CLINICAL PRACTICE GUIDELINES

MODULE 2: HAEMODIALYSIS

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Dr. Robert Mactier,
Consultant Nephrologist,
Glasgow Royal Infirmary,
NHS Greater Glasgow & Clyde

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Introduction

The basis for the management of advanced chronic kidney disease is the seamless integration of renal replacement therapy (HD, peritoneal dialysis, and transplantation) with evidence based medical treatment of its complications. The National Service Framework Part 1: Dialysis and Transplantation has stressed the need for a patient-centred approach in the planning and provision of renal replacement therapy with an emphasis on patient education and choice as well as the provision of adequate resources for elective access surgery, dialysis and transplantation (1). It also identified that a small proportion of patients after counseling may opt for optimal conservative medical therapy without planning to initiate dialysis.

Innovations and changes in HD practice have seldom been underpinned by adequately powered randomised trials. Nevertheless, day-to-day clinical decisions on HD are required and standards need to be set on the best available evidence. Consequently clinical practice guidelines for HD have been developed in Australasia, Canada, Europe and the USA as well as the UK (2-17). These guidelines serve to identify and promote best practice in the delivery of HD and have set clinical standards to allow comparative audit of the key aspects of the HD prescription, laboratory data and patient outcomes. The reports of the UK Renal Registry, Scottish Renal Registry and NHS Quality Improvement Scotland have demonstrated the benefits of performing regular audit to improve clinical standards in HD (2-4).

This module provides an expansion on the 2002 guidelines in HD to incorporate sections on patient-centred HD facilities and initiation of dialysis, an expansion on the section on vascular access and, most importantly, an update on the current guidelines based on evidence from new studies. The USA (NKF-KDOQI) and European (EBPG) guidelines have also been updated recently (9, 11, 13) and standardisation with these and other international guidelines has been attempted whenever possible. This module promotes the adoption of a range of standardized audit measures in HD and has been designed to permit easy modification on the website to incorporate future changes in practice recommendations based on evidence from new research. The proportions of patients who should achieve clinical and laboratory targets have not been specified for most of the clinical practice guidelines. This approach is designed to allow for greater achievement of audit measures in parallel with improvements in clinical practice.

References

1   The National Service Framework for Renal Services Part 1: Dialysis and Transplantation, Department of Health, London, UK, January 2004. (www.doh.gov.uk/nsf/renal/index.htm)

2   Clinical Standards for Adult Renal Services, NHS Quality Improvement Scotland, March 2003. (www.clinicalstandards.org)

3   Renal Association Standards & Audit Subcommittee "Treatment of adults & children with renal failure - Standards and audit measures". 3rd Edition, London: Royal College of Physicians 2002. (www.renal.org/Standards/standards.html)

4   Report of NHS Quality Improvement Scotland (www.nhshealthquality.org)

5   National Kidney Foundation-K/DOQI Clinical Practice Guidelines for chronic kidney disease: Evaluation, classification and stratification. Am J Kidney Dis 2002; 39: 2 Supplement 1 S1-S266. (www.kidney.org/professionals/kdoqi/guidelines.cfm)

6   Canadian Society of Nephrology Clinical Practice Guidelines. JASN 1999; 10: Supplement 13 (http://csnscn.ca)

7   CARI (Caring for Australians with Renal Impairment) Guidelines Part 1 - Dialysis Guidelines. Eds: Knight J and Vimalachandra D, Excerpta Medica Communications, 2000 (www.kidney.org.au/cari/)

8   National Kidney Foundation-K/DOQI Clinical Practice Guidelines for hemodialysis adequacy, Update 2000. Am J Kidney Dis 2000; 37:1 Supplement 1 S7-S62 (www.kidney.org/professionals/kdoqi/guidelines.cfm)

9   National Kidney Foundation-K/DOQI Clinical Practice Guidelines and Clinical Practice Recommendations for Haemodialysis Adequacy, 2005 (in press) (www.kidney.org/professionals/kdoqi/guidelines.cfm)

10   National Kidney Foundation-K/DOQI Clinical Practice Guidelines for vascular access 2000. Am J Kidney Dis 2000; 37: 1 Supplement 1 S137-S180 (www.kidney.org/professionals/kdoqi/guidelines.cfm)

11   National Kidney Foundation-K/DOQI Clinical Practice Guidelines for vascular access, Update 2005. (in press) (www.kidney.org/professionals/kdoqi/guidelines.cfm)

12   European Best Practice Guidelines for haemodialysis Part 1. Nephrol Dial Transplant 2002; 17: Supplement 7 S1-S111. (http://ndt.oupjournals.org/content/vol17/suppl_7/index.shtml)

13   European Best Practice Guidelines for haemodialysis Part 2. Nephrol Dial Transplant 2005;20 (suppl 5) 148-155 (http://ndt.oupjournals.org/content/vol17/suppl_7/index.shtml).

14   National Kidney Foundation-K/DOQI Clinical Practice Guidelines for bone metabolism and disease in chronic kidney disease. Am J Kidney Dis 2002;39:2 Supplement (www.kidney.org/professionals/kdoqi/guidelines.cfm)

15   National Kidney Foundation-K/DOQI Clinical Practice Guidelines for managing dyslipidaemias in chronic kidney disease. Am J Kidney Dis 2003; 41: 4 Supplement 3 S1-S92. (www.kidney.org/professionals/kdoqi/guidelines.cfm)

16   National Kidney Foundation-K/DOQI Clinical Practice Guidelines for nutrition of chronic renal failure. Am J Kidney Dis 2001; 37: 1 Supplement 2 S66-S70. (www.kidney.org/professionals/kdoqi/guidelines.cfm)

17   National Kidney Foundation-K/DOQI Clinical Practice Guidelines for anaemia of chronic kidney disease. Am J Kidney Dis 2001; 37: 1 Supplement 1 S182-S236. (www.kidney.org/professionals/kdoqi/guidelines.cfm)

Summary of clinical practice guidelines for haemodialysis

1 Haemodialysis facilities (Guidelines DIAL-HD 1.1 – 1.6)

Guideline 1.1 DIAL-HD
The specification of new or refurbished haemodialysis facilities should adhere to the guidelines that are described in the NHS Estates Health Building Note 53: Volumes 1 & 2.

Guideline 1.2 DIAL-HD
The haemodialysis facility should have sufficient specialist support staff to fulfill the criteria listed by the Renal Workforce Planning Group 2002.

Guideline 1.3 DIAL-HD
Except in remote geographical areas the travel time to a haemodialysis facility should be less than 30 minutes or a haemodialysis facility should be located with 25 miles of the patient's home.
In inner city areas travel times over short distances may exceed 30 minutes at peak traffic flow periods during the day.

Guideline 1.4 DIAL-HD
Haemodialysis patients who require transport should be collected from home within 30 minutes of the allotted time and be collected to return home within 30 minutes of finishing dialysis.

Guideline 1.5 DIAL-HD
All patients who may be suitable for home dialysis should receive full information and education about home haemodialysis.
Home haemodialysis training is not available in all renal units and some patients may need to travel to a sub-regional or regional centre to pursue their choice to train for home haemodialysis.

Guideline 1.6 DIAL-HD
Haemodialysis capacity in satellite and main renal units within a geographical area should increase in step with predicted need. To allow for patient choice regarding out of hours haemodialysis schedules, provision of holiday haemodialysis and expansion in patient numbers calculation of the required number of haemodialysis stations should be based on using each station for 2 patients per day three times per week.
The national average number of hospital haemodialysis patients per million catchment population reported for the previous year by the UK Renal Registry should be regarded as the minimum capacity for haemodialysis in each geographically based renal service. Alternatively up-to-date regional data may be used. For example the national average provision for 312 hospital haemodialysis

patients (78 stations) per million catchment population in Scotland at the end of 2005 may be regarded as a minimum haemodialysis capacity in all regions in 2006. The level of hospital haemodialysis provision will need to be higher in areas with a high ethnic and/or elderly population and increase nationwide over the next 10 years.

2 Haemodialysis equipment and disposables (Guidelines DIAL-HD 2.1 – 2.3)

Guideline 2.1 DIAL-HD

All equipment used in the delivery and monitoring of therapy should comply with the relevant standards for medical electrical equipment. General safety standards are covered by BS EN 60601-1: 2006 and specific dialysis machine requirements are covered by BS-EN 60601-2-16: 1998 (Medical electrical equipment: Particular requirements for the safety of haemodialysis (HD), haemodiafiltration and haemofiltration equipment).

Guideline 2.2 DIAL-HD

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 requirements of the statutory Medical Device Directive and also national and international standards where they exist for new products: BS-EN 1283: 1996 (haemodialysers, haemodiafilters, haemofilters, haemoconcentrators and their extra corporeal circuits), ISO 8638:2004 (Extracorporeal blood circuit for haemodialysers, haemodiafilters and haemofilters) or ISO 13960: 2003 (Plasma filters).

Guideline 2.3 DIAL-HD

Machines should be replaced after between seven and ten years' service or after completing between 25,000 and 40,000 hours of use for haemodialysis, depending upon an assessment of machine condition.

3 Concentrates and water for haemodialysis (Guidelines DIAL-HD 3.1 – 3.4)

Guideline 3.1 DIAL-HD

Ready made concentrates are classified as medical devices and should display the CE mark. Concentrates that are manufactured 'in house' should meet the requirements of BS EN 13867: 2002 (Concentrates for haemodialysis and related therapies) (good practice).

Guideline 3.2 DIAL-HD

Water used in the preparation of dialysis fluid should, as a minimum, meet the requirements stated in Table 1 for chemical and microbiological contaminants.

After consultation within the UK the limits for chemical contaminants are derived from AAMI RD-52 2004 (1), ISO 13959:2002 (2) and the European Pharmacopoeia (3), whilst the limits for bacterial counts (100 cfu/ml) and endotoxin (0.25 IU/ml) are based on the European Pharmacopoeia (3) and the European Renal Association Best Practice Guidelines (4). New equipment should be capable of producing 'ultrapure' dialysis fluid (bacterial counts <0.1 cfu/ml and endotoxin <0.03 IU/ml) in order to meet the best practice guidelines. Ideally this should be achieved using ultrapure water; however water that meets the minimum standard in Table 1 can be used together with point of use filtration of the dialysis fluid. If routine monitoring demonstrates continuous contamination in excess of the desired levels, a programme to improve this should start immediately **(good practice).**

Guideline 3.3 DIAL-HD

A routine testing procedure for water for dialysis should form part of the renal unit policy.

Guideline 3.4 DIAL-HD

The dialysate should contain bicarbonate as the buffer.

4 Haemodialysis membranes (Guidelines DIAL-HD 4.1 – 4.6)

Guideline 4.1 DIAL-HD

The balance of evidence supports the use of low flux synthetic and modified cellulose membranes instead of unmodified cellulose membranes.

The benefits of low flux synthetic and modified cellulose membranes over unmodified cellulose membranes are limited to advantages arising from different aspects of improved biocompatibility rather than better patient outcomes.

Guideline 4.2 DIAL-HD

The balance of evidence supports the use of a dialysis regimen with enhanced removal of middle molecules in incident patients who are predicted to remain on haemodialysis for several years and prevalent patients who have been on haemodialysis for more than 3.7 years. Such patients are at risk of developing symptoms of dialysis-related amyloidosis.

Treatments with better clearance of middle molecules include haemodialysis with high flux synthetic membranes and haemodiafiltration. The proven benefits of high flux synthetic membranes in randomized trials are limited to advantages arising from improved biocompatibility and enhanced removal of middle molecules, such as beta-2-microglobulin, rather than better patient survival rates. Chronic high flux dialysis in the HEMO study did not affect the primary outcome of all cause mortality or any of the secondary composite outcome measures

including the rates of first cardiac hospitalization or all cause mortality, first infectious hospitalization or all cause mortality, first 15% decrease in serum albumin or all cause mortality, or all non-vascular access-related hospitalizations.
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Guideline 4.3 DIAL-HD

Patients without increased bleeding risk should be given low-dose unfractionated heparin or LMWH during haemodialysis to reduce the risk of clotting of the extracorporeal system.

For patients with a risk of bleeding anticoagulation should be avoided or kept to a minimum by using a high blood flow rate and regular flushing of the extracorporeal circuit with saline every 15-30 minutes.

Guideline 4.4 DIAL-HD

If it is planned to reuse dialysers that are marked 'for single use only' the implications of dialyser reuse need to be considered carefully after reading MDA Device Bulletin DB 2000(04) Single-use medical devices: implications and consequences of reuse.

Guideline 4.5 DIAL-HD

The use of dialysers sterilized with ethylene oxide should be avoided.

Guideline 4.6 DIAL-HD

Haemodialysis patients should not be treated with ACE inhibitor drugs and AN 69 dialyser membranes at the same time.

5 Haemodialysis dose, frequency and duration (Guidelines DIAL-HD 5.1 – 5.7)

Guideline 5.1 DIAL-HD

HD should take place at least three times per week in nearly all patients with end-stage chronic renal failure.

Reduction of dialysis frequency to twice per week because of insufficient dialysis facilities is unacceptable.

Guideline 5.2 DIAL-HD

Every patient with end-stage chronic renal failure receiving thrice weekly HD should have consistently:

> **either urea reduction ratio (URR) > 65%**
> **or equilibrated Kt/V of >1.2 (or sp Kt/V of > 1.3) calculated from pre- and post-dialysis urea values, duration of dialysis and weight loss during dialysis.**

To achieve a URR above 65% or eKt/V above 1.2 consistently in the vast majority of the haemodialysis population clinicians should aim for a minimum target URR of 70% or minimum eKt/V of 1.4 in individual patients. Aiming for these target doses also addresses the concerns raised by recent data which suggest that women

and patients of low body weight may have improved survival rates if the URR is maintained above 70% or eKt/V is at least 1.4.

Guideline 5.3 DIAL-HD

The duration of thrice weekly HD in adult patients with minimal residual renal function should not be reduced below 4 hours without careful consideration.

Guideline 5.4 DIAL-HD

Patients receiving dialysis twice weekly for reasons of geography should receive a higher sessional dose of dialysis.

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.

Guideline 5.5 DIAL-HD

Measurement of the 'dose' or 'adequacy' of HD should be performed monthly in all hospital HD patients and may be performed less frequently in home HD patients.

All dialysis units should collect and report this data to their regional network and the UK Renal Registry.

Guideline 5.6 DIAL-HD

Standardisation of the method of post-dialysis blood sampling is essential since all measurements of dialysis dose require the measurement of the post-dialysis blood urea concentration. Post-dialysis blood samples should be collected either by the stop-dialysate flow method, the slow-flow method or the simplified stop-flow method.

The method used should remain consistent within renal units and should be reported to the Registry.

Guideline 5.7 DIAL-HD

Patients with acute renal failure should initially receive daily renal replacement therapy.

The frequency of renal replacement therapy may be reduced once the metabolic syndrome and fluid status of patients with acute renal failure is stable.

6 Laboratory and clinical indices of dialysis adequacy other than dialysis dose (Guidelines DIAL-HD 6.1 – 6.11)

Guideline 6.1 DIAL-HD

Blood sampling for biochemical and haematological measurements should be performed before a mid-week HD session using a dry needle or syringe.

Guideline 6.2 DIAL-HD
Monitoring of pre-dialysis biochemical and haematological parameters should be performed monthly in hospital HD patients and at least 3 monthly in home HD patients.

Guideline 6.3 DIAL-HD
Pre-dialysis serum bicarbonate concentrations measured with minimum delay after venepuncture should be between 20 and 26mmol/l.

Guideline 6.4 DIAL-HD
Pre-dialysis serum potassium should be between 3.5 and 6.5 mmol/l in HD patients.

Guideline 6.5 DIAL-HD
Pre-dialysis serum phosphate should be between 1.1 and 1.8mmol/l.

Guideline 6.6 DIAL-HD
Pre-dialysis serum calcium, adjusted for serum albumin, should be within the normal range.

Guideline 6.7 DIAL-HD
Pre-dialysis serum albumin corrected calcium x phosphate product should be less than 4.8 mmol2/l2.

Guideline 6.8 DIAL-HD
Serum PTH levels should be more than twice and less than 4 times the upper limit of normal for the intact PTH assay used.
 Serum PTH levels do not need to be performed routinely more often than every 3 months.

Guideline 6.9 DIAL-HD
Serum aluminium concentration should be measured every three months in all patients receiving oral aluminium containing phosphate binders.

Guideline 6.10 DIAL-HD
Pre-dialysis haemoglobin concentration should be 10.5-12.5g/dl.

Guideline 6.11 DIAL-HD
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 audited.

7 Vascular access (Guidelines DIAL-HD 7.1 – 7.16)

Guideline 7.1 DIAL-HD

To preserve veins for creation of vascular access venepuncture or insertion of peripheral venous cannulae should be avoided in the forearm or arm of all patients with advanced renal failure whenever possible.

Guideline 7.2 DIAL-HD

The preferred mode of vascular access for HD patients is a native arteriovenous fistula.

Guideline 7.3 DIAL-HD

There should be enough dedicated theatre sessions for access surgery to provide one session per week for every 120 patients on dialysis. With this level of access surgery provision no patient on dialysis, including those patients who present late, should wait more than four weeks for fistula construction.

Guideline 7.4 DIAL-HD

Patients should undergo fistula creation between 6 and 12 months before haemodialysis is expected to start to allow time for adequate maturation of the fistula or time for a revision procedure if the fistula fails or is inadequate for use.

Guideline 7.5 DIAL-HD

The time to first cannulation of an AVF should be a minimum of 1 month and preferably at least 2 months after creation.

First cannulation may be considered between 2 and 4 weeks after creation of an AVF if this is the alternative to insertion of a central venous catheter and a nephrologist or experienced haemodialysis nurse has assessed that the fistula has matured adequately for use for dialysis.

Guideline 7.6 DIAL-HD

At least 65% of patients presenting more than three months before initiation of dialysis should start HD with a usable native arteriovenous fistula.

Guideline 7.7 DIAL-HD

Investigation of the AVF or graft to assess for evidence of arterial or venous stenoses or access recirculation is required if there is a significant fall in the blood flow rate that can be achieved, a reduction in delivered dialysis dose or a persistent rise in venous pressure in sequential dialysis sessions.

Guideline 7.8 DIAL-HD

All patients should be evaluated for a secondary arteriovenous access after each episode of access failure.

Guideline 7.9 DIAL-HD
As few HD patients as possible should rely on central venous catheters for vascular access.
As an audit measure less than 20% of patients on long-term HD should use tunneled or non-tunneled central venous catheters as the form of vascular access.

Guideline 7.10 DIAL-HD
Cuffed, tunneled double-lumen central venous catheters are preferred if temporary vascular access is likely to be needed for more than 3 weeks. Non-cuffed double-lumen catheters may be used if temporary vascular access for haemodialysis is predicted to be required for less than 3 weeks.

Guideline 7.11 DIAL-HD
The preferred insertion site for central venous catheters is the internal jugular vein and the catheter should not be placed on the same side as a planned or maturing upper limb arterio-venous access, whenever possible.

Guideline 7.12 DIAL-HD
All renal units should use real-time ultrasound to guide insertion of central venous catheters.

Guideline 7.13 DIAL-HD
All renal units should have protocols to ensure that full barrier precautions are followed during insertion of temporary and tunneled central venous dialysis catheters.

Guideline 7.14 DIAL-HD
All central venous catheter connections and disconnections should be performed under aseptic conditions by trained staff.

Guideline 7.15 DIAL-HD
Peripheral and central line blood cultures should be taken prior to starting antibiotics in all cases of suspected catheter-related infection.

Guideline 7.16 DIAL-HD
All HD units should collect and audit data on the form of vascular access in use in incident and prevalent haemodialysis patients and the rates of bacteraemia per 1000 patient days using central venous catheters, arterio-venous grafts and arterio-venous fistulae.

8 Access to and withdrawal from dialysis (Guidelines DIAL-HD 8.1 – 8.5)

Guideline 8.1 DIAL-HD

All patients with advanced renal failure (eGFR < 30ml/min), who have a life expectancy of more than 3 months, should be considered for renal replacement therapy and should be referred to a nephrologist.

Guideline 8.2 DIAL-HD

If there is no medical contraindication the choice of initial dialysis modality should be based on patient choice.

Guideline 8.3 DIAL-HD

After full education and counseling a small proportion of patients may opt for active non-dialytic management of advanced chronic kidney disease, including nutritional, medical and psychological support, rather than plan to initiate dialysis.

The numbers of patients not taken on to dialysis and the reasons for this decision should be subject to audit.

Guideline 8.4 DIAL-HD

Renal replacement therapy should be commenced when a patient with an eGFR < 15ml/min/1.73m2 has symptoms or signs of uraemia, fluid overload or malnutrition in spite of medical therapy and considered carefully when an asymptomatic patient has an eGFR < 6ml/min/1.73m2.

Guideline 8.5 DIAL-HD

Any decision to discontinue haemodialysis 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.

The decision, and the reasons for it, must be recorded in the patient's notes. Renal units should develop guidelines for palliative care of such patients, including liaison with community services.

Summary of audit measures for haemodialysis

1 The distance and travel time between the patient's home and the nearest satellite or main haemodialysis unit.

2 The waiting time after arrival before starting dialysis and the waiting time for patient transport after the end of haemodialysis.

3 The proportion of dialysis patients in the main renal unit and its satellite units who are on home haemodialysis.

4 The number of haemodialysis patients and number of haemodialysis stations in the main renal unit and its satellite units expressed per million catchment population.

5 The proportion of patients in the main renal unit and its satellite units who are on twice weekly haemodialysis.

6 Cumulative frequency curves of urea reduction ratio measured using a standard method of post-dialysis sampling.

7 The proportion of patient non-attendances for haemodialysis sessions and the proportion of dialysis sessions shortened at the patient's request.

8 Cumulative frequency curves of pre-dialysis serum potassium concentration.

9 Cumulative frequency curves of pre-dialysis serum calcium, phosphate calcium x phosphate product and PTH concentrations.

