric dialysis programme should be able to provide both in-centre HD as well as home and in-centre PD. It is more usual for patients to be transferred from PD to HD because of complications rather than vice versa. The length of time on HD is usually short because of the shorter waiting times for transplantation in children. The relatively smaller numbers of paediatric patients means that there are few controlled comparative studies in children. Guidelines are based on opinions and reports of clinical experience to registries.

The dialysis centre

Standard

- ▶ All children requiring HD should be treated in a designated paediatric nephrology and dialysis centre. **(Good practice)**

Recommendations

- ▶ Children and parents should be free to choose a particular dialysis modality in discussion with the multi-professional team.⁸⁵ **(Good practice)**
- ▶ It is essential that children receiving chronic HD treatment are given a service that meets their physical and psychosocial needs. Children should be nursed in paediatric units where a renally trained children's nurse is always available for advice and support.⁸⁶ **(Good practice)**
- ▶ The child and family should be prepared either in hospital or at home for HD by their named nurse and play specialist using such materials as dolls, videos, story books and games.⁸⁷ **(Good practice)**
- ▶ The child's nutritional status should be managed and monitored by a paediatric renal dietician. **(Good practice)**

Vascular access

Standards

- ▶ Temporary central venous lines risk the loss of potential access points and their use should be kept to a minimum. **(Good practice)**
- ▶ When tunnelled, cuffed central venous catheters are used, the rate of infection should be better than one in every 12 patient months averaged over the total population for three years.⁸⁸ **(Good practice)**

Recommendations

- ▶ The choice of vascular access should take into account the age and size of the child. Although an arteriovenous fistula is regarded as the best long-term vascular access, this may not be possible in small children who can be managed using catheters that are tunnelled subcutaneously. Such catheters can also provide vascular access in older children where early transplantation is anticipated. **(Good practice)**
- ▶ Vascular access should be performed by an appropriately trained surgeon. **(Good practice)**
- ▶ Problems with needle phobia require referral to a child psychologist. **(Good practice)**

Dialysis frequency and dose

Standards

- ▶ Standards of adequacy recommended for adult patients should be regarded as the minimum for children. **(Good practice)**
- ▶ Adequacy tests should be performed monthly. **(Good practice)**

RATIONALE

3.33 In view of the lack of paediatric evidence, it is recommended that adult values for measures of small solute clearance, Kt/V , creatinine clearance and urea reduction ratio are extrapolated to children. It is worth stressing that in paediatric practice, as with adults, adequate dialysis is a combination of a number of factors and not just small solute clearance. If assessing urea reduction ratio, then this should occur at least monthly and may need to take place at least once every two weeks in young children. Residual renal function should be measured three monthly in children able to provide 24-hour urine collections. The HD prescription needs to be adjusted in line with growth and changing nutritional requirements.

3.34 Post-dialysis target weight should be reassessed monthly in order to allow for growth. Patients with regular weight gains of >6% of post-dialysis target weight should be identified and given help to achieve fluid control.

3.35 Untoward complications are prevented by thorough assessment and monitoring before, during and after HD of weight, blood pressure, temperature, pulse, general well-being and fluid assessment.

3.36 The extracorporeal blood volume in the HD circuit is recommended not to exceed 8–10% of the child's total blood volume (80 ml/kg).⁸⁹ All children should be dialysed with a machine offering volume controlled ultrafiltration and should receive bicarbonate dialysis using a bio-compatible dialyser. When choosing a dialyser, the urea clearance is estimated at 3–5 ml/kg/min where the effective surface area of the dialyser is less than three-quarters of the child's body surface area.⁹⁰

3.37 URR is a mathematically simple, transparent and easily applied measure of small solute clearances. It avoids assumptions required to perform more complex formal UKM.⁹¹

However, URR underestimates true urea clearance, as it does not measure urea removed by native kidney function and ultrafiltration. The greater the urine clearance, the greater the underestimate. It is likely in the near future that direct measurement on-line of urea removal will be available, thus removing the need for mathematical modelling. In children with no, or unmeasured, residual renal function, URR should be equal to or more than 65%. Children with residual renal function may be well dialysed with URR <65%.

3.38 The guideline for removing fluid in dialysis is no greater than 5% post-dialysis target weight per session (0.2ml/kg/min).⁸⁹ Weight gain between dialysis treatments should be recorded for each dialysis session, and should be encouraged to be 5% or less between sessions, often requiring a fluid restriction. For more fluid removal during the session, isolated ultrafiltration at the beginning of treatment may reduce symptoms.

