Peritoneal dialysis clinical practice guidelines for children and adolescents

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This document has been adapted for paediatric patients from the Renal Association Standards for Peritoneal Dialysis in Adults (www.renal.org/guidelines/index.html) written by Prof Simon Davies. Although the large majority of standards for adults also apply to children, there are some areas that differ significantly. There are also some important areas not covered in the adult standards, such as the specific requirements of the growing child and the need for a structured process for transfer of adolescents to adult services. For this reason, the renal association adult guidelines have been adapted where necessary. All standards that are taken directly from the adult guidelines are shown in regular font and paediatric guidelines are in italics.

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Summary of Clinical Practice Guidelines for Peritoneal Dialysis

1. Equipment and Resources

1.1 The dialysis unit should have sufficient specialist support staff to fulfil the criteria listed by the Renal Workforce Planning Group 2002.

Paediatric standard 1: PD for children should take place in specialised paediatric centres able to provide multidisciplinary support

1.2 Access to other paediatric sub-speciality services should be easily available.

1.3 Adolescents need to be prepared for transfer to adult services. It is important that the process is begun in good time, and that there is an appropriate transfer policy that is agreed by both the referring and receiving centres.

Paediatric standard 2: A transfer process for adolescents must be in place and agreed by referring and receiving units

1.4 Peritoneal dialysis should be delivered in the context of a comprehensive and integrated service for renal replacement therapies, including haemodialysis (including temporary backup facilities), transplantation and conservative care. Both continuous ambulatory peritoneal dialysis (CAPD) and automated peritoneal dialysis (APD), in all its forms should be available. Dedicated PD nursing staff (1 W.T.E. per 20 patients) should be part of the multidisciplinary team

1.5 All equipment used in the delivery and monitoring of therapies should comply with the relevant standards for medical electrical equipment [BS-EN 60601-2-39:1999, BS5724-2-39:1998, IEC 60601-2-39:1998, Particular requirements for the safety – specification for peritoneal dialysis equipment]. Tubing sets and catheters should carry the "CE" mark to indicate that the item conforms to the essential requirements of the Medical Devices Directive (93/42/EEC) and that its conformity has been assessed in accordance with the directive.

1.6 Fluids for peritoneal dialysis are required to satisfy the current European quality standards as indicated in the European good manufacturing practice and the European Pharmacopoeia Monograph "Solutions for Peritoneal Dialysis". Manufacturing facilities are required to meet the relevant standards (ISO 9001/2 and EN 46001/2). Product registration files must be submitted to and product approval given by the Medicines Control Agency.

1.7 The use of disconnect systems should be standard unless clinically contraindicated.

1.8 Biocompatible PD solutions (normal pH, low concentrations of glucose degradation products) should be used in patients experiencing infusion pain. Otherwise they should be considered in patients who are likely to remain on PD more than 4 years.

2. Preparation for Peritoneal Dialysis

2.1 All patients should, where possible, be adequately prepared for renal replacement therapy and this should include receiving information and education about PD treatment, delivered by experienced members of the MDT who have paediatric renal training. Patients commencing RRF in an unplanned fashion for whatever reason should receive this information once appropriate.

2.2 Where possible, timing of PD catheter insertion should be planned to accommodate patient convenience, commencement of training between 10 days and 6 weeks and before RRT is essential to enable correction of early catheter-related problems without the need for temporary haemodialysis.

2.3 Dialysis centres should have a dedicated team approach to catheter insertion. This is more important than the type of catheter or the implantation technique used. *In children, the most important thing is that the surgeon undertaking the procedure is appropriately trained and skilled.*

Paediatric standard 3: Peritoneal dialysis catheter insertion should be undertaken by appropriately trained and skilled staff

2.4 Peri-operative catheter care and catheter complications (leaks, hernias, obstruction) should be managed according to the International Society of Peritoneal Dialysis guidelines

3. Solute Clearance

3.1 Both residual urine and peritoneal dialysis components of small solute clearance should be measured at least six monthly or more frequently if clinically indicated. Both urea and/or creatinine clearances can be used to monitor dialysis adequacy and should be interpreted within the limits of the methods.

3.2 A combined urinary and peritoneal Kt/Vurea of 1.7/week or a creatinine clearance of 50L/week/1.73m2 should be considered as minimal treatment doses. The dose should be increased in patients experiencing uraemic symptoms.

Paediatric standard 4: A Kt/Vurea of 1.7/week and creatinine clearance 50L/week/1.73m^2 should be the minimum for children

4. Ultrafiltration and fluid management

4.1 Peritoneal membrane function should be monitored regularly (6 weeks after commencing treatment and at least annually or when clinically indicated) using a peritoneal equilibration test (PET) or equivalent. Daily urine and peritoneal ultrafiltration volumes, with appropriate correction for overfill, should be monitored at least six-monthly.