10 Cumulative frequency curves of pre-dialysis haemoglobin concentration.

11 The incidence of symptomatic hypotensive episodes during dialysis sessions.

12 The proportion of prevalent patients on long-term haemodialysis who use an arterio-venous fistula, arterio-venous graft and tunneled or non-tunneled central venous catheters as the mode of vascular access.

13 **The number of dedicated renal failure access surgery sessions per 120 dialysis patients.**

14 **The dates of first referral to nephrology, referral for creation of vascular access and creation of first vascular access and the date and mode of vascular access at the initiation of dialysis should be recorded and audited in all incident chronic haemodialysis patients.**

15 **The rates of bacteraemia (and specifically the rates of MRSA bacteraemia) observed per 1000 patient days using central venous catheters, arterio-venous grafts and arterio-venous fistulae.**

16 **The proportion of patients with advanced renal failure (CKD stage 5) who are treated with conservative medical therapy.**

17 **Record of the serum creatinine, estimated GFR and co-morbidity at initiation of chronic renal replacement therapy (dialysis or transplantation).**

Full clinical practice guidelines for haemodialysis

1 Haemodialysis facilities (Guidelines DIAL-HD 1.1 - 1.6)

Guideline 1.1 DIAL-HD
The specification of new or refurbished haemodialysis facilities should adhere to the guidelines that are described in the NHS Estates Health Building Note 53: Volumes 1 & 2 (good practice).

Rationale
The specification that is required for a modern haemodialysis (HD) unit has been detailed by NHS Estates and should be followed in all new and refurbished satellite and main renal unit HD facilities (1,2).

References
1   NHS Estates, Facilities for Renal Services, Health Building Note 53: Volume 1, Satellite dialysis unit & Volume 2, Main renal unit
2   The National Service Framework for Renal Services Part 1: Dialysis and Transplantation, Department of Health, London, UK, January 2004. (www.doh.gov.uk/nsf/renal/index.htm)

Guideline 1.2 DIAL-HD
The haemodialysis facility should have sufficient specialist support staff to fulfill the criteria listed by the Renal Workforce Planning Group 2002 (good practice).

Rationale
The number of medical, specialist nursing, technical and allied health professionals that are required to provide high quality HD therapy has been standardized by the Renal Workforce Planning Group (1). There should be great emphasis on teamwork, quality assurance and audit, health and safety and continuing professional development for all members of the multidisciplinary team (2).

References
1   Section 5 Workforce Planning Projections. National Renal Workforce Planning Group Recommendations 2002
2   The National Service Framework for Renal Services Part 1: Dialysis and Transplantation, Department of Health, London, UK, January 2004. (www.doh.gov.uk/nsf/renal/index.htm)

Guideline 1.3 DIAL-HD
Except in remote geographical areas the travel time to a haemodialysis facility should be less than 30 minutes or a haemodialysis facility should be located with 25 miles of the patient's home.
In inner city areas travel times over short distances may exceed 30 minutes at peak traffic flow periods during the day **(good practice).**

Audit measure 1
The distance and travel time between the patient's home and the nearest satellite or main haemodialysis unit.

Rationale
Equity of access to HD is self evident in a patient-centred service. Lack of local HD provision and the inadequacy of patient transport services are the commonest concerns cited by HD patients and Kidney Patient Associations. The acceptance rate for dialysis declines with increasing distance and travel time from the nearest dialysis unit and patients are less likely to be offered dialysis if the travel time from home to the dialysis unit is more than 37 minutes (1,2). The prevalence rate of HD patients remains significantly lower in the areas of Wales with travel times greater than a 30 minute drive to the nearest current dialysis unit (3). To reverse the inverse relationship between acceptance rates for HD and travel time to the nearest HD facility patients should not need to spend more than 30 minutes traveling to and from dialysis unless they live in a remote geographical area. NHS Quality Improvement Scotland has adopted 30 minutes as the maximum routine travel time to and from HD facilities in Scotland except in remote areas (4) but this guideline may be viewed as impractical in some urban areas because of transport delays due to traffic congestion.

Small satellite units should be established also in rural areas or islands to provide more local access to HD and permit travel distances or times that make thrice weekly HD acceptable to patients. Many of the prevalent HD population are elderly, have diabetes and/or overt cardiovascular disease and have suboptimal vascular access in the form of central venous catheters. Some of these patients therefore may not be medically suitable for treatment at a local satellite HD unit and may need to travel further to a main renal unit for dialysis. A comparison of the costs, quality of dialysis, quality of life and frequency of adverse events of HD in satellite and main renal units in England and Wales showed no major differences except the adequacy of HD, as assessed by measurement of the urea reduction ratio, was better in the patients treated in satellite units (5, 6). The provision of dialysis treatment at the 12 renal satellite units in the study potentially saved the HD patients an additional 19 minutes travel time for each dialysis session (5). This study has confirmed that HD in a satellite unit is an effective alternative to treatment in a main renal unit and provides support for a national network of HD facilities with adequate capacity to enable all medically suitable patients to receive chronic HD without having routine travel times in excess of 30 minutes. The location of satellite units should provide maximum geographic access to patients within the local catchment population and a centre

of population based approach has been used in the planning of small satellite HD units in some regions of the UK (7).

Better local access to HD can only be achieved if there are improvements in patient transport as well as the development of an extensive network of HD facilities. The Cross Party Group on Kidney Disease Report, 2004 reinforces this point since it identified that 49% of HD patients in Scotland had travel times in excess of 30 minutes even though only 10% patients lived more than a 30 minute drive from the nearest HD facility (8). The development of patient transport services that avoid the need to collect and drop off other patients at the dialysis centre or at other healthcare facilities would help keep travel times to a minimum.

References

1   Roderick P, Clements S, Stone N et al. What determines geographical variation in rates of acceptance onto renal replacement therapy in England? J Health Service Res Policy 1999; 4:139-146

2   Boyle PJ, Kudlac H, Williams, AJ. Geographical variation in the referral of patients with chronic end-stage renal failure for renal replacement therapy. QJM 1996; 89: 151-157

3   White P, James V, Ansell D et al. Equity of access to dialysis facilities in Wales. QJM 2006; 99:445-452

4   Clinical Standards for Adult Renal Services, NHS Quality Improvement Scotland, March 2003. (www.clinicalstandards.org)

5   Roderick P, Armitage A, Nicholson T et al. A clinical and cost evaluation of haemodialysis in renal satellite units in England and Wales. Am J Kidney Dis 2004; 44: 121-131

6   Roderick P, Nicholson T, Armitage A et al. An evaluation of the costs, effectiveness and quality of renal replacement therapy provision in renal satellite units in England and Wales. Health Technol Assess 2005; 9:1-178

7   MacGregor MS, Campbell J, Bain M et al. Using geographical information systems to plan dialysis facility provision. Nephrol Dial Transplant 2005; 20:1509-1511

8   Cross Party Group on Kidney Disease, April 2004

9   (www. show.scot.nhs.uk/srr/Publications/Cross party report renal disease in Scotland.pdf)

Guideline 1.4 DIAL-HD
Haemodialysis patients who require transport should be collected from home within 30 minutes of the allotted time and be collected to return home within 30 minutes of finishing dialysis (good practice).

Audit measure 2
The waiting time after arrival before starting dialysis and the waiting time for patient transport after the end of haemodialysis

Rationale
Patient travel to and from hospital is the main source of complaint of hospital HD patients (1). Reduction in the waiting times before traveling to or from the HD unit would significantly shorten the "dialysis day" for many patients (1).

Provision of designated parking adjacent to the dialysis area would encourage patients to organize their own transport to and from dialysis and so reduce the need for hospital provision of patient transport. Specialised, fully funded transport for dialysis patients is the gold standard and should be developed to facilitate timely transport by car or ambulance to meet these guidelines. The provision of dedicated or individualized HD patient transport services, which can avoid the need to collect and drop off other patients, and the use of staggered starting times for HD would help to reduce patient waiting times before starting and after completing dialysis. Audit of this patient-centred index of quality of HD provision has been reported in the Scottish HD population by Quality Improvement Scotland (QIS) (2).

References
1   Clinical Standards for Adult Renal Services, NHS Quality Improvement Scotland, March 2003. (www.clinicalstandards.org)
2   Report of NHS Quality Improvement Scotland (www.nhshealthquality.org)

Guideline 1.5 DIAL-HD
All patients who may be suitable for home dialysis should receive full information and education about home haemodialysis.
Home haemodialysis training is not available in all renal units and some patients may need to travel to a sub-regional or regional centre to pursue their choice to train for home haemodialysis **(good practice).**

Audit measure 3
The proportion of dialysis patients in the main renal unit and its satellite units who are on home haemodialysis

Rationale
HD may be performed in a variety of settings, including hospital-based units, free-standing units, and in the home. Patient survival and quality of life adjusted for co-morbid risk factors has been reported to be higher on home than hospital HD (1, 2). Home HD is more cost-effective than hospital HD if patients remain on dialysis for more than 14 months to offset training and setup costs (3). The choice between home and hospital HD for patients assessed as able to perform dialysis at home should be determined mainly by patient preference rather than economic grounds. Nevertheless the number of patients on home HD in the UK has continued to decline. Not all UK units provide home HD and, based on a review of the clinical-effectiveness and cost-effectiveness of home, satellite and hospital HD, the National Institute of Clinical Excellence (NICE) has recommended that the option to train to perform home HD should be available to all patients (4,5). NICE recommended that more than 10% of dialysis patients should be treated by home HD and, whilst this recommendation is achieved in Australasia (6), very few centres in the UK have more than 5% of dialysis patients on home HD (7). Higher prevalence rates of home HD may be achieved by having a designated home HD training centre serving several renal units within a region akin to current service provision for renal transplantation.

References

1   Woods JD, Stannard D, Blagg CR et al. Comparison of mortality with home haemodialysis and centre haemodialysis: A national study. Kidney Int 1996; 49: 1464- 1470

2   Saner E, Nitsch D, Descourdes C et al. Outcome of home haemodialysis patients: A case-control study. Nephrol Dial Transplant 2005, 20: 604- 610

3   Mackenzie P, Mactier RA. Home haemodialysis in the 1990's.

4   Nephrol Dial Transplant 1998; 13: 1944-1948

5   Mowatt G, Vale L, Perez J et al. Systematic review of the effectiveness and cost-effectiveness and economic evaluation of home versus hospital or satellite haemodialysis for people with end-stage renal failure. Health Technol Assess 2003; 7: 1-174

6   National Institute of Clinical Excellence.

7   Full guidance on home compared with hospital haemodialysis for patients with end-stage renal failure October 2002. (www.nice.org.uk)

8   MacGregor MS, Agar JW, Blagg CR. Home haemodialysis - international trends and variation. Nephrol Dial Transplant 2006; 21: 1934-45

9   The Renal Association UK Renal Registry, The Seventh Annual Report, December 2004. (www.renalreg.com Renal Association Standards & Audit Subcommittee)

Guideline 1.6 DIAL-HD

Haemodialysis capacity in satellite and main renal units within a geographical area should increase in step with predicted need. To allow for patient choice regarding out of hours haemodialysis schedules, provision of holiday haemodialysis and expansion in patient numbers calculation of the required number of haemodialysis stations should be based on using each station for 2 patients per day three times per week.

The national average number of hospital haemodialysis patients per million catchment population reported for the previous year by the UK Renal Registry should be regarded as the minimum capacity for haemodialysis in each geographically based renal service. Alternatively up-to-date regional data may be used. For example the national average provision for 312 hospital haemodialysis patients (78 stations) per million catchment population in Scotland at the end of 2005 may be regarded as a minimum haemodialysis capacity in all regions in 2006. The level of hospital haemodialysis provision will need to be higher in areas with a high ethnic and/or elderly population and increase nationwide over the next 10 years **(good practice).**

Audit measure 4

 The number of haemodialysis patients and number of haemodialysis stations in the main renal unit and its satellite units expressed per million catchment population.

Rationale

HD treatment has evolved rapidly since its introduction and HD is the main mode of dialysis in most developed countries. HD was the established mode of dialysis

at 90 days in 67.5% of the UK patient cohort in 2003 compared with 59% in 1998 (1). About 40% of patients starting renal replacement therapy (RRT) are referred as late uraemic emergencies with no time for the planning of, or counseling on, the options for dialysis, and such patients are more likely to remain on HD (2,3). HD is also 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. Many patients are maintained by HD after failure of renal transplants or because they have had to abandon PD. After the first 3 years of dialysis 3% of the 1998-2000 cohort of HD patients in the UK had converted to peritoneal dialysis, mostly within the first year, whereas almost 11% of the PD patients had switched to HD each year (1).

The provision of HD capacity within the UK has tended to lag behind patient demand and this has restricted both patient choice and access to hospital HD (4). UK Registry data from the end of 2004 showed that there were 261 patients per million population on hospital or satellite HD (5). 40.9% of the estimated 638 prevalent end-stage renal failure patients per million population were receiving hospital HD and only 1.2% were on home HD at the end of 2004 (5). Scottish Renal Registry data from the end of 2004 showed that 76% of dialysis patients were receiving hospital HD, 299 patients per million were receiving hospital HD and 725 prevalent patients per million were on chronic RRT (6). At the end of 2005 the Scottish Renal Registry data showed that 77% of dialysis patients were receiving hospital HD, 312 patients per million were receiving hospital HD and 758 prevalent patients per million were on chronic RRT (7). Hospital HD provision in Scotland increased by an average of 18 patients per million population each year between 2000 and 2005. Regional variation in the level of provision of HD within the UK continues and this needs to be addressed to permit equity of access to HD throughout the country (8).

Additional capacity is needed to allow for patient choice of HD schedule, holiday HD and anticipated expansion in patient numbers. For these reasons the calculated number of dialysis stations that are required in each geographical area should be based on using each machine only for two patients per day three days per week. The degree of flexibility in HD capacity and scheduling then depends on the proportion of HD patients who are on a third shift each day. The national average number of hospital HD patients per million catchment population reported for the previous year by the UK Renal Registry may be regarded as the minimum capacity for HD in each geographically based renal service. This approach should drive the provision of HD upwards in the areas with below average HD capacity. For example the provision for an average of 312 hospital HD patients (or 78 stations) per million catchment population in Scotland at the end of 2005 could be regarded as a minimum HD capacity in all regions in 2006. The required capacity for HD will be greater in areas with a high ethnic or elderly population due to their higher prevalence of ESRD and these areas will need proportionately greater HD capacity than the national average. HD capacity will need to expand greatly over the next 10 years as the number of prevalent ESRD patients rises progressively and the proportion of the patients who are elderly and/or have co-morbidity also increases (9). Regional and national audit of HD capacity will highlight if there is inequity of access to HD and provide support for the development of HD facilities in such geographical areas. Meeting the need for HD will be a major challenge

and regular audit should be used to raise HD capacity across the UK in step with the projected increase in demand over the next decade.

References

1   The Renal Association UK Renal Registry, The Seventh Annual Report, December 2004. (www.renalreg.com Renal Association Standards & Audit Subcommittee)

2   Metcalfe W, Khan IH, Prescott GJ et al. Can we improve early mortality in patients receiving renal replacement therapy? Kidney Int 2000; 57: 2539–45

3   Little J, Irwin A, Marshall T et al. Predicting a patient's choice of dialysis modality: experience in a United Kingdom renal department. Am J Kidney Dis 2001; 37: 981–6

4   Treatment of adults & children with renal failure - Standards and audit measures. 3rd Edition, London: Royal College of Physicians 2002. (www.renal.org/Standards/standards.html)

5   The Renal Association UK Renal Registry, The Eighth Annual Report, December 2005. (www.renalreg.com Renal Association Standards & Audit Subcommittee)

6   Report of the Scottish Renal Registry 2004 (www.show.scot.nhs.uk/srr)

7   Report of the Scottish Renal Registry 2005 (www.show.scot.nhs.uk/srr)

8   Blank L, Peters J, Lumsdon A et al. Regional differences in the provision of adult renal dialysis services in the UK. QJM 2005; 98:183-190

9   Feest TG, Rajamahesh J, Byrne C et al. Trends in adult renal replacement therapy in the UK: 1982-2002. QJM 2005: 98: 21-28

2 Haemodialysis equipment and disposables (Guidelines DIAL-HD 2.1 – 2.3)

Guideline 2.1 DIAL-HD

All equipment used in the delivery and monitoring of therapy should comply with the relevant standards for medical electrical equipment. General safety standards are covered by BS EN 60601-1: 2006 and specific dialysis machine requirements are covered by BS-EN 60601-2-16: 1998 (Medical electrical equipment: Particular requirements for the safety of haemodialysis (HD), haemodiafiltration and haemofiltration equipment (good practice).

The equipment used in renal units represents a substantial asset that must be carefully maintained. The selection of equipment should be in accordance with a policy that conforms to the recommendations of the MHRA (MHRA DB2006 (05): - Managing Medical Devices – Guidance for Healthcare & Social Services Organisations – Nov. 2006 (personal communication, Ged Dean, Nottingham University Hospitals Trust) and National Audit Office (The management of medical equipment in NHS acute trusts in England, National Audit Office, 1999). The above BS-EN 60601-2-16 standard for electrical equipment for renal replacement therapy was defined in 1998, superceded BS5724-2-16:1998 and IEC 60601-2-16:1998 and remains applicable in 2006 (personal communication, Andy Mosson, Association of Renal Technologists).

Guideline 2.2 DIAL-HD

Disposables such as dialysers and associated devices are classified as medical devices and should display the CE mark (good practice).

All disposable equipment such as haemodialysers, blood tubing sets and related devices should display the CE mark. The presence of such a mark signifies compliance with the requirements of the statutory Medical Device Directive and also national and international standards where they exist for new products: BS-EN 1283: 1996 (haemodialysers, haemodiafilters, haemofilters, haemoconcentrators and their extra corporeal circuits), ISO 8638:2004 (Extracorporeal blood circuit for haemodialysers, haemodiafilters and haemofilters) or ISO 13960: 2003 (Plasma filters).

Guideline 2.3 DIAL-HD

Machines should be replaced after between seven and ten years' service or after completing between 25,000 and 40,000 hours of use for haemodialysis, depending upon an assessment of machine condition (Good practice).

The routine maintenance of the equipment used for renal replacement therapy is essential and the service history of each machine should be documented fully throughout its use-life by the renal unit technicians. 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. Intensive use of HD machines for three 4 hour shifts per day, 6 days per week would complete 26208 hours of use after 7 years. We accept that there is no firm evidence that replacement, as suggested above, is the most cost-effective strategy.

3 Concentrates and water for haemodialysis (Guidelines DIAL-HD 3.1 – 3.4)

Guideline 3.1 DIAL-HD

Ready made concentrates are classified as medical devices and should display the CE mark. Concentrates that are manufactured 'in house' should meet the requirements of BS EN 13867: 2002 (Concentrates for haemodialysis and related therapies) (good practice).

Rationale

The presence of the CE mark signifies compliance with the requirements of the statutory Medical Device Directive and also national and international standards where they exist. Dialysis units that manufacture concentrates in-house should ensure that the fluid fulfils the requirements stated in BS EN 13867: 2002 (1).

References

1   BS EN 13867: 2002 Concentrates for haemodialysis and related therapies.
(http://www.bsonline.bsi-global.com)
Note: A revision of this standard is currently at the Committee Draft stage and should be available by 2008.

Guideline 3.2 DIAL-HD

Water used in preparation of dialysis fluid should, as a minimum, meet the requirements stated in Table 1 for chemical and microbiological contaminants.

Rationale

The limits for chemical contaminants are derived from AAMI RD-52 2004 (1), ISO 13959:2002 (2) and the European Pharmacopoeia (3) after consultation within the UK, whilst the limits for bacterial counts (100 cfu/ml) and endotoxin (0.25 IU/ml) are based on the European Pharmacopoeia (3) and the European Renal Association Best Practice Guidelines (4). New equipment should be capable of producing 'ultrapure' dialysis fluid (bacterial counts <0.1 cfu/ml and endotoxin <0.03 IU/ml) in order to meet the best practice guidelines. Ideally this should be achieved using ultrapure water, however water that meets the minimum standard in Table 1 can be used together with point of use filtration of the dialysis fluid. If routine monitoring demonstrates continuous contamination in excess of the desired levels, a programme to improve this should start immediately (good practice).

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. It is essential for the water used to produce dialysis fluid to have appropriate chemical and microbiological purity. Achieving this standard of purity usually requires softening, carbon filtration, reverse osmosis and an effective disinfection

programme for the pipework between the treatment plant and the dialysis machines.

The dialysis membrane was 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 (5-7). 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 bacterial endotoxin.

In patients treated with high flux membranes, a risk of pyrogen transfer due to backfiltration (a movement of dialysis fluid into the blood pathway of the device due to an inverted pressure gradient rather than the diffusion gradient discussed above) may exist. Lonneman et al, however, concluded that diffusion rather than convection is the predominant mechanism of transmembrane transport of pyrogens, and backfiltration across pyrogen adsorbing membranes does not necessarily increase their passage (5). 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.

A raised C-reactive protein (a sensitive marker of activation of the acute phase response) is associated with a significantly increased risk of death (8, 9), which has led to speculation that impure dialysis fluid may contribute to an increased risk of death in dialysis patients. The use of ultrapure water in a randomized study of 30 incident HD patients was associated with a reduction in CRP levels and a decrease in the rate of loss of residual renal function (10). Impure dialysis fluid has also been implicated in the pathogenesis of dialysis-related amyloidosis (11-13). While this suggestion has not been tested in clinical practice, it would seem prudent to ensure that water is as pure as reasonably possible.

Ultrapure water (< 0.1 cfu/ml and bacterial endotoxins < 0.03 IU/ml) is readily achievable using modern water treatment techniques and should be regarded as the standard for all newly installed water treatment plants (14). The European Best Practice Guidelines recommend the use of ultrapure water for conventional as well as high flux HD (4).

Reinfusion fluid, used in haemofiltration and haemodiafiltration, must be sterile (<1 cfu/1000 litres) and, particularly where large exchange volumes are required, have an endotoxin level of <0.03 IU/ml (15). Even with ultrapure water, this standard of purity can only be achieved with 'on-line' 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 1.