Psychosocial support (for HD and PD)

Standard

► Psychosocial support is an essential part of the care offered to children and families while on dialysis. All members of the multidisciplinary team contribute to such support, but the social worker and psychologist will play lead roles. **(Good practice)**

Recommendations

- Each paediatric unit should have a suitably qualified and experienced social worker allocated to the work of the unit and involved in arranging appropriate information and support for each family. In addition, the social worker should assess the economic impact of dialysis on the family and discuss possible sources of financial support. **(Good practice)**
- Dialysis, particularly in infants, imposes a large burden of care upon families. Strategies such as home-care nursing, respite care and holidays for children need to be considered to prevent family burn-out.⁹² **(Good practice)**
- Children attending the HD unit on a regular basis have the greatest need for educational support as they will miss considerable school time. Liaison between the hospital school-teacher and the child's school is essential for all hospitalised children.⁹³ **(Good practice)**
- Adolescent patients will require an additional profile of education plans, social issues and careers advice. The timing and practicalities of transition to adult units have to be actively discussed and planned.⁹⁴ **(Good practice)**

Research and audit

► Each paediatric renal unit should maintain mortality and morbidity data for patients on HD. All vascular access related problems, such as catheter malfunction, exit site and tunnel infections, septicaemia rates, results of dialysis adequacy parameters and their relationship to growth, should be maintained by each unit. The data should be reported to the British Paediatric Renal Registry to be used for comparative audit and setting of standards. **(Good epidemiological practice)**

Access to and withdrawal from dialysis

Recommendation

► The decisions to institute active non-dialytic management of the patient with ESRD, including nutritional, medical and psychological support, or to discontinue dialysis already in train, should be made jointly by the patient and the responsible consultant nephrologist after consultation with relatives, the family practitioner and members of the caring team, abiding by the principles outlined briefly below. The decision, and the reasons for it, must be recorded in the patient's notes. The numbers of patients not taken on to dialysis and the reasons for this decision should be subject to audit, as should the numbers and causes for those in whom dialysis is discontinued. Centres should develop guidelines for palliative care of such patients, including liaison with community services. **(Good practice)**

RATIONALE

3.39 Now that every patient in chronic renal failure, of whatever age and co-morbidity, is at least considered as a potential recipient of dialysis, questions of deciding not to start or to terminate dialysis have assumed increasing importance. Until recently, the UK dialysis scene was characterised by accidental – but also sometimes deliberate – failure of referral, so that the decision not to treat was taken by family members or referring physicians alone, rather than in conjunction with a nephrologist,⁹⁵ and there have been few studies of the decision not to start dialysis.^{96–7} Equally, there is only one study from the UK of withdrawal from dialysis⁹⁸ suggesting that this plays a major role (17%) in overall death rates on dialysis, as it does in the USA and Canada.^{99–101}

3.40 In practice, the decision not to take a patient on to dialysis has much in common with the decision to withdraw dialysis. This is because caring staff, patients and relatives, all face similar difficult¹⁰² judgements and decisions about the likely quality and quantity of life on dialysis. Also, two approaches may be taken when a patient presents in uraemia whose ability to cope with, and to enjoy and benefit from, dialytic treatment is doubtful. The first approach attempts to make a 'clean' decision on whether or not to start dialysis after a process of consultation and discussion; the second, often called 'trial of dialysis', involves starting a proportion of such patients on dialysis, but with a pre-discussed plan to review whether this should continue beyond a specified point in the near future – usually a few weeks or months. Clearly the expectation is that the outcome in this case will be withdrawal of some patients from dialysis.

3.41 In addition to patients who clearly present greater than average problems from the outset, there are individuals who have had a period of worthwhile life on dialysis, but whose quality of life worsens because of medical or psychological deterioration, or both simultaneously. Additional difficulty arises when dementia, often fluctuating, makes it hard or impossible to ascertain what the patient's own feelings and wishes might be.

3.42 It is impossible to set quantitative standards in this difficult area of care, but principles of action can be enunciated and agreed. All patients in renal failure should be

considered for dialysis, and neither age *per se* nor the social situation and support (or lack of it) should be a factor leading to exclusion. Nor should lack of facilities for dialysis be acceptable on its own as grounds for exclusion, or fear of litigation a basis for a decision in either direction.