Knowledge of the potentially harmful effects of bacterial products, trace elements and chemicals is still growing, and techniques of water treatment are continuously being developed. The maximum acceptable levels of chemical contaminants in water for dialysis have been established by AAMI (1), ISO 13959 (2) and the European Pharmacopoeia (3). These standards differ in the number and limits of the contaminants specified. Table 1 lists all the contaminants for which a limit is defined for water for dialysis in one or more of the standards. With the exception of nitrate, where the standards differ in their recommendations, the most stringent limit has been adopted. These limits should not be difficult to meet with a correctly specified and maintained water plant. For nitrate, the European Pharmacopoeia specifies a maximum of 2 mg/l nitrate (NO3) compared to the AAMI standard and ISO 13959 which recommend a limit of 2 mg/l of nitrate as nitrogen (N) which equates to approximately 9 mg/l of NO3. The more stringent EP limit is often difficult to meet in home HD installations and since the development of the AAMI standard, no new evidence for a lower limit for nitrate has emerged. As the benefits of home HD are well established, the less stringent recommendation has been adopted for nitrate.

Table 1 defines a subset of contaminants that should always be included in routine testing because they occur in relatively high levels and are not restricted in drinking water (chlorine, calcium, magnesium and potassium), or where the drinking water limit (16) is more than five times the recommended limit for water for dialysis. Sodium is included in the 'mandatory' group because, although the drinking water limit is 200 mg/l, additional sodium is introduced by softening. Table 1 also defines a group of contaminants for which the drinking water limit is 2 to 5 times the recommended limit for dialysis. In water treated by reverse osmosis, these contaminants will only exceed the limits in table 1 if they occur at relatively high levels in the water supplied to the unit. These contaminants can be omitted from routine tests if data is available to show that the levels in the water supplied to the unit rarely exceed the limit in the table. These data should be obtained from the municipal water supplier, or from tests on the raw water if it is obtained from a private source.

Table 1: Maximum recommended concentrations for chemical and microbial contaminants in water for dialysis

Contaminant	Criteria for inclusion in routine tests	Maximum recommended concentration (mg/l = ppm)	Standards on which limit is based	Initial Test Frequency (if not omitted)
Aluminium	Mandatory	0.01	EP, AAMI, ISO	3 monthly
Calcium	Mandatory	2 (0.05 mmol/l)	EP, AAMI, ISO	3 monthly
Total chlorine	Mandatory	0.1	EP	Not less than weekly
Copper	Mandatory	0.1	AAMI, ISO	3 monthly

Fluoride	Mandatory	0.2	EP, AAMI, ISO	3 monthly
Magnesium	Mandatory	2 (0.08 mmol/l)	EP	3 monthly
Nitrate (as N)	Mandatory	2 (equates to 9 mg/l NO3)	AAMI, ISO	3 monthly
Potassium	Mandatory	2 (0.05 mmol/l)	EP	3 monthly
Sodium	Mandatory	50 (2.2 mmol/l)	EP	3 monthly
Bacteria (TVC)	Mandatory	100 cfu/ml	EP, ISO	Not less than monthly
Endotoxin	Mandatory	0.25 IU/ml	EP	Not less than monthly
Ammonium	Omit if evidence permits	0.2	EP	3 monthly
Arsenic	Omit if evidence permits	0.005	AAMI, ISO	3 monthly
Cadmium	Omit if evidence permits	0.001	AAMI, ISO	3 monthly
Chloride	Omit if evidence permits	50	EP	3 monthly
Chromium	Omit if evidence permits	0.014	AAMI, ISO	3 monthly
Lead	Omit if evidence permits	0.005	AAMI, ISO	3 monthly
Mercury	Omit if evidence permits	0.0002	AAMI, ISO	3 monthly
Sulphate	Omit if evidence permits	50	EP	3 monthly
Barium	Include on indication only	0.1	AAMI, ISO	As indicated
Beryllium	Include on indication only	0.0004	AAMI	As indicated
Silver	Include on indication only	0.005	AAMI, ISO	As indicated
Thallium	Include on indication only	0.002	AAMI	As indicated
Tin	Include on indication only	0.1	ISO	As indicated
Zinc	Include on indication only	0.1	EP, AAMI, ISO	As indicated

Notes: Antimony (AAMI limit 0.006 mg/l) and selenium (AAMI and ISO limit 0.09 mg/l) have been excluded from this table as the limit for drinking water in the UK is lower than the limit for water for dialysis. The limit for tin may be omitted from the next revision of ISO 13959.

The final group of contaminants (barium, beryllium, silver, thallium, tin and zinc) are those for which a limit has been defined for water for dialysis and there is no

limit specified for drinking water in the UK. These trace elements are not considered to occur in levels that give cause for concern and, if low levels are present, they are removed effectively by reverse osmosis. Testing is only required if there is evidence of high levels in the local water supply (zinc, for example, can be introduced in the pipework).

Although the standards specify laboratory test methods to be used for chemical contaminant, any test method validated by the United Kingdom Accreditation Service is acceptable provided the detection limit is not less than 50% of the limit given in Table 1.

The tests used for monitoring microbial contamination of water for dialysis should be appropriate to the type of organisms found in water. A low nutrient agar, such as Tryptone Glucose Extract Agar or Reasoner's 2A, should be used [17-19] and samples should be incubated for at least 7 days at 20-22ºC [20]. These conditions have been shown to give good recovery for most environmental bacteria found in purified water. Some species are better adapted for growth at a higher temperature and/or on richer media, but the long incubation time will allow most of these to grow. Details of methods for sampling and culturing of water for dialysis are available in the Appendix of European Best Practice Guidelines for Haemodialysis Part 1 (3) and in the EDTNA/ERCA Guidelines on Control and Monitoring of Microbiological Contamination in Water for Dialysis (21), which also gives specific test conditions for fungi.

Procedures for providing quality assurance of the reinfusion fluid produced 'on-line' for haemofiltration or haemodiafiltration will be reviewed before the next edition of these guidelines as dialysis units gain experience managing this technology.

References

2   Association for the Advancement of Medical Instrumentation. Standard RD52:2004 -- Dialysate for haemodialysis. AAMI, Arlington, VA.

3   International standard reference number ISO 13959: 2002 (E). Water for haemodialysis and related therapies. (www.iso.org).
Note: A revision of this standard is currently at the Committee Draft stage and should be available by 2008.

4   Monograph 1167:1997 (corrected 2000, republished 2001) Haemodialysis solutions, concentrated, water for diluting. European Pharmacopoeia Supplement 2001.

5   European Best Practice Guidelines for haemodialysis Part 1. Section IV. Dialysis fluid purity. Nephrol Dial Transplant 2002; 17: Supplement 7 S45-S62 (http://ndt.oupjournals.org/content/vol17/suppl_7/index.shtml)

6   Lonnemann G, Behme TC, Lenzner B et al. Permeability of dialyzer membranes to TNF alpha-inducing substances derived from water bacteria. Kidney Int 1992; 42:61–68

7   Evans RC, Holmes CJ. In vitro study of the transfer of cytokine inducing substances across selected high flux hemodialysis membranes. Blood Purif 1991; 9: 92–101

8   Laude-Sharp M, Caroff M, Simard L et al. Induction of IL-1 during hemodialysis: transmembrane passage of intact endotoxins (LPS). Kidney Int 1990; 38: 1089–94

9   Owen WF, Lowrie EG. C-reactive protein as an outcome predictor for maintenance hemodialysis patients. Kidney Int 1998; 54:627–36

10   Zimmermann J, Herrlinger S, Pruy A et al. Inflammation enhances cardiovascular risk and mortality in hemodialysis patients. Kidney Int 1999; 55:648–58

11   Schiffl H, Lang SM, Fischer R. Ultrapure dialysis fluid slows loss of residual renal function in new dialysis patients. Nephrol Dial Transplant 2002; 17: 814-1818

12   Lonnemann G. The quality of dialysate: an integrated approach. Kidney Int Suppl 2000; 58(Suppl 76):S112–19

13   Lonnemann G. Chronic inflammation in haemodialysis: the role of contaminated dialysate. Blood Purif 2000; 18: 214–23

14   Lonnemann G. Should ultra-pure dialysate be mandatory? Nephrol Dial Transplant 2000; 15(Suppl 1): 55–9

15   Ward RA. Ultrapure dialysate: a desirable and achievable goal for routine haemodialysis. Semin Dial 2000; 13: 378–80

16   Nystrand R. Endotoxin and 'on line' production of substitution fluid in haemodiafiltration and haemofiltration. EDTNA-ERCA J 2002; 28: 127-9

17   The Water Supply (Water Quality) (England and Wales) Regulations 2000. Statutory Instrument No. 3184. Prescribed concentrations and values. http://www.dwi.gov.uk/regs/si3184/3184.htm#sch1

18   Van der Linde K, Lim BT, Rondeel JM, Antonissen LP, de Jong GM. Improved bacteriological surveillance of haemodialysis fluids: a comparison between Tryptic soy agar and Reasoner's 2A media. Nephrol Dial Transplant 1999;14: 2433-7

19   Ledebo I, Nystrand R. Defining the microbiological quality of dialysis fluid. Artif Organs 1999;23: 37-43

20   Harding GB, Pass T, Million C, Wright R, DeJarnette J, Klein E. Bacterial contamination of haemodialysis center water and dialysate: are current assays adequate? Artif Organs 1989;13:155-9

21   Pass T, Wright R, Sharp B, Harding GB. Culture of dialysis fluids on nutrient-rich media for short periods at elevated temperatures underestimate microbial contamination. Blood Purif 1996; 14:136-45

22   Guidelines for the control and monitoring of microbiological contamination in water for dialysis. EDTNA-ERCA J 2002; 28: 107-115 http://www.associationhq.com/edtna/pdf/WTguidelinesmicrob.pdf

Guideline 3.3 DIAL-HD
A routine testing procedure for water for dialysis should form part of the renal unit policy (good practice).

Rationale
The manufacturer of the water treatment plant and distribution system should demonstrate that the requirements for microbial contamination are met throughout the complete system at the time of installation.

The frequency for testing of water for dialysis for microbial contamination should not fall below monthly in main units and should be sufficiently frequent to detect trends. This is particularly important after installation and when alterations to the system are carried out. For home installations, it is usually impractical to maintain a monthly testing programme. In this situation, the dialysis machine should be fitted with point of use filtration.

The absence of any type of bacteriostat in the water following treatment makes it susceptible to bacterial contamination down stream of the water treatment plant.

Such contamination may be further enhanced by stagnant areas within the distribution network as well as irregular cleaning all of which contribute to the development of a biofilm which may also be present in the dialysate pathway of the proportionating system, particularly when non sterile liquid bicarbonate concentrate is used. Such biofilm is difficult to remove and results in the release of bacteria, bacterial fragments (endotoxins, muramylpeptides, and polysaccharides). The dialysis membrane prevents intact bacteria from crossing, however fragments have molecular weights that allow them to pass across the membrane into the bloodstream. Considerable differences exist in the adsorption capacity of such membranes, which may permit the passage of short bacterial DNA fragments (1,2). Current proportionating systems incorporate filters for the removal of such fragments on the basis of size exclusion and hydrophobic interaction. Monitoring as well as disinfection should be scheduled to prevent formation rather than to eliminate biofilm that may be present and a routine testing procedure for dialysate and feed water should form part of the renal unit policy.

Testing for chemical contaminants will normally include continuous conductivity monitoring of the water leaving the reverse osmosis system, and regular in-house checks of hardness and total chlorine (3). There is increasing use of chlorine dioxide to prevent growth of Legionella bacteria in hospital water systems. There is currently no guidance on the control and monitoring of chlorine dioxide in water for dialysis. Confirmation that the standard DPD test used to monitor chlorine and chloramines gives an accurate measure of the levels of chlorine dioxide and its breakdown products (chlorite and chlorates) is needed as is data on the carbon filter empty bed contact time required for effective removal. New data will be reviewed before the next edition of these guidelines.

The laboratory tests required to demonstrate compliance with the recommendations in Table 1 should be carried out during commissioning and within 3 months of setting up a new water system or making alterations to the water treatment plant. The frequency of laboratory tests may be modified once local trends have been established, but should not fall below annually. An initial full test on the supply water may be advisable and regular monitoring of water quality data from the supplier is essential when tests are omitted based on low levels of contamination in the water supply.

Records should be kept of all chemical and microbiological test results and remedial actions.

References
1   Differences in the permeability of high-flux dialyzer membranes for bacterial pyrogens. Schindler R, Christ-Kohlrausch F, Frei U, Shaldon S. Clin Nephrol 2003; 59:447-54

2   Short bacterial DNA fragments: detection in dialysate and induction of cytokines. Schindler R, Beck W, Deppisch R, Aussieker M, Wilde A, Gohl H, Frei U. J Am Soc Nephrol. 2004; 15:3207-14

3   Guidelines for the control of chlorine and chloramine in water for haemodialysis using activated carbon filtration. Morgan I. EDTNA ERCA J. 2004; 30:106-12

Guideline 3.4 DIAL-HD
The dialysate should contain bicarbonate as the buffer. (Evidence)

Rationale
One of the critical functions of dialysis is the correction of the metabolic acidosis caused by the failure of the diseased kidneys 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 buffer (1) 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 (2,3). 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 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 (4). 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 (5)

It is not possible to set evidence-based standards for other components of the dialysate. However there is recent evidence that non-diabetic HD patients using glucose-free dialysate have a surprisingly high rate of asymptomatic hypoglycaemia without an associated counter-regulatory response (6,7) The long-term effects of repeated dialysis-induced hypoglycaemia are uncertain. Hypoglycaemia is not observed if the dialysate contains glucose, but glucose-containing dialysate is slightly more expensive. Individualisation of dialysate potassium may be required in patients with hypokalaemia and adjustment of dialysate sodium concentrations during HD (sodium profiling) may be beneficial in some patients with haemodynamic instability.

References
1   Mion CM, Hegstrom RM, Boen ST et al. Substitution of sodium acetate for sodium bicarbonate in the bath fluid for hemodialysis. Trans Am Soc Artif Intern Organs 1964; 10:110–15

2   Novello A, Kelsch RC, Easterling RE. Acetate intolerance during haemodialysis. Clin Nephrol 1976; 5:29–32

3   Aizawa Y, Ohmori T, Imai K et al. Depressant action of acetate upon the human cardiovascular system. Clin Nephrol 1977; 8:477–80

4   MacLeod A, Grant A, Donaldson C et al. Effectiveness and efficiency of methods of dialysis therapy for end-stage renal disease: systematic reviews. Health Technol Assess 1998; 2:1–166

5   Veech RL. The untoward effects of the anions of dialysis fluids. Kidney Int 1988; 34:587–97

6   Jackson MA, Holland MR, Nicholas J et al. Occult hypoglycemia caused by hemodialysis. Clin Nephrol 1999; 51:242–7

7   Catalano C, Bordin V, Fabbian F et al. Glucose-free standard haemodialysis and occult hypoglycemia. Clin Nephrol 2000; 53:235–6

4 Haemodialysis membranes (Guidelines DIAL-HD 4.1 - 4.6)

Guideline 4.1 DIAL-HD

The balance of evidence supports the use of low flux synthetic and modified cellulose membranes instead of unmodified cellulose membranes (good practice).

The benefits of low flux synthetic and modified cellulose membranes over unmodified cellulose membranes are limited to advantages arising from different aspects of improved biocompatibility rather than better patient outcomes.

Rationale

Synthetic membranes, which can have more porous characteristics (high flux) than standard cellulose membranes, started to be used 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, leucocytes and other cellular elements than standard cellulose and hence decrease the inflammatory response, i.e. they were more biocompatible. Cellulose membranes have been modified to make them both more biocompatible and of slightly higher flux (semi-synthetic membranes e.g. haemophan or cellulose triacetate), and synthetic membranes with lower flux properties have also been produced (e.g. low-flux polysulphone). The more biocompatible membranes may have other advantages as a result of reduced activation of the systemic inflammatory response during dialysis but this is less certain (1).

A systematic Cochrane 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 (2). Comparison of unmodified cellulose and modified cellulose membranes was not undertaken. Despite the relatively large number of randomised controlled trials 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 lower with synthetic membranes in the single study that measured this outcome in this systematic review but a recent randomized study has shown no difference in serum lipid levels in the patient group treated with high-flux biocompatible membranes (3). Serum albumin was slightly higher at certain time points in some studies when synthetic membranes of both high and low flux were used and this may be an important finding given the adverse prognostic impact of hypoalbuminaemia in dialysis patients (4,5). The lower complement and leucocyte activation and greater adsorptive capacity for cytokines and beta-2-microglobulin of the more biocompatible dialysis membranes have potentially beneficial biological effects but have not been shown so far to provide better patient survival rates than unmodified cellulose membranes (2,6). Low-flux synthetic and modified cellulose dialysers are now no more expensive than unmodified cellulose dialysers and the use of these more biocompatible dialysers

instead of unmodified cellulose therefore seems justifiable on the basis of evidence of biological benefits and equivalent costs.

References

1   Ikizler TA, Wingard RL, Harvell J et al. Association of morbidity with markers of nutrition and inflammation in chronic haemodialysis patients: A prospective study. Kidney Int 1999; 55: 1945–51

2   Macleod AM, Campbell M, Cody JD et al. Cellulose, modified cellulose and synthetic membranes in the haemodialysis of patients with end-stage renal disease. The Cochrane Database of Systematic Reviews 2005 Issue 3. Art No: CD003234.DOI: 10.1002/14651858.CD003234.pub2

3   House AA, Wells GA, Donnelly JG et al. Randomised trial of high-flux versus low-flux haemodialysis: effects on homocysteine and lipids. Nephrol Dial Transplant 2000; 15:1029-1034

4   Foley RN, Parfrey PS, Harnett JD et al. Hypoalbuminemia, cardiac morbidity, and mortality in end-stage renal disease. J Am Soc Nephrol 1996; 7:728–36

5   Goldwasser P, Mittman N, Antignani A et al. Predictors of mortality in hemodialysis patients. J Am Soc Nephrol 1993; 3:1613–22

6   Grooteman MPC, Nube MJ. Impact of the type of dialyser on clinical outcome in chronic haemodialysis patients: does it really matter? Nephrol Dial Transplant 2004; 19:2965-2970

Guideline 4.2 DIAL-HD

The balance of evidence supports the use of a dialysis regimen with enhanced removal of middle molecules in incident patients who are predicted to remain on haemodialysis for several years and prevalent patients who have been on haemodialysis for more than 3.7 years. Such patients are at risk of developing symptoms of dialysis-related amyloidosis (good practice).

Treatments with better clearance of middle molecules include haemodialysis with high flux synthetic membranes and haemodiafiltration. The proven benefits of high flux synthetic membranes in randomized trials are limited to advantages arising from improved biocompatibility and enhanced removal of middle molecules, such as beta-2-microglobulin, rather than better patient survival rates. Chronic high flux dialysis in the HEMO study did not affect the primary outcome of all cause mortality or any of the secondary composite outcome measures including the rates of first cardiac hospitalization or all cause mortality, first infectious hospitalization or all cause mortality, first 15% decrease in serum albumin or all cause mortality, or all non-vascular access-related hospitalizations.

Rationale

Dialysis-related amyloidosis is a disabling, progressive condition caused by the polymerisation within tendons, synovium, and other tissues of beta-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 cellulose membranes. Exposure to bio-incompatible membranes may increase beta-2-microglobulin generation. Symptoms are typically first reported 7–10 years after commencing HD although tissue accumulation of dialysis-related amyloid can be demonstrated much earlier. A systematic review of 27 randomised trials comparing cellulose, modified cellulose and synthetic membranes, showed a significant reduction in end of study

beta-2-microglobulin values when high flux synthetic membranes were used and one small study showed amyloid occurred less frequently with this treatment (1). High flux HD membranes remove beta-2-microglobulin by a combination of diffusive clearance and adsorption and haemodiafiltration removes substantially more as a result of convective clearance. Both treatments are thought to reduce the risk of developing dialysis-related amyloid.

The effect of dialyser membrane flux was examined in the HEMO study, which was a prospective randomized trial of prevalent HD patients who had been on dialysis for a median of 3.7 years at the time of recruitment to the study (2,3). After a mean follow-up period of 2.8 years, during which 871 of the 1846 randomised patients died, no significant difference was observed in all cause mortality or secondary endpoints between the high and low flux treatment groups in spite of a ten fold increase in beta-2-microglobulin clearances in the high flux group (beta-2-microglobulin clearances of at least 20ml/min). Secondary analyses of the patients who had been on HD for greater than the median of 3.7 years before enrolment showed that the patients on high flux dialysis membranes had a 32% reduction in all cause mortality (CI 14-47% ; p = 0.001) and 37% reduction in cardiac death (CI 37-57% ; p = 0.016) compared with the low flux patients (4). However, when the number of prevalent years on HD was analysed as a continuous variable, the interaction of flux and years of dialysis on patient survival was not significant. The HEMO study was designed to have adequate power to detect a 25% reduction in the predicted baseline all cause mortality rate of the interventions (5). However the limited benefit observed with high flux membranes has been attributed to several factors in the design of the HEMO study such as the inclusion of prevalent rather than incident patients, the exclusion of patients with major co-morbidity, the failure to utilize ultra-pure water whilst using dialyser reuse and the high and low flux groups may have been separated inadequately since pre-dialysis beta-2-microglobulin levels were only 19% lower in the high flux group. Most of these confounding factors have been addressed in the Membrane Permeability Outcome (MPO) study which is a randomized, multicentre European study of high flux membranes in incident HD patients who have few exclusion criteria and do not reuse dialysers (6). In addition a multicentre, randomized controlled trial has failed to show a beneficial effect on anaemia in stable HD patients using a high flux biocompatible membrane compared with conventional cellulose membranes over a 12 week study period (7). A multivariate Cox proportional hazards analysis of a prospective non-randomised study of 1610 prevalent HD patients from 20 centres in France showed that age, diabetes, lower serum albumin and the use of low-flux dialyser membranes were associated with poorer survival (8). The patients on high-flux dialysers had a 38% lower risk of death (p=0.01) than patients on low-flux membranes. This non-randomised study (8) and post hoc analysis of the HEMO study (4) provide some evidence that long-term HD patients may have better survival from the use of high flux dialysers but this observation needs to be confirmed in a large prospective randomized study, such as the MPO study which has completed recruitment (6). One small prospective study has shown better preservation of residual renal function when using high flux membranes combined with ultrapure water (9). Preservation of residual renal function is desirable as residual renal function is a predictor of survival in HD patients (10), decreases beta-2-microglobulin levels and lessens the need for ultrafiltration.

As long as the cost of high flux membranes is significantly higher than low flux synthetic and modified cellulose membranes and the single use of dialysers remains routine practice the use high flux membranes should be a higher priority in patients who are likely to remain on or have been on HD for at least 3.7 years as this group of patients is at the greatest risk of developing dialysis-related amyloidosis. Appropriate incident patients include patients who are unlikely to receive a transplant either 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 and age) and prevalent patients with high risk of dialysis-related amyloidosis because of long-term dialysis or absence of residual renal function at the start of dialysis.

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 and this 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 haemodiafiltration. 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 before (pre-dilutional) or after (post-dilutional) the dialyser. However a recent systematic review of the existing 18, albeit mainly small, randomized trials showed no difference in patient outcomes between HD, haemodiafiltration and haemofiltration (11). The authors have acknowledged that there was a small arithmetic error in this systematic review although this did not alter its main conclusion (12). Haemodynamic variables were found to be similar in a further recent study comparing haemodiafiltration and low-flux HD under conditions of equivalent dialysis dose, ultrafiltration volume and core temperature (13). In a retrospective observational study of 2165 patients from 1998-2001 in five European countries, stratified into 4 groups (low-flux HD, high-flux HD, low-efficiency haemodiafiltration and high-efficiency haemodiafiltration), the subgroup on high-efficiency haemodiafiltration had a 35% lower mortality risk compared with patients on low-flux HD after adjusting for the dialysis dose and co-morbidity (p = 0.01) (14). In view of the potential influence of selection bias and other confounding factors the authors of this study stated that a controlled clinical trial was required to document the benefits of haemodiafiltration before it can be recommended in clinical practice guidelines (13). The Dutch CONvective TRAnsport STudy (CONTRAST) is a 3 year randomized study that addresses if all cause mortality and/or fatal and non-fatal cardiovascular events differ between haemodiafiltration and low flux HD in almost 800 HD patients (15). At present there is no objective evidence to support the routine use of haemofiltration or haemodiafiltration instead of HD in the management of end-stage chronic renal failure.

References

1 Macleod AM, Campbell M, Cody JD et al. Cellulose, modified cellulose and synthetic membranes in the haemodialysis of patients with end-stage renal disease. The Cochrane Database of Systematic Reviews 2005 Issue 3. Art No: CD003234.DOI:10.1002/14651858.CD003234.pub2

2 Eknoyan G, Levey AS, Beck GJ et al. The haemodialysis (HEMO) study: rationale for selection of interventions. Semin Dial 1996;9:24–33

3 Eknoyan G, Beck GJ, Cheung AK et al. Effect of dialysis dose and flux on mortality and morbidity in maintenance hemodialysis patients: Primary results of the HEMO study. N Engl J Med 2002; 347:2010-2019

4 Cheung AK, Levin NW, Greene T et al. Effects of high-flux haemodialysis on clinical outcomes: Results of the HEMO study. J Am Soc Nephrol 2003; 14:3251-3263

5 Greene T, Beck GJ, Gassman JJ et al. Design and statistical issues of the haemodialysis (HEMO) study. Control Clin Trials 2000; 21: 502-525

6 Locatelli F, Pozzoni P, Di Filippo S. What are we expecting to learn from the MPO study? Contrib Nephrol 2005; 149: 83-89

7 Locatelli F, Andrulli S, Pecchini F et al. Effect of high-flux dialysis on the anaemia of haemodialysis patients. Nephrol Dial Transplant 2000; 15: 1399-1409

8 Chauveau P, Nguyen H, Combe C et al. Dialyser membrane permeability and survival in haemodialysis patients. Am J Kidney Dis 2005; 45:564-571

9 Schiffl H, Lang SM, Fischer R. Ultrapure dialysis fluid slows loss of residual renal function in new dialysis patients. Nephrol Dial Transplant 2002; 17: 1814-1818

10 Termorshuizen F, Dekker FW, van Manen JG et al. Relative contribution of residual renal function and different measures of adequacy to survival in hemodialysis patients: an analysis of the Netherlands Cooperative Study on the Adequacy of Dialysis (NECOSAD)-2. J Am Soc Nephrol 2004; 15: 1061-1070

11 Rabindranath KS, Strippoli GF, Roderick P et al. Comparison of haemodialysis, hemofiltration, and acetate free biofiltration for ESRD: systematic review. Am J Kidney Dis 2005; 45:437-447

12 Locatelli F. Comparison of haemodialysis, haemodiafiltration and haemofiltration: systematic review or systematic error. Am J Kidney Dis 2005; 46: 787-788 (and reply from the authors of reference 9, 788-789)

13 Karamperis N, Sloth E, Jensen JD. Predilution haemofiltration displays no hemodynamic advantage over low-flux haemodialysis under matched conditions. Kidney Int 2005;67:1601-1608

14 Canaud B, Bragg-Gresham JL, Marshall MR et al. Mortality risk for patients receiving haemodiafiltration versus haemodialysis: European results from the DOPPS. Kidney Int 2006; 69: 2087-2093

15 Penne EL, Blankestijn PJ, Bots ML et al. Effect of increased convective clearance by on-line haemodiafiltration on all cause mortality in chronic haemodialysis patients - the Dutch CONvective TRAnsport STudy (CONTRAST): rationale and design of a randomised controlled trial. Curr Control Trail Cardiovasc Med 2005; 6: 8

Guideline 4.3 DIAL-HD

Patients without increased bleeding risk should be given low-dose unfractionated heparin or LMWH during HD to reduce the risk of clotting of

the extracorporeal system. (Evidence) For patients with a risk of bleeding anticoagulation should be avoided or kept to a minimum by using a high blood flow rate and regular flushing of the extracorporeal circuit with saline every 15-30 minutes.

Rationale

Extracorporeal anticoagulation is usually required to prevent thrombosis of all forms of dialyser and extracorporeal circuit. Unfractionated heparin may be used as the standard anticoagulant in view of its proven efficacy, ease of use and safety record unless the patient has a history of recent or active bleeding or heparin induced thrombocytopenia (1, 2). Heparin with a mean half-life of 1.5 hours is best administered as a loading dose followed by a continuous infusion of 500-1500 units/hour that is discontinued approximately 30 minutes before the end of the dialysis session. Monitoring when required can be performed by measuring the activated partial thromboplastin time or the whole-blood activated clotting time aiming for around 150% of predialysis or normal values. The dosage of heparin may need to be increased if there has been a substantive rise in the haematocrit after correction of renal anaemia or reduced if the patient is on warfarin or antiplatelet drugs. Low molecular weight heparin (LMWH) is an alternative agent that has been associated with lower risk of bleeding, less frequent episodes of hyperkalaemia and an improved lipid profile compared with standard heparin. However a systematic review of 11 trials comparing the use of LMWH and unfractionated heparin in HD patients concluded that there was no difference in the incidence of bleeding complications, bleeding from the vascular access after HD or thrombosis of the extracorporeal circuit (3).

For patients with a risk of bleeding anticoagulation should be avoided or kept to a minimum by using a high blood flow rate and regular flushing of the extracorporeal circuit with saline every 15-30 minutes (2). Alternatively heparin may be replaced by a prostacyclin infusion or regional citrate anticoagulation. The former may induce hypotension and is expensive whilst the latter requires careful replacement of calcium and magnesium, monitoring of serum calcium and magnesium levels during HD and is too complex for routine use. For patients with heparin induced thrombocytopenia (HIT) or heparin induced thrombocytopenia and thrombotic syndrome (HITTS) anticoagulation with either Argatroban, heparinoids (danaparoid) or hirudin should be utilized instead of heparin.

References

1 Ouseph R, Ward RA. Anticoagulation for intermittent haemodialysis. Semin Dial 2000; 13:181-187

2 European Best Practice Guidelines for haemodialysis Part 1. Nephrol Dial Transplant 2002; 17: Supplement 7 S1-S111 (http://ndt.oupjournals.org/content/vol17/suppl_7/index.shtml)

3 Lim W, Cook DJ, Crowther MA. Safety and efficacy of low molecular weight heparins for haemodialysis in patients with end-stage renal failure: a meta-analysis of randomised trials. J Am Soc Nephrol 2004; 15:3192-3206

Guideline 4.4 DIAL-HD

If it is planned to reuse dialysers that are marked 'for single use only' the implications of dialyser reuse need to be considered carefully after reading MDA Device Bulletin DB 2000(04) Single-use medical devices: implications and consequences of reuse (good practice).

Rationale

Haemodialysers and their extracorporeal circuits contain sterile non-pyrogenic pathways. Dialysers 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 dialyser. 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. With reuse high flux biocompatible membranes can be used more cost effectively. In recognition of this 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 dialysers that are so labelled in the USA.

Re-use has been shown to be safe in a number of studies and may have benefits, specifically a reduction in beta-2-microglobulin [1]. Some studies report an overall reduction in mortality among patients treated with re-used dialysers [1] 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 the use of formalin [2,3]. Changing from multiple to single use of dialysers has been reported recently to result in a reduction in the mortality rate in a large USA population [4]. It is standard practice to discard the dialyser whenever the hollow fibre volume (total cell volume) is less than 80% of the initial measured value but this method may not always be reliable in detecting dialyser dysfunction [5]. The significant costs and health and safety issues associated with reprocessing of dialysers and the ongoing concerns about patient safety, reduced dialyser efficiency and patient outcomes with reuse have led to reuse being discontinued in the UK. The cost of high-flux dialysers is falling gradually and it is anticipated that mass production will result in similar prices for high flux biocompatible dialysers thus making them cost-effective without having to consider re-use.

References
1   Pollak VE, Kant KS, Parnell SL et al. Repeated use of dialyzers is safe: longterm observations on morbidity and mortality in patients with end-stage renal disease. Nephron 1986; 42:217–23

2   Held PJ, Pauly MV, Diamond L. Survival analysis of patients undergoing dialysis. Jama 1987; 257:645–50

3   Port FK, Wolfe RA, Hulbert-Shearon TE et al. Mortality risk by haemodialyser reuse practice and dialyzer membrane characteristics: results from the USRDS dialysis morbidity and mortality study. Am J Kidney Dis 2001; 37:276–86

4   Lowrie EG, Li Z, Ofsthun N, Lazarus JM. Reprocessing dialysers for multiple uses: recent analysis of death risks for patients. Nephrol Dial Transplant 2004; 19: 2823-2830

5   Delmez JA, Weerts CA, Hasamear PD, Windus DW. Severe dialyser dysfunction undetectable by standard reprocessing validation tests. Kidney Int 1989; 36: 478-484.

Guideline 4.5 DIAL-HD
The use of dialysers sterilized with ethylene oxide should be avoided (good practice).

Rationale
Chemical sterilization of dialysers and tubing with ethylene oxide has been associated with anaphylactoid reactions (1) and this risk can be avoided by using alternatives, such as steam or gamma radiation, for the sterilization of dialysers (2).

References
1   Bommer J, WilhelmsOH, Barth HP et al. Anaphylactoid reactions in dialysis patients: role of ethylene oxide. Lancet 1985; 2:1382-1385

2   European Best Practice Guidelines for haemodialysis Part 1. Nephrol Dial Transplant 2002; 17: Supplement 7 S1-S111 (http://ndt.oupjournals.org/content/vol17/suppl_7/index.shtml).

Guideline 4.6 DIAL-HD
Haemodialysis patients should not be treated with ACE inhibitor drugs and AN 69 dialyser membranes at the same time. (Evidence)

Rationale
The concurrent use of AN 69 dialyser membranes in patients on ACE inhibitors has been reported to cause haemodynamic instability attributable to bradykinin (1). This interaction is preventable by changing the ACE inhibitor to an angiotensin II antagonist or changing to a different dialysis membrane (2).

References
1   Verresen L, Fink E, Lemke HD, Vanrenterghem Y. Bradykinin is a mediator of anaphylactoid reactions on AN69 membranes in patients receiving ACE inhibitors. Kidney Int 1994; 45:1497-1503

2   European Best Practice Guidelines for haemodialysis Part 1. Nephrol Dial Transplant 2002; 17: Supplement 7 S1-S111 (http://ndt.oupjournals.org/content/vol17/suppl_7/index.shtml).

5 Haemodialysis dose, frequency and duration (Guidelines DIAL-HD 5.1 – 5.7)

Guideline 5.1 DIAL-HD
HD should take place at least three times per week in nearly all patients with end-stage chronic renal failure. Reduction of dialysis frequency to twice per week because of insufficient dialysis facilities is unacceptable (good practice).

Audit measure 5
The proportion of patients in the main renal unit and its satellite units who are on twice weekly haemodialysis.

Rationale
Twice weekly HD as a long-term form of chronic renal replacement therapy should be discouraged. The most powerful determinant of solute removal is dialysis frequency rather than duration. Twice per week HD is no longer regarded as adequate and should be avoided. The frequency of twice weekly dialysis has decreased world wide, including in the USA where it fell from 12.9% to 3.6% of new patients between 1990 and 1996 (1). Some patients who live at far distances from a HD unit remain on twice weekly HD and this small subgroup of patients should be kept to minimum and receive much longer duration sessions. Twice weekly HD without an increase in treatment time may be acceptable if patients have a significant level of residual renal function, such as either a combined urinary urea and creatinine clearance or eGFR above 5ml/min/1.73m2, provided that residual renal function is monitored at least every 3 months and the frequency of dialysis is increased when renal function decreases.

The three times per week HD 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 within a 7 day treatment cycle. Furthermore, all outcome data from randomized prospective trials have so far been derived from patient groups undergoing such dialysis schedules. The National Co-operative Dialysis Study (NCDS), an historical US randomised trial where cellulose membranes and acetate dialysate were used, has addressed the issue of optimal dialysis time. This 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 (2). Longer dialysis gave a better outcome (2, 3). A combination of better patient tolerance using improved machines and higher efficiency HD, economic constraints and patient preference for shorter times has resulted in a gradual reduction in the average length of dialysis sessions around the world.

More recently two approaches to more frequent dialysis sessions have been re-evaluated. The first is dialysis for around two-three hours per day for five-six days per week (often termed short daily HD) (4-8). The other approach is a renewed interest in slow overnight treatment for 5–7 nights per week (often termed nocturnal daily HD) that can (9-12):

a) deliver very large doses of dialysis (weekly Kt/V of almost 6 and much greater removal of middle molecules)
b) remove sodium and water so that anti-hypertensive treatment can be reduced to a minimum
c) permit regression of left ventricular hypertrophy
d) allow patients to follow an unrestricted diet
e) permit phosphate binders to be discontinued
f) improve sleep disturbance and sleep apnoea

Both regimes have been reported to give improved clinical outcomes such as higher quality of life, fewer hospital admissions and reduced need for erythropoietin when compared with the more conventional regime of three sessions per week each of four hours (4-12). Daily HD may also be indicated in the short term when patients develop an acute intercurrent illness or pericarditis. On the basis of the successful reports from these observational studies of short daily and nocturnal daily HD the National Institutes of Health (NIH) has sponsored 2 prospective randomized studies in 250 patients to compare each form of "daily" or frequent HD with standard thrice weekly HD. These NIH studies **(Frequent Haemodialysis Network Studies)** are due to be completed in 2008/2009 (13).

References

1   Port FK, Orzol SM, Held PJ, Wolfe RA. Trends in treatment and survival for haemodialysis patients in the United States. Am J Kidney Dis 1998; 32(Suppl 4): S34–38

2   Lowrie EG, Parker TF, Parker TF, Sargent JA. Effect of the haemodialysis prescription on patient morbidity: report from the National Cooperative Dialysis Study. N Engl J Med 1981; 305:1176–1181

3   Lowrie EG, Teehan BP. Principles of prescribing dialysis therapy: implementing recommendations from the National Cooperative Dialysis Study. Kidney Int Suppl 1983; 13:S113–122

4   Mastrangelo F, Alfonso L, Napoli M et al. Dialysis with increased frequency of sessions (Lecce dialysis). Nephrol Dial Transplant 1998; 13(Suppl 6): 139–147

5   Twardowski ZJ. Daily dialysis: is this a reasonable option for the new millennium? Nephrol Dial Transplant 2001; 16:1321–1324

6   Galland R, Traeger J, Arkouche W et al. Short daily haemodialysis and nutritional status. Am J Kidney Dis 2001; 37(Suppl 2): S95–98

7   Goldfarb-Rumyantzev AS, Leypoldt JK, Nelson N et al. A crossover study of short daily haemodialysis. Nephrol Dial Transplant 2005; 21: 166-175

8   Woods JD, Port FK, Orzol S et al. Clinical and biochemical correlates of starting "daily" haemodialysis. Kidney Int 1999; 55: 2467-2476

9   Fagugli RM, Reboldi G, Quintaliani G et al. Short daily haemodialysis: blood pressure control and left ventricular mass reduction in hypertensive haemodialysis patients. Am J Kidney Dis 2001; 38: 371-376

10 Pierratos A. Nocturnal home haemodialysis: an update on a 5-year experience. Nephrol Dial Transplant 1999; 14:2835-2840

11 Mucsi I, Hercz C, Uldall R et al. Control of serum phosphate without any phosphate binder in patients treated with nocturnal haemodialysis. Kidney Int 1998; 53:1399-1404

12 Raj DS, Charra B, Pierratos A, Work J. In search of ideal haemodialysis: is prolonged frequent dialysis the answer? Am J Kidney Dis 1999; 34:597–610

13 Walsh M, Culleton B, Tonelli M, Manns B. A systematic review of the effect of nocturnal haemodialysis on blood pressure, left ventricular hypertrophy, anaemia, mineral metabolism and health-related quality of life. Kidney Int 2005; 67:1500-1508

14 www.niddk.nih.gov/patient/hemodialysis/hemodialysis.htm

Guideline 5.2 DIAL-HD

Every patient with end-stage chronic renal failure receiving thrice weekly HD should have consistently:

- **either urea reduction ratio (URR) > 65%**
- **or equilibrated Kt/V of >1.2** (or sp Kt/V of > 1.3) **calculated from pre- and post-dialysis urea values, duration of dialysis and weight loss during dialysis (Evidence)**

To achieve a URR above 65% or eKt/V above 1.2 consistently in the vast majority of the haemodialysis population clinicians should aim for a minimum target URR of 70% or minimum eKt/V of 1.4 in individual patients. 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 maintained above 70% or eKt/V is at least 1.4.

Audit measure 2
Cumulative frequency curves of urea reduction ratio measured using a standard method of post-dialysis sampling

Rationale
Dialysis adequacy is a global concept that includes the clinical assessment of general well-being, nutrition, the impact on the patient's quality of life, anaemia, blood pressure and fluid status as well as measures of clearance of putative uraemic toxins 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 (beta-2-microglobulin). Adequate clearance of the whole range of molecules by dialysis is important and in the future monitoring of beta-2-microglobulin levels may be used to assess dialysis adequacy. For practical reasons HD adequacy thus far has been measured using small, easily measured solutes such as urea (1-3)

Three methods of assessing urea removal are in current use (1, 2):

a) The URR (4) is the simplest. The percentage fall in blood urea achieved by a dialysis session is measured as follows:

{(pre-dialysis [urea] – post-dialysis [urea])}/pre-dialysis (urea) • 100%.

The URR is easy to perform and is the most widely used index of dialysis dose used in the UK. URR does not take solute removal via ultrafiltration or residual renal function or urea generation during dialysis into account (5, 6) and hence

adjustment of dialysis dose to achieve a particular target will result in higher overall urea removal than predicted from the percentage reduction in blood urea. However these drawbacks are not important 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% (7-10).

b) 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. Kt/V can be calculated using several formulae giving different results (11) and hence, if Kt/V is being used 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. The second generation formula validated and reported by Daugirdas is recommended (12).

c) Urea kinetic modeling (Formal UKM), the most complex measure, involves analysis of the fall in (urea) during HD, 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. Therefore UKM requires collection of additional data on dialyser clearance, an interdialytic urine collection for measurement of urea concentration and volume, and measurement of pre-dialysis urea concentration on the subsequent dialysis. These data are fed into a computer programme which, assuming steady state, calculates Kt/V urea and normalised protein catabolic rate (5). Kt/V measured by formal UKM is more accurate than URR, particularly at high values of URR and Kt/V (3). Its use allows accurate prediction of the effects of changing one particular component of the dialysis prescription (e.g. dialyser size, dialysis duration, blood flow rate) on the delivered dialysis dose although this benefit has been overstated given the limited number of practical options for changing the dialysis prescription. UKM also may give 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 may be a useful adjunct to other methods of assessment of nutritional status.

However doubts have been raised whether Kt/V is 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 (13, 14). Non-normalised dialysis dose (Kt) has been proposed as an alternative and better index of dialysis dose adequacy to Kt/V since the former index obviates the trend for smaller patients with poorer nutritional status to be accorded a higher dialysis dose (15,16). In a large cross-sectional analysis using Kt as the index of dialysis 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 (13). 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.

Most UK haemodialysis units only collect pre- and post-dialysis urea concentration, and only a very few perform UKM. For comparative audit, the choice therefore currently lies between calculation of URR and estimation of Kt/V urea from such data.