3.43 Careful medical assessment of any co-morbid conditions from which the patient may suffer is needed, together with whatever medical measures (short of dialysis) are required to correct them or minimise their effects.¹⁰³ Particular attention needs to be paid to potentially reversible mental states. Similarly, patients who have deteriorated will need careful medical and psychological assessment. If it appears that only a brief period of survival of unacceptable quality is likely on dialysis (eg less than three months), then the possibility of not starting or stopping dialysis needs to be considered. The interest of the individual patient must remain paramount, and although the opinions of relatives should be consulted, they should not be binding. The responsible consultant nephrologist should solicit views of the patient's family doctor, next of kin, and all carers within the multidisciplinary caring team. The decision must be taken by both the consultant (who must assess the patient personally), and the patient. The patient will need to be fully informed throughout, and to be aware of their options, so far as their mental status permits. The most realistic and accurate description of starting or not starting, continuing or not continuing dialysis should be given. The substance of these discussions must be recorded in the patient's notes. If the decision is taken not to initiate, or to stop dialysis, then a management plan of supportive care must be put in place. This must then be carried through in a way that ensures continued support, achieves what seems best *from the patient's point of view*, and finally enables the patient to die with dignity, when the time comes. Achieving this will often require co-ordinated work with the palliative care team, who should be involved early in the management plan.¹⁰⁴ Certain patients who are severely ill, often with conditions affecting several organs, may have a concurrent acute deterioration of their chronic renal failure. The referring physician (who may be in a different hospital) and the nephrologist, may feel, after discussion, that dialysis is inappropriate given the very poor prognosis from the underlying conditions. Under these circumstances the referring physician would discuss matters with the patient, if possible, and with the family.⁹⁷

Paediatric section

3.44 In paediatric practice, in particular, the decision to focus on palliative care often evolves gradually. Different members of staff and family may be working towards the decision at different rates, and time and discussion are essential for the transition. This time can be helpful in providing an opportunity for planning, as medical, nursing, psychosocial and spiritual care needs to be provided.

Recommendations

- ▶ Centres should have guidelines for palliative care.
- ▶ Symptom management should include assessment of current problems as well as prediction of future ones, and a management plan should be prepared.
- ▶ Plans for any equipment necessary should be made before it is needed.

- ▶ Possible drug requirements and their routes of administration should be predicted.
 - ▶ Community nursing support should be arranged.
 - ▶ Access to 24-hour support should be arranged. A key worker, usually a hospital or community nurse, should take on the task of coordinating care.
 - ▶ Information should be provided as to how the child may die and what to do after death.
 - ▶ Support should be available for the child to discuss their illness if they are old enough, and should be available for siblings and other family members.
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Appendix 1

Specification for chemical analysis of treated water for dialysis

(Based on AAMI standards¹⁰⁵ but modified in accordance with current British and European Pharmacopoeias)

1. pH	5.0–7.0	10. Calcium	Limit 2 ppm
2. Chlorine	Limit 0.1 ppm/mg/l*	11. Magnesium	Limit 2 ppm
3. Chloramine	Limit 0.1 ppm	12. Copper	Limit 0.1 ppm
4. Chlorides	Limit 50 ppm	13. Zinc	Limit 0.1 ppm
5. Nitrate	Limit 2 ppm	14. Lead	Limit 0.005 ppm
6. Sulphate	Limit 50 ppm	15. Mercury	Limit 0.001 ppm
7. Fluoride	Limit 0.2 ppm	16. Silver	Limit 0.005 ppm
8. Sodium	Limit 50 ppm	17. Aluminium	Limit 0.01 ppm
9. Potassium	Limit 2 ppm	18. Ammonium	Limit 0.2 ppm

* The units ppm and mg/l are equivalent

Appendix 2

Methods for post-dialysis sampling

Slow-flow method

Guidelines developed by F Gotch and M Keen, Davis Medical Centre, San Francisco and used since 1990 by Lister Renal Unit, East & North Herts NHS Trust.⁶⁴

- ▶ At the end of dialysis, turn the blood pump down to 100 ml per min.
- ▶ Override alarms to keep blood flowing.
- ▶ Wait 15–30 seconds and take samples from the 'A' line sampling post.
- ▶ If more than one sample is required, the urea should be the first one taken.
- ▶ Wash back blood; take patient off as normal.

Simplified stop-flow method

Guidelines developed by EJ Lindley, V Osborne, S Sanasy, D Swales and M Wright. The Leeds Teaching Hospitals NHS Trust.

- ▶ When you are ready to take the sample, turn the blood pump slowly down to 50 ml/min.
- ▶ Start counting to five; if the venous pressure alarm has not already stopped the blood pump when you get to five, stop the pump manually.
- ▶ Disconnect the arterial line and take a sample from the needle tubing (or the arterial connector of the catheter) within 20 seconds of slowing the blood pump to 50 ml/min.
- ▶ If more than one sample is required, the urea sample should be the first one taken.
- ▶ Wash back blood; take patient off as normal.

Stop-dialysate-flow method

Developed by Dr Mactier, Geddes, and Traynor at Stobhill Hospital Glasgow, and now currently used by all dialysis units in Scotland.⁷⁰

- ▶ Stop dialysate flow, but keep blood pump running for five minutes.
- ▶ Take a blood sample from anywhere in the blood circuit.

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