The optimal dialysis dose has not been well defined but minimum targets of delivered dose measured by URR and Kt/V have been established. A retrospective analysis of the National Co-operative Dialysis Study suggested that a Kt/V of 1.0 was the watershed between 'good' dialysis (Kt/V >1.0) and inadequate dialysis (Kt/V <1.0). Thereafter Kt/V survived as an index of dialysis adequacy (17). More recent studies (7-9,18-20) have shown a reduction in mortality rates with increases in dialysis dose measured in various ways with some of the studies adjusting for co-morbidity (8,20). One study has shown no further reduction in mortality above Kt/V of 1.3 or URR of 70% (7). Many commentators, however, believed that some further improvement in mortality risk could be achieved with Kt/Vs of up to 1.6 or even higher (21-23). The HEMO trial was a prospective randomised controlled trial in which 1846 patients were randomised to achieve a standard-dose goal of an equilibrated Kt/V of 1.05 (URR circa 65%) or a high-dose goal of an eKt/V of 1.45 (URR circa 75%) and to synthetic or semi-synthetic membranes of high or low flux in a 2 x 2 factorial design. (24). The HEMO study showed no difference in patient survival or secondary end-points between the two groups after a mean follow-up period of 2.8 years. No difference in patient outcomes was observed in the two groups even although dialysis doses were well separated with achieved eKt/V of 1.16 in the standard-dose group (spKt/V 1.3 + 0.1 ; URR 66.3 + 2.5%) and eKt/V of 1.53 in the high-dose group (spKt/V 1.7 + 0.1 ; URR 75.2 + 2.5%). Subgroup analysis of the HEMO study showed that 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) and this association persisted after adjusting for different indices of body size (25). An association between higher dose and lower mortality rates in women but not in men was confirmed using the average URR of incident HD patients in the USA and eKt/V of HD patients in the DOPPS data from 7 countries (26). Further analyses of the HEMO study showed that differences in dialysis dose and membrane flux had no effect on the proportion of infection-related deaths (27).

Based upon the above evidence we have retained the standard dose as a URR of 65% or an eKt/V of 1.2, which should be regarded as the minimum dialysis dose delivered thrice weekly. To ensure as many patients as possible achieve this standard consistently the target dose should be a URR of 70% or eKt/V of 1.4. As with all standards, achievement is dependent on patients' concordance with treatment. This includes the agreement of the patient to increase treatment duration if the delivered dialysis dose is inadequate after the dialyser blood flow rate, dialysate flow rate and dialyser performance have been increased to the maximum that can be achieved. Increased understanding amongst patients of the benefits of an adequate dialysis dose should help to improve outcomes. The proportion of dialysis sessions that are missed or shortened by the patient should be audited in each unit.

Time-dependent Cox regression analysis of the HEMO study has shown that mean pre-dialysis serum beta-2-microglobulin levels but not dialyser beta-2-microglobulin clearances were associated with all cause mortality with a relative risk of 1.11 per 10mg/L rise in the beta-2-microglobulin concentration above a reference value of 27mg/L (CI 1.05-1.19 ; p = 0.001) after adjusting for residual renal function and pre-study years on dialysis (28). This evidence provides support for the use of beta-2-microglobulin to assess adequacy of HD in future both as an indicator of patient outcome and a surrogate marker of middle molecule removal (29). The apparent disparity between the prognostic effects of serum beta-2-microglobulin levels and dialyser beta-2-microglobulin clearances (28) is most likely due to the limited mass removal of beta-2-microglobulin in high-efficiency dialysis due to intercompartmental transfer resistance within the patient which results in rebound of serum beta-2-microglobulin levels at the end of therapy (30). This observation on beta-2-microglobulin intradialytic kinetics provides further support for the use of longer duration and/or more frequent dialytic therapies (29).

References

1   Depner T. Hemodialysis kinetic modeling. In: Henrich WL (ed). The principles and practice of dialysis, 2nd edn. Philadelphia: Lippincott, Williams and Wilkins,1999: Chapter 7.

2   Gotch F. Urea kinetic modelling to guide haemodialysis therapy in adults. In: Nissenson AR, Fine RN (eds). Dialysis therapy, 2nd edn. Philadelphia: Hanley and Belfus, 2002; Section 6:117–121

3   Sherman RA, Hootkins R. Simplified formulas for monitoring haemodialysis adequacy. In: Nissenson AR, Fine RN (eds). Dialysis therapy, 3rd edn. Philadelphia: Hanley and Belfus, 2002; Section 6:122–126

4   Lowrie EG, Lew NL. The urea reduction ratio (URR): A simple method for evaluating haemodialysis treatment. Contemp Dial Nephrol 1991; 12(2): 11–20

5   Depner TA. Assessing adequacy of haemodialysis: urea modeling. Kidney Int 1994; 45:1522–35

6   Sherman RA, Cody RP, Rogers ME et al. Accuracy of the urea reduction ratio in predicting dialysis delivery. Kidney Int 1995; 47:319-321

7   Held PJ, Port FK, Wolfe RA et al. The dose of haemodialysis and patient mortality. Kidney Int 1996; 50:550–556

8   McClellan WM, Soucie JM, Flanders WD. Mortality in end-stage renal disease is associated with facility-to-facility differences in adequacy of haemodialysis. J Am Soc Nephrol 1998; 9:1940–1947

9   Parker T, Husni L, Huang W et al. Survival of haemodialysis patients in the United States is improved with a greater quantitiy of dialysis. Am J Kidney Dis 1994; 23: 670-680

10 Owen WF, Lew NL, Lowrie EG et al. The urea reduction ratio and serum albumin concentration as predictors of mortality in patients undergoing haemodialysis. N Eng J Med 1993; 329: 1001-1006

11 Movilli E. Simplified approaches to calculate Kt/V. Its time for agreement. Nephrol Dial Transplant 1996; 11:24–27

12 Daugirdas JT. Second generation logarithmic estimates of single-pool variable3volume Kt/V; an analysis of error. J Am Soc Nephrol 1993; 4:1205-1213

13 Lowrie EG, Chertow G, Lazarus JM. Owen WF. The mortality effect of the clearance x time product. Kidney Int 1999; 56: 729-737

14 Lowrie EG, Chertow GM, Lew NL et al. The urea clearance x dialysis time product (Kt) as an outcome-based measure of haemodialysis dose. Kidney Int 1999; 56: 729-737

15 Li Z, Lew NL, Lazarus JM, Lowrie EG. Comparing the urea reduction ratio and urea product as outcome-based measures of haemodialysis dose. Am J Kidney Dis 2000; 35: 598- 605

16 Lowrie EG, Li Z, Ofsthun N, Lazarus JM. Measurement of dialyser clearance, dialysis time, and body size: death risk relationships among patients. Kidney Int 2004; 66: 2077- 2084

17 Gotch FA, Sargent JA. A mechanistic analysis of the National Cooperative Dialysis Study (NCDS). Kidney Int 1985; 28:526–534

18 Hakim RM, Breyer J, Ismail N, Schulman G. Effects of dose of dialysis on morbidity and mortality. Am J Kidney Dis 1994; 23:661–669

19 Collins AJ, Ma JZ, Umen A et al. Urea index and other predictors of haemodialysis patient survival. Am J Kidney Dis 1994; 23:272–282

20 Bloembergen WE, Hakim RM, Stannard DC et al. Relationship of dialysis membrane and cause-specific mortality. Am J Kidney Dis 1999; 33:1–10

21 Hornberger JC. The haemodialysis prescription and quality-adjusted life expectancy. Renal Physicians Association Working Committee on Clinical Guidelines. J Am Soc Nephrol 1993; 4:1004–1020

22 Hornberger JC. The hemodialysis prescription and cost effectiveness. Renal Physicians Association Working Committee on Clinical Guidelines. J Am Soc Nephrol 1993; 4:1021–1027

23 Wolfe RA, Ashby VB, Daugirdas JT et al. Body size, dose of haemodialysis, and mortality. Am J Kidney Dis 2000; 35:80–88

24 Eknoyan G, Beck GJ, Cheung AK et al. Effect of dialysis dose and flux on mortality and morbidity in maintenance hemodialysis patients: Primary results of the HEMO study. N Engl J Med 2002; 347:2010-2019

25 Depner T, Daugirdas J, Greene T et al. Dialysis dose and the effect of gender and body size on outcome in the HEMO study. Kidney Int 2004; 65: 1386-1394

26 Port FK, Wolfe RA, Hulbert-Shearon TE et al. High dialysis dose is associated with lower mortality among women but not among men. Am J Kidney Dis 2004; 43: 1014-1023

27 Allon M. Depner TA, Radeva M, et al. Impact of dialysis dose and membrane on infection-related hospitalisation and death: Results of the HEMO study. J Am Soc Nephrol 2003; 14: 1863- 1870

28 Cheung AK, Rocco MV, Yan G et al. Serum beta-2-microglobulin levels predict mortality in dialysis patients: results of the HEMO study. J Am Soc Nephrol 2006; 17: 546-555

29 Canaud B, Morena M, Cristal JP, Krieter D. Beta-2-microglobulin, a uraemic toxin with a double meaning. Kidney Int 2006; 69; 1297-1299

30 Ward RA, Greene T, Hartmann B, Samtleben W. Resistance to intercompartmental mass transfer limits beta-2-microglobulin removal by post-dilution haemodiafiltration. Kidney Int 2006; 69:1431-1437

Guideline 5.3 DIAL-HD
The duration of thrice weekly HD in adult patients with minimal residual renal function should not be reduced below 4 hours without careful consideration (good practice).

Audit measure 7
The proportion of patient non-attendances for dialysis and the proportion of dialysis sessions shortened at the patient's request.

Rationale
It is difficult to separate the influence of dialysis time and dose on patient outcomes (1). Early studies showed that the risk of death is associated with short dialysis duration (2). Dialysers with higher mass transfer area coefficients in combination with higher blood and dialysis fluid flow rates have been used to provide higher efficiency HD than in the past. The urea clearance will depend on whichever is the lowest of the blood flow rate, dialyser urea mass transfer coefficient and dialysate flow rate. Since small solute urea removal can be formally quantified by validated techniques, dialysis times have been reduced while maintaining 'equivalence' in the degree of blood urea purification. A crossover study of standard and higher efficiency HD prescriptions delivering equal dialysis dose (urea removal) measured by direct dialysate quantification has shown lower phosphate and beta-2-microglobulin removal and less bicarbonate absorption during the shorter duration, higher efficiency prescription (3). Improved clearance of iohexol was also observed on longer duration HD with similar Kt/V. Thus, when short and standard duration HD provide equal urea clearances, delivered dialysis therapy should not be regarded as equivalent. Alternatively changing to treatment modalities that provide both convective and diffusive removal of solutes such as haemodiafiltration have been used to lower treatment times although shortening the duration of haemodiafiltration will tend to negate its benefits of providing higher middle molecule clearances.

Retrospective data from a large Japanese population have shown that dialysis duration up to 5.5 hours was associated with improved patient survival after adjusting for dialysis dose (4). Very low mortality rates were observed in Tassin in patients treated with long duration thrice weekly HD with mean spKt/V of 1.67 + 0.41 (5). However, a Cox analysis showed that patient survival was linked to improved blood pressure control and lower cardiovascular mortality related to the achievement of better long-term control of dry body weight (5). Conversely high efficiency HD has been associated with poor blood pressure control. In the USA patients who received dialysis for less than 3.5 hours per session three times per week had approximately twice the risk of death of patients on HD for more than 4 hours three times per week (2). Cox regression analyses of data from the Dialysis Outcomes and Practice Patterns Study (DOPPS) and the Australian and New Zealand Dialysis and Transplant Registry have shown that patient survival was greater in patients if treatment times were above 4 hours and 4.5 hours, respectively (6,7) and both of these observational studies have concluded that a randomised controlled study of longer dialysis sessions in thrice weekly HD is needed. These observations suggest that the duration of thrice weekly HD should be reduced below 4 hours with caution unless the patient has significant residual renal function or low body weight.

Delivered treatment times and hence weekly dialysis dose are reduced if either the patient requests to discontinue the dialysis session early or if the patient attends for dialysis irregularly. Non-adherence to the prescribed dialysis schedule should be kept to a minimum and monitored.

References

1   Kjellstrand CM. Duration and adequacy of dialysis Overview: the science is easy, the ethic is difficult. Asaio J 1997; 43:220–224

2   Held PJ, Levin NW, Bovbjerg RR et al. Mortality and duration of haemodialysis treatment Jama 1991; 265:871–875

3   Mactier RA, Madi AM, Allam BF. Comparison of high-efficiency and standard haemodialysis providing equal urea clearances by partial and total dialysate quantification Nephrol Dial Transplant 1997; 12: 1182-1186

4   Shinzato T, Nikai S, Akiba T et al. Survival in long-term haemodialysis patients results from the annual survey of the Japanese Society of Dialysis Therapy. Nephrol Dial Transplant 1997; 12: 884-888

5   Charra B, Calemard E, Ruffet M et al. Survival as an index of adequacy of dialysis. Kidney Int 1992; 41:1286-1291

6   Saran R, Bragg-Gresham JL, Levin NW et al. Longer treatment time and slower ultrafiltration in haemodialysis: Associations with lower mortality in the DOPPS. Kidney Int 2006; 69: 1222-1228

7   Marshall MR, Byrne BG, Kerr PG, McDonald SP. Associations of haemodialysis dose and session length with mortality risk in Australian and New Zealand patients. Kidney Int 2006; 69:1229-1236

Guideline 5.4 DIAL-HD
Patients receiving dialysis twice weekly for reasons of geography should receive a higher sessional dose of dialysis (good practice).

Rationale
A wider distribution of small satellite HD units would help reduce the need to accept twice weekly HD for lifestyle reasons. Twice weekly HD effectively means that the patient will require longer duration HD, usually at least 6 hours twice per week. It should be acknowledged if this cannot be achieved and patients who are receiving twice weekly HD without an increase in treatment time should be informed explicitly that this is a compromise between the practicalities of dialysis and their long-term health.

Guideline 5.5 DIAL-HD
Measurement of the 'dose' or 'adequacy' of HD should be performed monthly in all hospital HD patients and may be performed less frequently in home HD patients (good practice).

Rationale

Monthly measurement of dialysis dose in hospital HD patients should be used to optimize the HD prescription and may facilitate early detection of poorly functioning vascular access. Monitoring of dialysis dose in home HD patients on a monthly basis is impractical and may be performed on a less frequent basis such as every 3 months. All dialysis units should collect and report data on dialysis adequacy to their regional network and the UK Renal Registry. Meaningful comparative audit within a renal unit or regional network requires the use of the same methodology of measurement of dialysis dose and blood sampling during a mid-week HD session in the census week.

Guideline 5.6 DIAL-HD

Post-dialysis blood samples should be collected either by the stop-dialysate flow method, the slow-flow method or the simplified stop-flow method. The method used should remain consistent within renal units and should be reported to the Registry. (Evidence)

Rationale

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

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

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 as the effects of access and cardiopulmonary recirculation dissipate (1). 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 (2-6); 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 USA (7) and in the UK (8,9). Techniques of post-dialysis blood sampling that involve taking the sample immediately at the end of the HD session were used commonly in the USA in the past (7), generate a higher apparent URR and may have contributed to the rise in the URR deemed necessary for optimum survival in observational studies.

Several methods of post-dialysis blood sampling are in use in the UK:

   a) Stop dialysate flow method (validated by Drs. Geddes, Traynor and Mactier, NHS Glasgow, and used by all of the HD units in Scotland since 1999; ref 8-10).

At the end of the dialysis time stop dialysate flow but keep the blood pump running.
After 5 minutes with no dialysate flow take a blood sample from anywhere in the blood circuit.

b) Slow-flow method (developed by F Gotch and M Keen, Davis Medical Centre, San Francisco and used by Lister Renal Unit, East & North Herts NHS Trust since 1990; ref 3).

At the end of the dialysis time turn the blood pump speed down to 100 ml per min.
Override alarms to keep blood pump operating.
Wait 15–30 seconds and take samples from the "arterial" line sampling port.
If more than one blood sample is required, the sample for urea should be the first one taken.

c) Simplified stop-flow method (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 speed slowly down to 50 ml per 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 speed to 50 ml per min.
If more than one blood sample is required, the urea sample should be the first one taken.

The stop dialysate flow method avoids the dilutional effects of access and cardiopulmonary recirculation and is a 2 step process involving switching off the dialysate flow for 5 minutes at the end of the HD session and then taking a blood sample from the arterial or venous port (8). The stop dialysate flow method is simple, easily reproducible, suitable for all forms of vascular access, validated in haemodiafiltration as well as HD (8,9) and is currently the most widely used method in the UK. The slow-flow method and the stop-flow method were devised to give early post-dialysis measurements which avoid the effects of access re-circulation but do not allow for cardiopulmonary recirculation which continues for the first 2 minutes after the end of HD using a fistula or graft as vascular access (1). The stop and slow flow methods will underestimate post-dialysis "equilibrated" blood urea concentrations more than the stop dialysate flow method and consequently overestimate urea removal by HD.

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 efficiency of dialysis and the size of the patient. Formulae have been validated for predicting 30 minute post-dialysis or "equilibrated" blood urea from blood samples using either the stop dialysate flow method (10) or similar sampling methods to the slow flow and stop flow methods (3,6,11). A standardized approach to post-dialysis blood sampling is preferable for comparative audit (12) and the stop dialysate flow method was adopted by all of the adult renal units in Scotland since it is simple, practical, well validated and the least likely method to overestimate the URR or Kt/V. The stop dialysate flow and slow-flow methods are the two methods included in Guideline 3.4 of the latest update of the KDOQI Clinical Practice Guidelines on Haemodialysis Adequacy (13).

References

1   Schneditz D, Kaufman AM, Polaschegg HD et al. Cardiopulmonary recirculation during haemodialysis. Kidney Int 1992; 42: 1450-1456

2   Lai YH, Guh JY, Chen HC, Tsai JH. Effects of different sampling methods for measurement of post dialysis blood urea nitrogen on urea kinetic modeling derived parameters in patients undergoing long-term haemodialysis. Asaio J 1995; 41:211–215

3   Tattersall JE, De Takats D, Chammey P et al. The post-haemodialysis rebound: predicting and quantifying its effect on Kt/V. Kidney Int 1996; 50:2094–2102102

4   Tattersall JE, Chammey P, Aldridge C et al. Recirculation and the post-dialysis rebound. Nephrol Dial Transplant 1996; 11(Suppl 2):75–80

5   Daugirdas JT, Smye SW. Effect of a two compartment distribution on apparent urea distribution volume. Kidney Int 1997; 51:1270–1273

6   Smye SW, Tattersall JE, Will EJ. Modeling the postdialysis rebound: the reconciliation of current formulas. Asaio J 1999; 45:562–567

7   Beto JA, Bansal VK, Ing TS et al. Variation in blood sample collection for determination of haemodialysis adequacy. Am J Kidney Dis 1998; 31:135-141

8   Geddes C C, Traynor J P, Walbaum D et al. A new method of post-dialysis blood urea sampling: the "stop dialysate flow" method. Nephrol Dial Transplant 2000; 15:517-523

9   Traynor JP, Oun HA, McKenzie P et al. Assessing the utility of the stop dialysate flow method in patients receiving haemodiafiltration. Nephrol Dial Transplant 2005; 20: 2479-2484

10 Traynor JP, Geddes CC, Ferguson C, Mactier RA. Predicting 30-minute postdialysis rebound blood urea concentrations using the stop dialysate flow method. Am J Kidney Dis 2002; 39:308-314

11 Daugirdas JT. Second generation logarithmic estimates of single-pool variable3volume Kt/V; an analysis of error. J Am Soc Nephrol 1993; 4:1205-1213

12 The Renal Association UK Renal Registry, The Seventh Annual Report, December 2004.

13 (www.renalreg.com Renal Association Standards & Audit Subcommittee)

14 National Kidney Foundation-K/DOQI Clinical Practice Guidelines and Clinical Practice Recommendations for Haemodialysis Adequacy, 2005 (in press) (www.kidney.org/professionals/kdoqi/guidelines.cfm)

Guideline 5.7 DIAL-HD
Patients with acute renal failure should initially receive daily renal replacement therapy. (Evidence)

Rationale
At present there is no evidence to show whether continuous or intermittent renal replacement therapies or whether haemofiltration or HD provide better survival in patients with acute renal failure. In a randomised, risk stratified, dose equivalent prospective comparison of continuous veno-venous HD (CVVHD) versus intermittent HD in 80 intensive care unit patients with acute renal failure the CVVHD group had greater daily fluid volume removal but no improvement in patient survival, preservation of urinary output or recovery of renal function (1). A randomized study of extended daily HD and continuous HD in intensive care patients with acute renal failure showed no difference in haemodynamic stability (2). However there is evidence that survival in patients with acute renal failure is better with daily than alternate day renal replacement therapy (3). In this randomized prospective study of 160 critically ill patients with acute renal failure the mortality rate using an intention-to-treat analysis was 28% with daily HD and 46% with alternate day HD ($p < 0.01$). The frequency of renal replacement therapy may be reduced once the metabolic syndrome and fluid status of patients with acute renal failure is stable. Initial randomized studies showed that the use high flux biocompatible membranes were associated with improved patient survival rates in acute renal failure but this has not been confirmed in follow-up studies (4). 58% of the 90 patients randomly assigned to bioincompatible Cuprophan dialysers survived compared with 60% of the 90 patients assigned to polymethylmethacrylate membranes (4). A randomized study of continuous veno-venous haemofiltration in acute renal failure has shown improved patient survival in patients prescribed at least 35ml/hour/kg body weight (5). Extended daily HD and post-dilutional continuous veno-venous haemofiltration are widely utilized in the management of acute renal failure in the UK and both provide long duration therapy to help maintain adequate fluid balance with minimal adverse haemodynamic effects in this critically ill patient group.

References
4   Augustine JJ, Sandy D, Seifert TH, Paganini EP. A randomized controlled trial comparing intermittent with continuous dialysis in patients with acute renal failure. Am J Kidney Dis 2004; 44:1000-1007

5   Kumar VA, Yeun JY, Depner TA, Don BR. Extended daily dialysis versus continuous haemodialysis for ICU patients with acute renal failure: a two-year single centre report. Int J Artif Organs 2004; 27: 371-379

6   Schiffl H, Lang SM, Fischer R. Daily haemodialysis and the outcome of acute renal failure. N Eng J Med 2002; 346: 305-310

7   Jorres A, Gahl, GM, Dobis C et al. Haemodialysis-membrane biocompatibility and mortality of patients with dialysis-dependent acute renal failure: a prospective randomized multicentre trial. International Multicentre Study Group. Lancet 1999; 354: 1337-1341

8   Ronco C, Bellomo R, Homel P et al. Effects of different doses in continuous veno-venous haemofiltration on outcomes of acute renal failure: a prospective randomized trial. Lancet 2000; 356: 26-30

6 Laboratory and clinical indices of dialysis adequacy other than dialysis dose (Guidelines DIAL-HD 6.1 – 6.11)

Guideline 6.1 DIAL-HD

Blood sampling for biochemical and haematological measurements should be performed before a mid-week HD session using a dry needle or syringe (good practice).

Rationale

Too much emphasis may have been placed in the past on achieving a given standard of small solute clearance at the expense of addressing a wide range of other important clinical and laboratory parameters of dialysis adequacy. A global assessment of dialysis adequacy includes achievement of good control of:

- hyperkalaemia and metabolic acidosis
- bone metabolism
- anaemia
- hypertension and fluid balance
- traditional and non-traditional cardiovascular risk factors
- nutritional status

Variability in interdialysis fluid weight gains after the 1 or 2 day intervals between HD sessions may be expected to cause differing degrees of haemodilution and so influence pre-dialysis haemoglobin and albumin concentrations. A recent study has shown higher pre-dialysis serum calcium and phosphate concentrations after the longer interdialysis interval in the absence of evidence of different levels of haemodilution between short and long interdialysis intervals (1). These findings indicate that time-interval related interdialytic and non-dialytic factors may influence pre-dialysis biochemical and haematological results and reinforce the need for standardization of timing of pre-dialysis blood sampling in HD patients. The UK Renal Registry and Scottish Renal Registry have employed audit measures using measurement of laboratory values from samples that were collected before commencing HD after a one day interdialysis interval. To avoid blood sampling at weekends blood sampling is effectively limited to either a Wednesday or Thursday dialysis session. This restricted timing of blood sampling allows standardization of interpatient and intrapatient interdialysis fluid weight gains and it is important that all samples are taken using a dry needle or syringe to ensure dilutional sampling errors are avoided.

References

1   Sigrist MK, Devlin L, Taal MW, Fluck RJ, McIntyre CW. Length of interdialysis interval influences serum calcium and phosphorus concentrations. Nephrol Dial Transplant 2005; 20:1643-1646

Guideline 6.2 DIAL-HD

Monitoring of pre-dialysis biochemical and haematological parameters should be performed monthly in hospital HD patients and at least 3 monthly in home HD patients (good practice).

Rationale

Standardised analytical methods of measuring laboratory indices are required if comparative audit against target standards is to be meaningful. Difficulties still arise since laboratories across the UK use different methods to measure serum albumin and different correction factors for adjusting serum calcium levels (1).

References

2   The Renal Association UK Renal Registry, The Seventh Annual Report, December 2004. (www.renalreg.com)

Guideline 6.3 DIAL-HD

Pre-dialysis serum bicarbonate concentrations measured with minimum delay after venepuncture should be between 20 and 26mmol/l. (good practice).

Rationale

The main causal factors of metabolic acidosis in stable HD patients are inadequate dialysis delivery, excessive animal protein (sulphur containing amino acid) intake and high interdialysis weight gains. Whole-body base balance studies in 18 anuric HD patients have highlighted the importance of interdialysis dilution in the aetiology of predialysis acidosis (1). In ill patients metabolic acidosis may also be due to increased protein catabolism, hypotension or hypoxia induced lactate production or bicarbonate losses associated with co-morbid illness. Pre-dialysis metabolic acidosis has a range of adverse consequences: an increase in protein catabolism and anti-anabolic effects, negative inotropic effect, loss of bone mineral, insulin resistance, growth retardation in children, reduced thyroxine levels, altered triglyceride metabolism, hyperkalaemia, lower serum leptin levels and greater accumulation of beta-2-microglobulin.

Pre-dialysis venous bicarbonate levels between 17.5 and 20 mmol/l were associated with the lowest risk of death in a large cohort study of 13535 hemodialysis patients whilst the relative risk of death was increased threefold if the pre-dialysis venous bicarbonate was < 15 mmol/l (2). In a DOPPS study of more than 7000 unselected HD patients the corrected mid-week serum bicarbonate concentration averaged 21.9 mmol/l and correlated inversely with the nPCR and serum albumin (3). The adjusted risk of death, hospitalization or malnutrition was higher in patients with serum bicarbonate levels less than 16 or above 24 when compared with patients in the reference group with moderate pre-dialysis acidosis (3). Short-term benefits of correcting pre-dialysis acidosis from below 19mmol/l to 24mmol/l, by either increasing the dialysate bicarbonate concentration (4-7) or the addition of oral bicarbonate supplements (8), have been shown in several small crossover studies. Correction of acidosis reduced whole body protein degradation in a study of 6 patients (4), increased the sensitivity of the parathyroid

glands to serum calcium in studies of 21 and 8 patients (5,6), improved triceps skin thickness as an index of nutritional status in 46 patients (7) and increased serum albumin after 3 months in 12 patients without any change in body weight, Kt/V, and nPCR (8). Other studies have shown no increase in serum albumin after correction of acidosis. Complete correction of pre-dialysis metabolic acidosis in HD patients may lead to post-dialysis metabolic alkalosis and consequently hypoventilation, phosphate transfer into cells and a higher risk of soft tissue and vascular calcification. The prerequisite additional oral or dialysate bicarbonate (and sodium) load may contribute to higher sodium (and fluid) retention and hypertension. Review of the target pre-dialysis serum bicarbonate levels set by international clinical practice guidelines indicates that a mild degree of pre-dialysis acidosis is recommended to minimize the risk of adverse events.

References

1   Mioni R, Gropuzzo M, Messa M et al. Acid production and base balance in patients in chronic haemodialysis. Cli Sci 201;101:329-37

2   Lowrie EG, Lew NL. Death risk in haemodialysis patients: The predictive value of commonly measured variables and an evaluation of death rate differences between facilities. Am J Kidney Dis 1990; 15: 458-482

3   Bommer J, Locatelli F, Satayathum S et al. Association of predialysis serum bicarbonate levels with risk of mortality and hospitalisation in the Dialysis Outcomes and Practice Patterns Study (DOPPS). Am J Kidney Dis 2004;44:661-71

4   Graham KA, Reaich D, Channon SM et al. Correction of acidosis in haemodialysis decreases whole-body protein degradation. J Am Soc Nephrol 1997;8: 632-7

5   Lefebvre A, de Verneioul MC, Gueris J et al. Optimal correction of acidosis changes progression of dialysis osteodystrophy. Kidney Int 1989;36:1112-8

6   Graham KA, Hoenich NA, Tarbit M et al. Correction of acidosis in haemodialysis patients increases the sensitivity of the parathyroid glands to calcium. J Am Soc Nephrol;1997;8:627-31

7   Williams AJ, Dittmer ID, McArley A, Clarke J. High bicarbonate dialysate in haemodialysis patients: effects on acidosis and nutritional status. Nephrol Dial Transplant 1997;12:2633-7

8   Movilli E, Zani R, Carli O et al. Correction of metabolic acidosis increases serum albumin concentrations and decreases kinetically evaluated protein intake in haemodialysis patients: a prospective study. Nephrol Dial Transplant 1998;13:1719-22

Guideline 6.4 DIAL-HD
Pre-dialysis serum potassium should be between 3.5 and 6.5 mmol/l in HD patients (good practice).

Audit measure 8
Cumulative frequency curves of pre-dialysis serum potassium concentration.

Rationale
The risk of developing hyperkalaemia is inversely related to renal function. Hyperkalaemia is a common indication for emergency dialysis in patients already on HD and 3-5% of deaths in dialysis patients have been attributed to hyperkalaemia (1). Non-compliance with the HD prescription and/or diet is the main cause of hyperkalaemia in dialysis patients but drug therapy, such as ACE

inhibitors, angiotensin receptor blockers, non-steroidal anti-inflammatory drugs, beta-blockers and potassium supplements, may be implicated.

HD is the most reliable and immediate treatment of hyperkalaemia in dialysis patients and the serum potassium will usually fall by 1 mmol/l after the first hour of HD and a further 1mmol/l after the next 2 hours of HD (2). The rate of potassium removal may be enhanced by an increase in the dialyser blood flow rate, a rise in the dialysate bicarbonate concentration or a decrease in the dialysate potassium concentration (3). A recent review paper (4) has highlighted the benefit in performing an urgent electrocardiogram to guide management in patients with serum potassium above 6mmol/l and help decide which patients need emergency administration of intravenous 10ml 10% calcium chloride over 5 minutes. A Cochrane meta-analysis of non-dialytic emergency interventions for hyperkalaemia concluded that intravenous glucose with insulin and nebulised or inhaled salbutamol were effective in reducing serum potassium levels but the studies were limited by the absence of data on cardiac arrhythmia or mortality rates (3). Whilst the combination of salbutamol and intravenous glucose with insulin was probably more effective than either therapy alone the evidence for efficacy of intravenous bicarbonate or potassium exchange resins in this Cochrane review of randomized or quasi-randomised trials was equivocal and neither should be used as monotherapy for severe hyperkalaemia .

Hypokalaemia towards the end or immediately after HD is not uncommon and may be corrected by relaxing dietary potassium restriction or, if necessary, by increasing the dialysate potassium concentration (5, 6).

References

1   Morduchowicz G, Winkler J, Drazne E et al. Causes of death in patients with end-stage renal disease treated by dialysis in a centre in Israel. Isr J Med Sci 1992;28:776-9

1   Ahmed J, Weisberg LS. Hyperkalaemia in dialysis patients. Semin Dial 2001;14:348-56

2   Mahoney BA, Smith WAD, Lo DS, Tsoi K, Tonelli M, Clase CM. Emergency interventions for hyperkalaemia (Cochrane Review). In: The Renal health Library, 2005. Oxford: Update Software Ltd (www.update-software.com)

3   Alfonzo AVM, Isles C, Geddes C, Deighan C. Potassium disorders - clinical spectrum and emergency management. Resuscitation 2006;70:10-25

4   Wiegand CF, Davin TD, Raij L, Kjellstard CM. Severe hypokalemia induced by hemodialysis. Arch Int Med 1981;141: 167-70

5   Bleyer AJ, Hartman J, Brannon PC et al. Characteristics of sudden death in hemodialysis patients. Kidney Int 2006; 69: 2268-73

Guideline 6.5 DIAL-HD

Pre-dialysis serum phosphate should be between 1.1 and 1.8mmol/l. (good practice).

Guideline 6.6 DIAL-HD
Pre-dialysis serum calcium, adjusted for serum albumin, should be within the normal range (good practice).

Guideline 6.7 DIAL-HD
Pre-dialysis serum albumin corrected calcium x phosphate product should be less than 4.8 mmol2/l2. (good practice).

Guideline 6.8 DIAL-HD
Serum PTH levels should be more than twice and less than 4 times the upper limit of normal for the intact PTH assay used.

Serum PTH levels do not need to be performed routinely more often than every 3 months **(good practice).**

Audit measure 9
Cumulative frequency curves of pre-dialysis serum calcium, phosphate, calcium x phosphate product and PTH concentrations

Guideline 6.9 DIAL-HD
Serum aluminium concentration should be measured every three months in all patients receiving oral aluminium containing phosphate binders (good practice).

Guideline 6.10 DIAL-HD
Pre-dialysis haemoglobin concentration should be 10.5-12.5g/dl. (evidence).

The target haemoglobin concentration should be at least 11g/dl to allow for the normal distribution around the mean haemoglobin value of the patient population and intraindividual variation of laboratory measurements and hydration status.

Audit measure 10
Cumulative frequency curves of pre-dialysis haemoglobin concentration.

Rationale
The detailed rationale for these guidelines (Guidelines 6.5 - 6.10) is available in the "Complications of Chronic Kidney Disease" module of the updated RA guidelines, 2007. Defined ranges of several biochemical variables (Guidelines 6.5 - 6.8) have been associated with better survival rates of HD patients in large observational studies (1-11). These laboratory indices, which have been associated with improved patient outcomes in large datasets of hospital HD patients, were used to develop the audit measures and clinical practice guidelines for thrice weekly HD within this update. The laboratory based guidelines that are recommended for thrice weekly HD in this update are consistent with previous versions of the Renal Association HD guidelines, the UK Renal Registry, Scottish Renal Registry and Quality Improvement Scotland (QIS) and also with the clinical

practice guidelines for HD that have been generated in Europe, Australasia and North America. There are no evidence-based guidelines for these laboratory parameters in patients with end-stage chronic renal failure on other than thrice weekly HD or in patients with dialysis dependent acute renal failure. The standards set in this module apply equally to home and hospital HD patients. Similar audit measures have been used in the preparation of previous UK Renal Registry Annual Reports (12).

References

6   Lowrie EG, Lew NL. Death risk in haemodialysis patients: The predictive value of commonly measured variables and an evaluation of death rate differences between facilities. Am J Kidney Dis 1990; 15: 458-482

7   Iseki K, Uehara H, Nishime K et al. Impact of the initial levels of laboratory variables on survival in chronic dialysis patients. Am J Kidney Dis 1996; 28:541–548

8   Iseki K, Miyasato F, Tokuyama K et al. Low diastolic blood pressure, hypoalbuminemia, and risk of death in a cohort of chronic haemodialysis patients. Kidney Int 1997; 51:1212–1217

9   Owen WF, Lew NL, Lowrie EG et al. The urea reduction ratio and serum albumin concentration as predictors of mortality in patients undergoing hemodialysis. N Engl J Med 1993; 329:1001–1006

10   Block GA, Hulbert-Shearon TE, Levin NW et al. Association of serum phosphorus and calcium x phosphorus product with mortality risk in chronic haemodialysis patients: a national study. Am J Kidney Dis 1998; 31:607-617

11   Young EW, Albert JM, Satayathum S et al. Predictors and consequences of altered mineral metabolism: The Dialysis Outcomes and Practice Study. Kidney Int 2005; 67: 1179-1187

12   Block GA, Klassen PS, Lazarus JM et al. Mineral metabolism, mortality and morbidity in maintenance hemodialysis. J Am Soc Nephrol 2004; 15: 2208-2218

13   Kestenbaum B, Sampson JN, Rudser KD et al. Serum phosphate levels and mortality risk among people with chronic kidney disease. J Am Soc Nephrol 2005; 16:520-528

14   Noordzij M, Korevaar JC, Boeschoten EW et al. The Kidney Disease Outcomes Quality Initiative (K/DOQI) guideline for bone metabolism and disease in CKD: association with mortality in dialysis patients. Am J Kidney Dis 2005; 46:925-932

15   Robinson BM, Joffe MM, Berns JS et al. Anaemia and mortality in haemodialysis patients: Accounting for morbidity and treatment variables updated over time. Kidney Int 2005; 68:2323-2330

16   Agarawal R. Hypertension and survival in chronic haemodialysis patients - past lessons and future opportunities. Kidney Int 2005; 67:1-13

17   The Renal Association UK Renal Registry, The Seventh Annual Report, December 2004. (www.renalreg.com)

Guideline 6.11 DIAL-HD
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 audited (good practice).

Audit measure 11
The incidence of symptomatic hypotensive episodes during dialysis sessions.

Rationale

Dialysis-related hypotension is the most frequent symptomatic complication of HD and historically in some studies occurred in more than 15% of HD sessions (1). As well as being extremely unpleasant hypotensive episodes can shorten the time on dialysis and reduce the efficiency of delivered dialysis (1). Dialysis-related hypotension also has been shown to be an independent predictor of poor patient survival (2). 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 (3). Patients experiencing frequent dialysis-related hypotension are at higher risk of death (4) and this may be because dialysis-related hypotension is a marker for severe cardiac disease (5). Adjustment of the rate of fluid removal, dialysate sodium concentration and dialysate temperature during dialysis, or combinations thereof, can reduce the incidence of this complication (6-9). Interdialysis weight gains can be reduced if dietary sodium intake is kept below 100 mmol/day and thereby reduce thirst and subsequent fluid intake. Dialysate sodium modeling or ramping can reduce intradialysis cramps and hypotension but incurs the risk of greater problems with interdialysis thirst, weight gain and hypertension (7). A recent randomized trial of intradialytic blood volume monitoring and conventional monitoring showed no difference in weight, blood pressure or frequency of dialysis-related complications whilst hospitalization and mortality rates were lower in the group assigned to conventional monitoring (10). However the conventional monitoring group had atypically low hospitalisation and mortality rates in comparison with local prevalent HD patients (10). There is also the question of increased cost if on-line monitoring of changes in relative blood volume (by measurement of changes in optical density of blood) is used to assess dry body weight in an attempt to reduce the incidence of intradialytic hypotension (11). A recent systematic review of 22 studies has concluded that a reduction in dialysate temperature is effective in decreasing the incidence of intradialytic hypotension without affecting dialysis adequacy (12). Increasing the dialysis treatment time to reduce the fluid ultrafiltration rate or decreasing the dialysate fluid temperature are the most reliable and practical methods of reducing the incidence of intradialytic hypotension without causing adverse sequelae.

References

1   Ronco C, Brendolan A, Milan M et al. Impact of biofeedback-induced cardiovascular stability on haemodialysis tolerance and efficiency. Kidney Int 2000; 58:800–808

2   Shoji T, Tsubakihara Y, Fujii M et al. Haemodialysis-associated hypotension as an independent risk factor for two-year mortality in haemodialysis patients. Kidney Int 2004; 66:1212-1220

3   Daugirdas JT. Dialysis hypotension: a hemodynamic analysis. Kidney Int 1991; 39:233–46

4   Koch M, Thomas B, Tschope W et al. Survival and predictors of death in dialysed diabetic patients. Diabetologia 1993; 36:1113–1117

5   Poldermans D, Man in 't Veld AJ, Rambaldi R. Cardiac evaluation in hypotension-prone and hypotension-resistant haemodialysis patients. Kidney Int 1999; 56:1905–1911

6   Dheenan S, Henrich WL. Preventing dialysis hypotension: A comparison of usual protective maneuvres. Kidney Int 2001; 59:1175–1181

7   Sang GLS, Kovithavongs C, Ulan R, Kjellstrand K. Sodium ramping in hemodialysis: A study of beneficial and adverse effects. Am J Kidney Dis 1997; 29: 669-677

8   Yu AW, Ing TS, Zabaneh RJ, Daugirdas JT. Effect of dialysate temperature on central hemodynamics and urea kinetics. Kidney Int 1995; 48: 237-243

9   Maggiore Q, Pizzarelli F, Santoro A et al. The effects of control of thermal balance on vascular stability in hemodialysis patients: results of the European randomised clinical trial. Am J Kidney Dis 2002; 40: 280-290

10   Reddan DN, Szczech LA, Hasseblad V et al. Intradialytic blood volume monitoring in ambulatory haemodialysis patients: a randomised trial. J Am Soc Nephrol 2005; 16:2162-2169

11   Rodriguez HJ, Domenici R, Diroll A, Goykhman I. Assessment of dry weight by monitoring changes in blood volume during haemodialysis using Crit-Line. Kidney Int 2005; 68:854-861

12   Selby NM, McIntyre CW. A systematic review of the clinical effects of reducing dialysate fluid temperature. Nephrol Dial Transplant 2006; 21: 1883-98

7 Vascular access (Guidelines 7.1 - 7.16)

Guideline 7.1 DIAL-HD

To preserve veins for creation of vascular access venepuncture or insertion of peripheral venous cannulae should be avoided in the forearm or arm of all patients with advanced renal failure whenever possible (good practice).

Rationale

To preserve veins for vascular access all healthcare staff and patients with progressive renal failure should be aware of the need to avoid venepunctures and insertion of peripheral intravenous catheters in the forearm and elbow, especially the cephalic veins of the non-dominant arm (1).

References

2   National Kidney Foundation-K/DOQI Clinical Practice Guidelines for vascular access 2000. Am J Kidney Dis 2000; 37: 1 Supplement 1 S137-S180 (www.kidney.org/professionals/kdoqi/guidelines.cfm)

Guideline 7.2 DIAL-HD

The preferred mode of vascular access for haemodialysis patients is a native arteriovenous fistula (good practice).

Audit measure 12

The proportion of prevalent patients on long-term haemodialysis who use an arterio-venous fistula, arterio-venous graft and tunneled or non-tunneled central venous catheters as the mode of vascular access.

Rationale

A native arteriovenous fistula (AVF) is the preferred access in the great majority of HD patients as it produces the highest flows, minimises sepsis and has the greatest longevity (1-4). 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 tunneled central venous catheters and 18.4 per 1000 dialysis sessions with temporary central venous catheters (5). The CHOICE study of the effect of the type of vascular access on survival among 616 incident patients showed that the adjusted relative risk of death compared with AVF was 1.2 for an arteriovenous graft and 1.5 for a central venous catheter (6). Clinical assessment of the upper limbs prior to access placement has been used successfully to indicate if Doppler ultrasound is required to select the most appropriate site for access creation (7). A radio-cephalic and then brachial-cephalic fistula is the preferred order of access placement whenever possible. Thereafter a transposed brachial-basilic vein fistula or arterio-venous synthetic graft should be considered before relying on a central venous catheter for long-term vascular access. In a small number of patients with severe cardiac dysfunction fistula construction may be contra-indicated since a high flow AVF can contribute to high output cardiac failure. An active program of AVF creation in an USA centre using vascular

mapping increased the prevalence of functional AVF from 24% to 44% which was associated with a significant reduction in hospitalization rates (p< 0.001) (8).

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% (1). This study reports on data from the UK, France, Germany, Italy and Spain (1). Quality Improvement Scotland has recommended that at least 70% of prevalent chronic HD patients should have a functioning AVF whilst the National Service Framework Part 1 has indicated that 90% of prevalent chronic HD patients should have an AVF for vascular access. The National Dialysis Access Survey showed that only 69.9% of prevalent HD patients in the UK in 2005 had definitive access for dialysis (65.6% AVF and 4.3% arteriovenous graft) (9). Rather than specify a minimum proportion of HD patients who should have a functioning AVF this guideline emphasizes that as many patients as possible should have a functioning AVF in preference to other forms of vascular access and the prevalent form of vascular access should be audited in each unit at least annually.

References

1. Pisoni RL, Young EW, Dykstra DM et al. Vascular access use in Europe and the United States; Results from the DOPPS. Kidney Int 2002; 61:305–316

2. Woods JD, Port FK. The impact of vascular access for haemodialysis on patient morbidity and mortality. Nephrol Dial Transplant 1997; 12: 657-659

3. Nassar GM, Ayus JC. Infectious complications of haemodialysis access. Kidney Int 2001; 60:1–13

4. Hirth RA, Turenne MN, Woods JD et al. Predictors of type of vascular access in haemodialysis patients. JAMA 1996; 276: 1303-1308

5. Stevenson KB, Adcox MJ, Mallea MC et al. Standardized surveillance of haemodialysis vascular access infections: 18-month experience at an outpatient, multifacility, haemodialysis centre. Infect Control Hosp Epidemiol 2000; 21: 200-203

6. Astor BC, Eustace JA, Powe NR et al. Type of vascular access and survival among incident haemodialysis patients: the Choices for Healthy Outcomes in Caring for ESRD (CHOICE) Study. J Am Soc Nephrol 2005; 16:1449-1455

7. Wells AC, Fernando B, Butler A et al. Selective use of ultrasonographic vascular mapping in the assessment of patients before haemodialysis access surgery. Br J Surg 2005; 92:1439-1443

8. Ackad A, Simonian GT, Steel K et al. A journey in reversing practice patterns: a multidisciplinary experience in implementing DOQI guidelines for vascular access. Nephrol Dial Transplant 2005; 20:1450-1455

9. The Renal Association UK Renal Registry, The Eighth Annual Report, December 2005, Chapter 6. (www.renalreg.com Renal Association Standards & Audit Subcommittee)

Guideline 7.3 DIAL-HD

There should be enough dedicated theatre sessions for access surgery to provide one session per week for every 120 patients on dialysis. With this level of access surgery provision no patient on dialysis, including those who present late, should wait more than four weeks for fistula construction (good practice).

Audit measure 13
The number of dedicated renal failure access surgery sessions per 120 dialysis patients.

Rationale
Vascular access surgery for haemodialysis needs to improve in the UK. The UK has been lagging behind most countries in Europe with regard to the proportion of HD patients using natural AVFs. 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. Secondly, most renal units in the UK have insufficient access to surgical support including theatre sessions dedicated to renal failure surgery. One dedicated access surgery session per 120 dialysis patients has been identified as best practice but only 4 of the 10 adult renal units in Scotland achieved this audit standard of access surgery provision in 2003 (1). This level of access surgery provision should decrease the waiting time for access surgery, which is particularly important for patients who are either already on dialysis or predicted to start dialysis within a few months.

References
1   Report of NHS Quality Improvement Scotland (www.nhshealthquality.org)

Guideline 7.4 DIAL-HD
Patients should undergo fistula creation between 6 and 12 months before haemodialysis is expected to start to allow time for adequate maturation of the fistula or time for a revision procedure if the fistula fails or is inadequate for use (good practice).

Audit measure 14
The dates of first referral to nephrology, referral for creation of vascular access and creation of first vascular access and the date and mode of vascular access at the initiation of dialysis should be recorded and audited in all incident chronic haemodialysis patients.

Rationale
Ideally patients should undergo AVF creation between 6 and 12 months before HD is expected to start to allow time for adequate maturation of the AVF or time for a revision procedure if the AVF fails or is inadequate for use (1). The frequent need for revision surgery is emphasized by a meta-analysis of 8 prospective and 30 retrospective studies of the outcome of radiocephalic AVF creation that showed an initial failure rate of 15% and primary and secondary patency rates of radio-cephalic AVF at 1 year of 62% and 66% respectively (2). Patients more than 65 years old were shown to have a relative risk of 1.7 of an AVF failing to mature compared to patients less than 65 years old (3). The recommendation that an AVF should be created early in the year before dialysis is anticipated to start is supported further by a retrospective study of 5924 Canadian HD patients which showed that the subgroup (n=1240) with fistula creation more than 4 months before beginning dialysis had a lower risk of sepsis and death, primarily related to

their reduced use of central venous catheters for vascular access (4). Patients with timely creation of an AVF ready for use at the start of HD were shown to have better survival than patients who started HD with a catheter and converted to an AVF who in turn had improved survival rates in comparison to patients who continued to use a catheter for vascular access (5).

The creation of vascular access ready for use at the initiation of HD in the majority of patients would be a major step in achieving improved patient outcomes on dialysis (6). The Dialysis Outcomes and Practice Pattern Study (DOPPS) has identified that there is wide variation in the time delay among European countries between referral to a nephrologist and creation of an arterio-venous fistula (7) and improvements in planning the creation of vascular access should be a high priority in the UK. The National Dialysis Access Survey indicated that only 31% of incident HD patients started dialysis with definitive access and of those known to a renal unit for at least a year only half started HD with definitive access (8). This survey also indicated that avoidable delay in referral for vascular access in patients known to a renal unit for at least 6 months was common; only 33% of this patient group were referred for access creation more than 6 months before starting dialysis only 48% were referred for vascular access surgery more than 3 months before starting dialysis (8). The temporal relationships between first nephrology referral, referral for and creation of vascular access and mode of functioning access at the time of starting HD should be audited to promote quality improvements in the planning of vascular access.

References

1   National Kidney Foundation-K/DOQI Clinical Practice Guidelines for vascular access 2000. Am J Kidney Dis 2000; 37: 1 Supplement 1 S137-S180 (www.kidney.org/professionals/kdoqi/guidelines.cfm)

2   Rooijens PP, Tordoir JH, Stijnen T et al. Radiocephalic wrist arteriovenous fistula for haemodialysis: meta-analysis indicates a high primary failure rate. Eur J Endovasc Surg 2004; 28:583-589

3   Lok CE, Oliver MJ, Su J et al. Arteriovenous fistula outcomes in the era of the elderly dialysis population. Kidney Int 2005; 67:2462-2469

4   Oliver MJ, Rothwell DM, Fung K et al. Late creation of vascular access for hemodialysis and increased risk of sepsis. J Am Soc Nephrol 2004; 15: 1936-1942

5   Ortega T, Ortega F, Diaz-Corte C et al. The timely construction of arteriovenous fistulae: a key to reducing morbidity and mortality and to improving cost management. Nephrol Dial Transplant 2005; 20:598-603

6   Pereira B. Optimisation of pre-ESRD care: The key to improved dialysis outcomes. Kidney Int 2000; 57:351-365

7   Rayner HC, Pisoni RL, Gillespie BM et al. Creation, cannulation and survival of arterio-venous fistulae - data from the Dialysis Outcomes and Practice Patterns Study (DOPPS). Kidney Int 2003; 63:323-330.

8   The Renal Association UK Renal Registry, The Eighth Annual Report, December 2005, Chapter 6. (www.renalreg.com Renal Association Standards & Audit Subcommittee)

Guideline 7.5 DIAL-HD

The time to first cannulation of an AVF should be a minimum of 1 month and preferably at least 2 months after creation (good practice).

Rationale

First cannulation may be considered between 2 and 4 weeks after creation if this is the alternative to insertion of a central venous catheter and a nephrologist or experienced haemodialysis nurse has assessed that the fistula has matured adequately for use for dialysis.

The time required before an AVF is considered to have adequate blood flow rates and vessel wall "maturity" to allow safe, repeated cannulation for HD varies in different countries from less than 2 weeks to more than 3 months (1). A shorter maturation time would reduce dependence on temporary vascular access but may reduce AVF survival. The use of a central venous catheter for HD and nephrology referral within a month before starting dialysis were both predisposing factors to first cannulation within 28 days after creation of an AVF in a DOPPS study of first AVF in 642 incident HD patients (2). Both of these DOPPS studies also showed that maturation times of less than 14 days before first cannulation of an AVF were associated with lower AVF survival (1,2). An Italian multi-centre study of first AVF in incident patients confirmed the strong association between late referral, use of central venous catheters for vascular access and earlier first cannulation time and showed that shorter maturation times of an AVF before first cannulation were associated with lower unassisted and assisted patency rates (3). This contrasts with the findings of the DOPPS report (1) that showed no difference in fistula failure rates whether the fistula was first cannulated between 15 and 28 days or between 43 and 84 days. In an Italian multicentre study first cannulation within 1 month of creation was associated with a 94% higher risk of primary failure (p < 0.001) and within 2 weeks was associated with 111% increased risk of failure (p < 0.009) (3). These observational studies lend support to the current recommendation in the K/DOQI guidelines that there should be a minimum of 1 month and preferably at least 2 months before first utilization of an AVF (4) except when the fistula has matured adequately before 4 weeks and using the fistula is the alternative to insertion of a central venous catheter. A recent commentary on the available evidence has concluded that cannulation of newly created fistulae within 2 weeks should be avoided, first cannulation between 2 and 4 weeks may be possible in individual cases if the fistula is deemed mature by the nephrologist or surgeon and it is probably safe to cannulate a fistula after 4 weeks of creation (5). Conversely a mature access that has required surgical or radiological intervention to restore adequate blood flow rates may be cannulated as soon as clinically indicated.

References
1   Rayner HC, Pisoni RL, Gillespie BM et al. Creation, cannulation and survival of arterio-venous fistulae - data from the Dialysis Outcomes and Practice Patterns Study (DOPPS). Kidney Int 2003; 63:323-330

2   Pisoni RL, Young EW, Dykstra DM et al. Vascular access use in Europe and the United States; Results from the DOPPS. Kidney Int 2002; 61:305–316

3   Ravani P, Brunori G, Mandolfo S et al. Cardiovascular comorbidity and late referral impact arterio-venous fistula survival: a prospective multicentre study. J Am Soc Nephrol 2004; 15:204-209

4   National Kidney Foundation-K/DOQI Clinical Practice Guidelines for vascular access 2000. Am J Kidney Dis 2000; 37: 1 Supplement 1 S137-S180 (www.kidney.org/professionals/kdoqi/guidelines.cfm)

5   Saran R, Pisoni RL, Young EW. Timing of first cannulation of arteriovenous fistula: are we waiting too long? Nephrol Dial Transplant 2005; 20:688-690

Guideline 7.6 DIAL-HD

At least 65% of patients presenting more than three months before initiation of dialysis should start HD with a usable native arteriovenous fistula (good practice).

Audit measure 14
The dates of first referral to nephrology, referral for creation of vascular access and creation of first vascular access and the date and mode of vascular access at the initiation of dialysis should be recorded and audited in all incident chronic haemodialysis patients.

Rationale
With this audit measure the proportion of incident patients on long-term haemodialysis who present more than three months before initiation of dialysis and have permanent vascular access at the start of dialysis can continue to be assessed.

The time period between fistula creation and first use of a fistula for HD varies considerably amongst European countries from less than 1 month up to 4 months. Only 47% of UK patients started dialysis with a functioning AVF, compared with the European average of 66% in the DOPPS (1). The National Dialysis Access Survey indicated that only 31% of incident HD patients in the UK in April 2005 started dialysis with definitive access (2). If European practices for vascular access were extended to the UK at least 65% of patients presenting more than three months before initiation of dialysis should be able to start HD with a usable native AVF. Four of the 10 adult renal units in Scotland achieved this standard when audited in 2003 (3).

References
1   Pisoni RL, Young EW, Dykstra DM et al. Vascular access use in Europe and the United States; Results from the DOPPS. Kidney Int 2002; 61:305–316.

2   The Renal Association UK Renal Registry, The Eighth Annual Report, December 2005, Chapter 6. (www.renalreg.com Renal Association Standards & Audit Subcommittee)

3   Report of NHS Quality Improvement Scotland (www.nhshealthquality.org)

Guideline 7.7 DIAL-HD

Investigation of the AVF or graft to assess for evidence of arterial or venous stenoses or access recirculation is required if there is a significant fall in the blood flow rate that can be achieved, a reduction in delivered dialysis dose or a persistent rise in venous pressure in sequential dialysis sessions (good practice).

Rationale

There is no consensus on the effectiveness of interventions to prolong the use-life of AVFs and grafts for vascular access (1,2). The rate of AVF thrombosis is 0.2-0.4 per patient year compared with 0.8-1.2 per patient year for synthetic arteriovenous grafts (3). Clinical monitoring of the fistula or graft function can help detect the vascular access at risk. A significant fall in the blood flow rate that can be achieved, a reduction in delivered dialysis dose or a persistent rise in venous pressure at the same blood flow rate and using the same gauge of needle in sequential dialysis sessions should prompt further investigation of the AVF or graft to assess for evidence of arterial or venous stenoses or access recirculation (3-5). If there is evidence of greater than 50% stenosis of the fistula percutaneous angioplasty or surgical revision should be considered to prolong the use-life of the fistula. Interventions once thrombosis of a fistula has occurred have not shown good results unless there is no history of fistula dysfunction and the fistula has become occluded recently. Routine surveillance of fistula blood flow rates has not yet been shown to enhance the use-life of fistulae and regular access monitoring may or may not extend the use-life of arteriovenous grafts (6-10). The K/DOQI guidelines recommend that all patients undergo a program of regular access monitoring preferably by assessing access flow rates combined with prompt imaging and elective correction of stenosis in low flow accesses (11). However recent randomized studies suggest that radiological and/or surgical intervention is more likely to be clinically effective and cost-effective if assessment of the AVF or graft for intervention is restricted to patients with the aforementioned clinical indicators of poor vascular access function (6, 10).

References

1   Sands SS. Vascular access monitoring improves outcomes. Blood Purif 2005; 23:45-49

2   Paulson WD. Access monitoring does not really improve outcomes. Blood Purif 2005; 23:50-56

3   Woods JD, Turenne MN, Strawderman RL et al. Vascular access survival among incident haemodialysis patients in the United States. Am J Kidney Dis 1997; 30: 50-57

4   Sherman RA. The measurement of dialysis access recirculation. Am J Kidney Dis 1993; 22: 616-621

5   Tattersall JE, Farrington K, Raniga PD et al. Haemodialysis recirculation detected by the three-sample method is an artefact. Nephrol Dial Transplant 1993; 8: 60-63

6   Shahin H, Reddy G, Sharafuddin M et al. Monthly access flow monitoring with increased prophylactic angioplasty did not improve fistula patency. Kidney Int 2005; 68:2352-2361

7   Malik J, Slavikowa M, Svobodova J, Tuka V. Regular ultrasonagraphic screening significantly prolongs patency of PTFE grafts. Kidney Int 2005; 67:1554-1558

8   Besarab A, Sullivan KL, Ross RP et al. Utility of intra-access pressure monitoring in detecting and correcting venous outlet stenoses prior to thrombosis. Kidney Int 1995; 47: 1364-1373

9   Schwab SJ, Raymond JR, Saeed M et al. Prevention of hemodialysis fistula thrombosis: Early detection of venous stenoses. Kidney Int 1989; 36: 707-711

10   Moist LM, Churchill DN, House AA et al. Regular monitoring of access flow compared with monitoring of venous pressure fails to improve graft survival. J Am Soc Nephrol 2003; 14:2645-2653

11   National Kidney Foundation-K/DOQI Clinical Practice Guidelines for vascular access 2000. Am J Kidney Dis 2000; 37: 1 Supplement 1 S137-S180 (www.kidney.org/professionals/kdoqi/guidelines.cfm)

Guideline 7.8 DIAL-HD

All patients should be evaluated for a secondary arteriovenous access after each episode of access failure (good practice).

Rationale

To maximize the use of arteriovenous access for HD the NKF-KDOQI guidelines on vascular access have recommended that the patient should be assessed fully for secondary arteriovenous access creation after every episode of AVF or graft loss (1). This approach has been shown to be successful in subsequent reports (2).

References
1   National Kidney Foundation-K/DOQI Clinical Practice Guidelines for vascular access 2000. Am J Kidney Dis 2000; 37: 1 Supplement 1 S137-S180 (www.kidney.org/professionals/kdoqi/guidelines.cfm)

2   Asif A, Unger SW, Briones P et al. Creation of secondary arteriovenous fistulas: maximising fistulas in prevalent hemodialysis patients. Semin Dial   2005; 18:420-424

Guideline 7.9 DIAL-HD

As few HD patients as possible should rely on central venous catheters for vascular access.

As an audit measure less than 20% of patients on long-term HD should use tunneled or non-tunneled central venous catheters as the form of vascular access **(good practice).**

Audit measure (2.12 DIAL-HD)

The proportion of prevalent patients on long-term haemodialysis who use an arterio-venous fistula, arterio-venous graft and tunneled or non-tunneled central venous catheters as the mode of vascular access.

Rationale

Insertion of a non-cuffed (temporary) or cuffed tunneled (semi-permanent) central venous catheter is an unfortunate necessity for many patients who need to start HD before there has been time for creation or maturation of an AVF. Once established on HD via a catheter some patients may, despite counseling, refuse to

have an AVF constructed. Use of dialysis catheters and PTFE grafts for dialysis is associated with a greatly increased risk of hospitalisation and sepsis than use of AVFs (1-4). In a large prospective cohort of incident HD patients the relative risk of bacteraemia was 1.95 for HD with tunneled catheters and 1.05 for HD with grafts when compared to patients with an AVF (4). Infection-related hospitalization in the HEMO study was also shown to be more frequent in patients relying on central venous catheters for vascular access but was not reduced by the use of high flux dialysers or a higher dialysis dose (5). Patients with central venous dialysis catheters and consequent risk of catheter-related infection have been shown to require higher doses of erythropoietin stimulating agents (ESAs) to maintain similar or slightly lower mean haemoglobin values (6). Vascular access using dialysis catheters is also associated with a higher risk of central venous stenoses and lower blood flow rates. Loss of patency of central venous catheters is common (7). Each unit should have standardized protocols to attempt thrombolysis of tunneled central venous catheters using either urokinase or thromboplastin activator (7). Using a program of vascular access counseling, vascular mapping, a full range of surgical techniques and salvage procedures the majority of patients using tunneled dialysis catheters were provided with a functional arteriovenous access, mainly AVFs (8). The National Dialysis Access Survey of prevalent HD patients in the UK on 31st March 2005 showed that 27.5% of the 13,260 patients were using non-tunneled central venous catheters for vascular access and a further 2.0% were using non-tunneled venous catheters (9).

References

1   Chesser AM, Baker LR. Temporary vascular access for first dialysis is common, undesirable and usually avoidable. Clin Nephrol 1999; 51:228–232

2   Schwab SJ, Beathard G. The haemodialysis catheter conundrum: hate living with them, but can't live without them. Kidney Int 1999; 56:1–17

3   Schwab SJ, Harrington JT, Singh A et al. Vascular access for haemodialysis. Kidney Int 1999; 55:2078–90

4   Ishani A, Collins AJ, Herzog CA, Foley RN. Septicaemia, access and cardiovascular disease in dialysis patients: the USRDS Wave 2 study. Kidney Int 2005; 68:311-318

5   Allon M. Depner TA, Radeva M, et al. Impact of dialysis dose and membrane on infection-related hospitalisation and death: Results of the HEMO study. J Am Soc Nephrol 2003; 14: 1863-1870

6   Roberts TL, Obrador GT, St Peter WL et al. Relationship among catheter insertions, vascular access infections and anaemia management in haemodialysis patients. Kidney Int 2004; 66:2429-2436

7   National Kidney Foundation-K/DOQI Clinical Practice Guidelines for vascular access 2000. Am J Kidney Dis 2000; 37: 1 Supplement 1 S137-S180 (www.kidney.org/professionals/kdoqi/guidelines.cfm)

8   Asif A, Cherla G, Merrill D et al. Conversion of tunneled haemodialysis catheter-consigned patients to arteriovenous fistula. 2005; 67:2399-2406

9   The Renal Association UK Renal Registry, The Eighth Annual Report, December 2005, Chapter 6. (www.renalreg.com Renal Association Standards & Audit Subcommittee)

Guideline 7.10 DIAL-HD
Cuffed, tunneled double-lumen central venous catheters are preferred if temporary vascular access is likely to be needed for more than 3 weeks. Non-cuffed double-lumen catheters should be used if temporary vascular access for haemodialysis is predicted to be required for less than 3 weeks (good practice).

Rationale
The incidence of bacteraemia in a prospective study of non-tunneled HD catheters was 5% after 3 weeks of placement in the internal jugular vein (1). Cuffed, tunneled rather than non-tunneled central venous catheters are preferred if vascular access is likely to be required for more than 3 weeks since tunneled catheters are associated with a lower rate of infections and can provide higher blood flow rates (2-5). This approach permits immediate vascular access for a period of months with multiple options of site of catheter insertion.

References
1   Oliver MJ, Callery SM, Thorpe KE et al. Risk of bacteraemia from temporary hemodialysis catheters by site of insertion and duration of use: A prospective study. Kidney Int 2000; 58:2543-2545
2   Moss AH, Vasilakis C, Holley JL et al. Use of a silicone dual-lumen catheter with a Dacron cuff as a long-term vascular access for hemodialysis patients. Am J Kidney Dis 1990; 16: 211-215
3   Bander SJ, Schab SJ. Central venous angioaccess for hemodialysis and its complications. Semin Dial 1992; 5:121-128
4   Lee T, Barker J, Allon M. Tunnelled catheters in hemodialysis patients: reasons and subsequent outcomes. Am J Kidney Dis 2005; 46: 501-508
5   National Kidney Foundation-K/DOQI Clinical Practice Guidelines for vascular access 2000. Am J Kidney Dis 2000; 37: 1 Supplement 1 S137-S180 (www.kidney.org/professionals/kdoqi/guidelines.cfm)

Guideline 7.11 DIAL-HD
The preferred insertion site for central venous catheters is the internal jugular vein and the catheter should not be placed on the same side as a planned or maturing upper limb arterio-venous access, whenever possible (good practice).

Rationale
Central venous catheters should be inserted in the internal jugular vein, preferably the right internal jugular vein, since this site provides a more direct route to the superior vena caval-atrial junction than the left side and is more likely to be contralateral to the non-dominant arm, which is more frequently used for first attempts at fistula and graft placement (1). The subclavian veins should be avoided as sites of catheter placement to reduce the risk of compromising the successful use of an AVF or graft in the ipsilateral arm (2). Nevertheless central venous stenosis remains relatively common in the era of minimal use of subclavian venous catheters and was observed on venography in 55 of 133 patients with poor vascular access, 52 of whom had had previous dialysis

catheters (3). Femoral venous catheters may be used for emergency HD without need for radiological confirmation of catheter position or exclusion of complications. However femoral dialysis catheters are prone to problems with patency and dislodgement if used in patients who are not bed bound and non-cuffed femoral catheters should be removed within 1 week to reduce the risk of infection (1). The incidence of bacteraemia in a prospective study of non-tunneled femoral HD catheters was 11% after 1 week of placement (4).

References
1   National Kidney Foundation-K/DOQI Clinical Practice Guidelines for vascular access 2000. Am J Kidney Dis 2000; 37: 1 Supplement 1 S137-S180 (www.kidney.org/professionals/kdoqi/guidelines.cfm)

2   Barrett N, Spences S, McIvor J, Brown EA. Subclavian stenosis: A major complication of subclavian dialysis catheters. Nephrol Dial Transplant 1988;   3: 423-425

3   MacRae JM, Ahmed A, Johnson N et al. Central vein stenosis: a common problem in patients on hemodialysis. ASAIO J 2005; 51:77-81

4   Oliver MJ, Callery SM, Thorpe KE et al. Risk of bacteraemia from temporary hemodialysis catheters by site of insertion and duration of use: A prospective study. Kidney Int 2000; 58:2543-2545

Guideline 7.12 DIAL-HD
All renal units should use real-time ultrasound to guide insertion of central venous catheters (good practice).

Rationale
Real-time ultrasound is recommended to guide insertion of central venous catheters to improve the success rate of placement and reduce insertion-related complications (1). With the use of ultrasound guidance relatively inexperienced operators can insert internal jugular dialysis catheters reliably and safely (2). Fluoroscopy screening is mandatory for optimum localization of the catheter tip of tunneled central venous catheters (1).

References
1   National Kidney Foundation-K/DOQI Clinical Practice Guidelines for vascular access 2000. Am J Kidney Dis 2000; 37: 1 Supplement 1 S137-S180 (www.kidney.org/professionals/kdoqi/guidelines.cfm)

2   Geddes CC, Walbaum D, Fox JG, Mactier RA. Insertion of internal jugular temporary haemodialysis cannulae by direct ultrasound guidance - a   prospective comparison of experienced and inexperienced operators. Clin Nephrol 1998; 50:320-325

Guideline 7.13 DIAL-HD
All renal units should have protocols to ensure that full barrier precautions are followed during insertion of temporary and tunneled central venous dialysis catheters. (Evidence)

Rationale

The risk of infection with central venous catheters can be reduced by using full barrier precautions during catheter insertion and ensuring that all catheter connections and disconnections are performed under aseptic conditions by trained staff (1). Catheter removal is usually indicated in all episodes of bacteraemia related to temporary central venous dialysis catheters and in episodes of bacteraemia related to tunneled catheters associated with exit-site or tunnel infection, persistent fever after commencing antibiotics or metastatic infection (2).

References
1   Raad II, Hohn DC, Gilbreath BJ et al. Prevention of central venous catheter-related infections using maximal sterile barrier precautions during insertion.

2   Infect Control Hosp Epidemiol 1994; 15: 231-238

3   Allon M. Dialysis catheter-related bacteraemia: treatment and prophylaxis.   Am J Kidney Dis 2004; 45: 779-791 (review)

Guideline 7.14 DIAL-HD

All central venous catheter connections and disconnections should be performed under aseptic conditions by trained staff (good practice).

Rationale

Prevention of vascular access-related infection should be a high priority in the renal unit. Each unit should have strict concordance with infection control measures and protocols whenever cannulating AVFs and grafts or manipulating central venous catheters to connect/disconnect to the patient's bloodstream. Because of the relatively high risk of catheter-related infection all connections and disconnections should be performed under aseptic conditions by fully trained staff wearing a face mask or visor and preferably with the patient wearing a surgical mask to decrease the risk of infection from nasal carriage of Staphylococcus aureus (1). Local protocols may incorporate infection control measures that previous randomized studies have shown can lead to a reduction in catheter-related infections. These procedures include the use of dry gauze instead of transparent dressings (2), disinfection with chlorhexidine solutions instead of povidone-iodine (3), topical mupirocin, Medihoney or antiseptic at the catheter exit site (4-7) and citrate or antibiotics with heparin as a catheter locking solution (8-10). The need for effective procedures to prevent catheter-related infections has been reviewed recently (11).

References
1   Yu VL, Goetz A, Wagener M et al. Staphylococcus aureus carriage rate of patients receiving long-term haemodialysis. New Engl J Med 1986; 315: 91-   96

2   Conly JM, Grieves K, Peters B. A prospective, randomised study comparing transparent and dry gauze dressings for central venous catheters. J Infect Dis 1989; 159: 310-319

3   Chaiyakunapruk N, Veenstra DL, Lipsky BA, Saint S. Chlorhexidine compared with povidone-iodine solution for vascular catheter-site care: a meta-analysis. Ann Intern Med 2002; 136:792-801

4   Maki DG, Band JD. A comparative study of polyantibiotic and iodophor ointments in prevention of vascular catheter-related infection. Am J Med 1981; 70: 739-744

5   Levin A, Mason AJ, Jindal KK et al. Prevention of haemodialysis subclavian vein catheter infections by topical povidone-iodine. Kidney Int 1991; 40: 934-938

6   Maki DG, Ringer M, Alvarado CJ. Prospective randomised trial of povidone-iodine, alcohol and chlorhexidine for prevention of infection associated with central venous and arterial catheters. Lancet 1991; 338: 339-343

7   Sesso R, Barbosa D, Leme IL et al. Staphylococcus aureus prophylaxis in haemodialysis patients using central venous catheter: effect of mupirocin ointment. J Am Soc Nephrol 1998; 9:1085-1092

8   Weijmer MC, van den Dorpel MA, Van de Ven PJ et al. Randomised clinical trial comparison of trisodium citrate 30% and heparin as catheter-locking solution in hemodialysis patients. J Am Soc Nephrol 2005; 16: 2769-2777

9   Johnson DW, van Eps C, Mudge DW et al. Randomised, controlled trial of topical exit-site application of honey (Medihoney) versus mupirocin for prevention of catheter-associated infection in haemodialysis patients. J Am Soc Nephrol 2005; 16: 1456-1462

10   Dogra GK, Herson H, Hutchison B et al. Prevention of tunneled haemodialysis catheter-related infections using catheter-restricted filling with gentamicin and citrate: a randomised controlled study. J Am Soc Nephrol 2002; 13:2133-2139

11   McIntyre CW, Hulme IJ, Taal M, Fluck RJ. Locking of tunneled haemodialysis catheters with gentamicin and heparin. Kidney Int 2004; 66:801-85

12   Jaber BL. Bacterial infections in haemodialysis patients: Pathogenesis and prevention. Kidney Int 2005; 67:2508-2519

Guideline 7.15 DIAL-HD

Peripheral and central line blood cultures should be taken prior to starting antibiotics in all cases of suspected catheter-related infection (good practice).

Rationale

Multiple sets of blood cultures taken from both the central venous catheter and peripheral veins increase the diagnostic yield in patients with catheter-related bacteraemia. As well as helping treatment by identifying the causative organism(s) and antimicrobial sensitivities the higher positive culture rate facilitates microbiological surveillance within the renal unit and hospital, especially the incidence of antibiotic resistant organisms such as MRSA (1,2). The National Dialysis Access Survey indicated that the incidence of Staphylococcus aureus and MRSA bacteraemia during 2004 averaged 13 and 4 episodes per 100 HD patients per year, respectively (3).

References

1   Allon M, Radeva M, Bailey J et al HEMO Study Group. The spectrum of infection-related morbidity in hospitalised haemodialysis patients. Nephrol Dial Transpant 2005; 20: 1180-1186

2   National Kidney Foundation-K/DOQI Clinical Practice Guidelines for vascular access 2000. Am J Kidney Dis 2000; 37: 1 Supplement 1 S137-S180 (www.kidney.org/professionals/kdoqi/guidelines.cfm)

3   The Renal Association UK Renal Registry, The Eighth Annual Report, December 2005, Chapter 6. (www.renalreg.com Renal Association Standards & Audit Subcommittee)

Guideline 7.16 DIAL-HD
All HD units should collect and audit data on the form of vascular access in use in incident and prevalent haemodialysis patients and the rates of infection per 1000 patient days using central venous catheters, arterio-venous grafts and fistulae (good practice).

Audit measure 15
The rates of bacteraemia (and specifically the rates of MRSA bacteraemia) observed per 1000 patient days using central venous catheters, polytetrafluoroethylene (PTFE) grafts and arterio-venous fistulae.

Rationale
Comparative audit of the different forms of vascular access that are used for HD and the incidence of access related infections should help identify to what extent the above guidelines have been achieved and promote good clinical practice.

8 Access to and withdrawal from dialysis (Guidelines DIAL-HD 8.1 - 8.5)

Guideline 8.1 DIAL-HD
All patients with advanced renal failure (eGFR <30ml/min), who have a life expectancy of more than 3 months, should be considered for renal replacement therapy and should be referred to a nephrologist (good practice).

Rationale
Estimated GFR (eGFR) is used to report measurements of renal function whenever the GFR is below 90 ml/min (England & Wales) or below 60ml/min (Scotland). The MDRD equation based on age, sex, race and serum creatinine is the preferred and most practical method of estimating GFR in advanced renal failure although the mean of 24 hour urinary urea and creatinine clearances is utilized in assessing the adequacy of peritoneal dialysis and estimating residual renal function in HD patients. The routine reporting of eGFR should promote universal access for consideration of RRT. This approach helps to identify patients with significant chronic kidney disease and promote timely referral to a nephrologist. Avoiding late referral provides the opportunity for intervention to prevent or reduce the complications of renal failure and time to plan for renal replacement therapy. Patients who have been under nephrology care for more than 1 month are more likely to start HD using an AVF (1). A retrospective analysis of 109,321 incident HD patients in the USA found that the relative risk of death of patients with no pre-dialysis nephrology care was 1.51 and the relative risk of death of patients with one or two months pre-dialysis nephrology care was 1.23 when compared with patients with at least 3 months nephrology pre-dialysis care (2).

Now that every patient with advanced chronic renal failure, regardless of age and co-morbidity, is at least considered as a potential recipient of dialysis, questions of whether or not to start dialysis have assumed increasing importance. Until recently, acceptance or non-acceptance for dialysis in the UK was predetermined by accidental and occasionally deliberate failure of referral so that the decision not to initiate renal replacement therapy was taken by family members or referring physicians alone, rather than in conjunction with a nephrologist (3). It is often difficult to decide if patients with major comorbidity will or will not benefit from starting dialysis, even if referred well in advance of needing renal replacement therapy, and there have been few studies of the decision not to start dialysis (4). Nevertheless the problems of late referral or non-referral can be avoided if all patients who have advanced chronic renal failure (eGFR <30ml/min) and a predicted life expectancy of at least 3 months are considered for RRT and are referred to a nephrologist.

References

1   Rayner HC, Besarab A, Brown WW et al. Vascular access results from the Dialysis Outomes and Practice Patterns Study (DOPPS): performance against Kidney Disease Outcomes Quality Initiative (K/DOQI) Clinical Practice Guidelines. Am J Kidney Dis 2004; 44 (Suppl 3): 22-26

2   Khan SS, Xue JL, Kazmi WH et al. Does pre-dialysis nephrology care influence patient survival after initiation of dialysis? Kidney Int 2005; 67:1038-1046

3   Challah S, Wing AJ, Bauer R et al. Negative selection of patients for dialysis in the United Kingdom. Br Med J 1984; 288:1119–1122

4   Hirsch DJ, West ML, Cohen AD, Jindal KK. Experience with not offering dialysis to patients with a poor prognosis. Am J Kidney Dis 1994; 23:463–466

Guideline 8.2 DIAL-HD

If there is no medical contraindication the choice of initial dialysis modality should be based on patient choice (good practice).

Rationale

The provision of patient choice and equity of access to dialysis and transplantation have been reinforced by the National Service Framework Part 1 Dialysis and Transplantation (1). There has been only one small prospective randomized trial comparing HD and peritoneal dialysis in incident patients and this showed no differences in short-term patient outcomes in the small numbers of patients that could be enrolled into the study but the study data were not powered adequately to reach any other conclusion (2). Local access to hospital HD should not be an influential factor in the patient reaching a decision about their preferred initial mode of dialysis. In the absence of evidence that either HD or peritoneal dialysis provide superior patient outcomes the selection of initial dialysis modality should be based on the patient's choice after full education about the different forms of renal replacement therapy that are available, including home HD and live donor and cadaveric transplantation (3).

References

1   The National Service Framework for Renal Services Part 1: Dialysis and Transplantation, Department of Health, London, UK, January 2004. (www.doh.gov.uk/nsf/renal/index.htm)

2   Korevaar JC, Feith GW, Dekker FW et al. Effects of starting with haemodialysis compared with peritoneal dialysis in patients new on dialysis treatment: A randomised controlled trial. Kidney Int 2003; 64 :2222-2228

3   National Institute of Clinical Excellence. Full guidance on home compared with hospital haemodialysis for patients with end-stage renal failure October 2002 (www.nice.org.uk)

Guideline 8.3 DIAL-HD

After full education and counseling a small proportion of patients may opt for active non-dialytic management of advanced chronic kidney disease, including nutritional, medical and psychological support rather than plan to initiate dialysis. The numbers of patients not taken on to dialysis and the reasons for this decision should be subject to audit (good practice).

Audit measure 16

The proportion of patients with advanced renal failure (CKD stage 5) who are treated with conservative medical therapy.

Rationale

The decision whether to start or not to start RRT may be difficult (1). It is impossible to set quantitative standards in this difficult area of care, but principles of action can be enunciated and agreed. All patients who are found to have advanced renal failure should be considered for dialysis, and the patient's age, social circumstances or required level of community support should not 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. 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 (2). 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 to start or not to start RRT 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 (3). Some 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. Guidelines on shared decision-making in the initiation or withdrawal of dialysis have been developed (4).

Two approaches may be taken when a patient presents in uraemia whose ability to cope with, and to enjoy and benefit from dialysis 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.

References
1   Tobe SW, Senn JS (for the End-Stage Renal Disease Group). Foregoing renal dialysis: case study and review of ethical issues. Am J Kidney Dis 1996; 28:147–153

2   Campbell ML. Terminal care of ESRD patients forgoing dialysis. ANNA J 1991; 18:202–204

3   Cohen LM, Germian M, Poppel DM et al. Dialysis discontinuation and palliative care. Am J Kidney Dis 2000; 36:140–144

4   Galla JH. Clinical practice guideline on shared decision-making in the appropriate initiation of and withdrawal from dialysis. J Am Soc Nephrol 2000; 11:1340-1342

Guideline 8.4 DIAL-HD
Renal replacement therapy should be commenced when a patient with an eGFR < 15ml/min/1.73m2 has symptoms or signs of uraemia, fluid overload or malnutrition in spite of medical therapy and be considered carefully when an asymptomatic patient has an eGFR < 6ml/min/1.73m2 (good practice).

Audit measure 17
Record of the serum creatinine, the estimated GFR and co-morbidity at initiation of chronic renal replacement therapy (dialysis or transplantation).

Rationale
There are no criteria based on definitive evidence to advise when to start dialysis. In the absence of severe hyperkalaemia or pericarditis there is no definitive evidence to indicate when an asymptomatic patient with advanced renal failure should initiate dialysis. There is consensus that patients should start dialysis when

they develop symptoms or signs of fluid overload, hypertension, poor nutrition or uraemia which cannot be controlled by medical therapy such as high dose diuretics, even if their estimated residual renal function is relatively high. Nutritional status and dietary protein intake decrease progressively as renal function declines (1). The medical treatment of the complications of renal failure such as anaemia has improved in the past 10 years and this may explain recent reports of a lack of any relationship between the presence or absence of traditional symptoms of uraemia and residual renal function in patients with stage 5 chronic kidney disease (2). The patients with a higher haemoglobin concentration had fewer symptoms (2) and so relying on the onset of symptoms may result in patients starting dialysis too late. Conversely studies in the Netherlands and Scotland comparing patients who started dialysis at two different levels of residual renal function have shown no advantage to patient survival if adjustments are made for lead time bias in the group of patients starting dialysis with higher residual renal function (3-6). In the multicentre prospective Netherlands study 94 of the 253 incident patients began dialysis later than recommended in the US NKF KDOQI guideline and the adjusted benefit in survival after 3 years on dialysis was 2.5 months in the timely starter group (4). However this benefit may be attributed to lead-time bias since the average delay in initiation of dialysis in the late starter group was 4.1 months. A randomized prospective study to compare 3 year morbidity and mortality after initiating dialysis when patients have a Cockcroft and Gault creatinine clearance of 10-14ml/min/1.73m2 or 5-7ml/min/1.73m2 is underway (IDEAL study) (7).

With the evidence that nutritional status deteriorates progressively as renal function declines (1) and symptoms of advanced renal failure are not closely related to the degree of residual renal function in the modern era (2) it is appropriate that international guidelines have attempted to identify the level of residual renal function at which an asymptomatic patient should initiate dialysis. The above considerations fit well with the European Best Practice Guidelines which recommended that renal replacement therapy should commence when a patient with an eGFR < 15ml/min/1.73m2 has symptoms or signs of uraemia, fluid overload or malnutrition in spite of medical therapy or before an asymptomatic patient has an eGFR < 6ml/min/1.73m2 (8).

References
1   Ikizler TA, Greene JH, Wingarde RL et al. Spontaneous dietary protein intake during progression of chronic renal failure. J Am Soc Nephrol 1995; 6: 1386-1391

2   Curtis BM, Barrett BJ, Jindal K et al. Canadian survey of clinical status at dialysis initiation 1998-1999: a multicentre prospective study. Clin Nephrol 2002; 58:282-288

3   Traynor JP, Simpson K, Geddes CC et al. Early initiation of dialysis fails to prolong survival in patients in end-stage renal failure. J Am Soc Nephrol 2002; 13:2125-2132

4   Korevaar JC, Jansen MA, Dekker FW et al. When to initiate dialysis: effect of proposed US guidelines on survival. Lancet 2001; 358:1046-1050

5   Korevaar JC, Dekker FW, Krediet RT. Initiation of dialysis: is the problem solved by NECOSAD? Nephrol Dial Transplant 2003; 18: 1228-1229

6   Termorshuizen F, Korevaar JC, Dekker FW et al. Time trends in initiation and dose of dialysis in end-stage renal disease patients in The Netherlands. Nephrol Dial Transplant 2003; 18: 552-558

7   Cooper BA, Branley P, Bulfone L et al. The Initiating Dialysis Early and Late
     (IDEAL) study: study rationale and design. Perit Dial Int 2004; 24: 176-181

8   European Best Practice Guidelines for haemodialysis Part 1. Nephrol Dial Transplant
     2002; 17: Supplement 7 S1-S111
     (http://ndt.oupjournals.org/content/vol17/suppl_7/index.shtml).

Guideline 8.5 DIAL-HD

Any decision to discontinue haemodialysis 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 (good practice).

Rationale

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, or irrecoverable neurological deficit after a cerebrovascular event makes it difficult or impossible to ascertain what the patient's own feelings and wishes might be (1). In practice, the decision to withdraw dialysis has much in common with decision not to start a patient on dialysis. This is because caring staff, patients and relatives all face similar difficult judgements and decisions about the likely quality and quantity of life on dialysis. A similar process to that outlined in deciding whether or not to plan to start dialysis (see above) should be followed when assessing if withdrawal of dialysis is appropriate. There is one study from the UK that suggests that withdrawal from dialysis plays a major role (17%) in overall death rates on dialysis (2), as it does in the USA and Canada (3,4). Recent data from the Dialysis Outcomes and Practice Patterns Study have shown that the rate for withdrawal from HD is 3.5 per 100 patient-years and that not surprisingly "do not resuscitate" orders are associated with older age and nursing home residence (5). In a recent UK study withdrawal of dialysis was the commonest cause of death (38%) in the group of patients commencing dialysis when more than 75 years old (6). Withdrawal of dialysis is an increasing cause of death in dialysis patients and the date of the decision and the reasons for it should be recorded in the patient's casenotes (7). Renal units should develop guidelines for withdrawal of dialysis that include liaison with palliative care and community services.

References
1   Singer J, Thiel EC, Naylor D et al. Life-sustaining treatment preferences of
     hemodialysis patients: implications for advance directives. J Am Soc Nephrol 1995;
     6:1410–1417

2   Catalano C, Goodship THJ, Graham KA et al. Withdrawal of renal replacement
     therapy in Newcastle upon Tyne: 1964-1993. Nephrol Dial Transplant 1996; 11:133–
     139

3   Cohen LM, McCue JD, Germain M, Kjellstrand CJ. Dialysis discontinued: a good
     death? Arch Intern Med 1995; 155:42–47

4   Friedman EA. The best and worst times for dialysis are now. ASAIO J 1994; 40:107–108

5   Fissell RB, Bragg-Gresham JL, Lopez AA et al. Factors associated with "do not resuscitate" orders and rates of withdrawal from haemodialysis in the international DOPPS. Kidney Int; 2005 68: 1282-1288

6   Munshi SK, Vijayakumar N, Taub NA et al. Outcome of renal replacement therapy in the very elderly. Nephrol Dial Transplant 2001; 16:1721-1722

7   McLean AM. Dialysis treatment withdrawal – Legal aspects (UK). Nephrol Dial Transplant 1998; 13:1152-1153

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