4.2 Dialysis regimens resulting in fluid reabsorption should be avoided. Patients with high or high average solute transport, at greatest risk of this problem, should be considered for APD and icodextrin.

4.3 Dialysis regimens resulting in routine utilisation of hypertonic (3.86%) glucose exchanges should be avoided. Where appropriate this should be achieved by using icodextrin or diuretics

4.4 Treatment strategies that favour preservation of renal function should be adopted where possible. These include avoidance of episodes of dehydration, and the use of diuretics, ACEi and ARBs

4.5 Anuric patients who consistently achieve a daily ultrafiltration of less than 750 ml/1.73m^2 should be closely monitored and the benefits of modality switch considered

5. Infectious complications

5.1 Prevention Strategies

5.1.1 PD units should undertake regular audit of their peritonitis and exit-site infection rates, including causative organism, treatment and outcomes. They should enter into active dialogue with their microbiology department and infection control team to develop optimal local treatment and prevention protocols

Paediatric standard 5: All units should collect and audit data on the incidence of exit site infection

Paediatric standard 6: All units should collect and audit data on the incidence of peritonitis

5.1.2 Flush-before-fill dialysis delivery systems should be used

5.1.3 Patients should undergo regular revision of their technique and receive intensified training if this is below standard

5.1.4 Initial catheter insertion should be accompanied by antibiotic prophylaxis

5.1.5 Invasive procedures should be accompanied by antibiotic prophylaxis and emptying the abdomen of dialysis fluid for a period commensurate with the procedure

5.1.6 Topical antibiotic administration should be used to reduce the frequency of *Staph. aureus* and Gram negative exit-site infection and peritonitis

5.2 Treatment

5.2.1 Exit site infection is suggested by pain, swelling, crusting, erythema and serous discharge; purulent discharge always indicates infection. Swabs should be taken for culture and initial empiric therapy should be with oral antibiotics that will cover *S. aureus and P. aeruginosa*

5.2.2 Methicillin resistant organisms (MRSA) will require systemic treatment (e.g vancomycin) and will need to comply with local infection control policies.

5.2.3 Initial treatment regimens for peritonitis should include cover for bacterial Gram positive and Gram negative organisms until result of culture and antibiotic sensitivities are obtained.

6. Metabolic Factors

6.1 Standard strategies to optimise diabetic control should be used; these should be complemented by dialysis prescription regimens that minimise glucose, including glucose free solutions (icodextrin and amino-acids), where possible.

6.2 Central obesity can worsen or develop in some PD patients. The risk of this problem, and associated metabolic complications, notably increased atherogenicity of lipid profiles and insulin resistance, can be reduced by avoiding excessive glucose prescription and using icodextrin.

6.3 Awareness of the effects of Icodextrin on assays for estimation of amylase and glucose (using glucose dehydrogenase) should be disseminated to patients, relatives, laboratory and clinical staff

7. Laboratory and clinical indices

7.1 Monitoring of biochemical and haematological parameters should be performed monthly or at each clinic visit if less often than monthly

7.2 Serum bicarbonate concentrations should be between 20 and 26mmol/l.

7.3 Serum potassium should be between 3.5 and 6.5 mmol/l.

7.4 Serum phosphate should be within, and preferably nearer to the 50th centile, for the age appropriate normal range.

7.5 Serum calcium, adjusted for serum albumin, should be within the age appropriate normal range.

7.6 Serum albumin corrected calcium x phosphate product should be less than 4.8 $mmol^2/l^2$.

7.7 The optimum range for serum PTH levels is controversial. There is emerging evidence that levels should be maintained at less than twice the upper limit of normal for the intact PTH assay used.

7.8 Serum aluminium concentration should be measured every three months in all patients receiving oral aluminium hydroxide. No patient whose ferritin level is <100 µg/l should have a serum aluminium concentration >60 µg/l (2.2 µmol/l).

7.9 Pre-dialysis haemoglobin concentration should be greater than the lower limit of the age appropriate normal range.

7.10 Ferritin levels should be between 100 and 800 mcg/L

7.11 Height and head circumference (in those under 2 years of age) should be measured monthly, and the rate of growth checked against normal centiles. Dry weight should be estimated regularly, at least monthly or every 2 weeks in infants. Pubertal stage should be assessed every 3 months in those over 10 years of age, or sooner if clinically indicated.

Paediatric standard 7: Growth and development should be measured regularly as part of the assessment of dialysis adequacy

Paediatric standard 8: Dry weight needs regular reassessment in the growing child

7.12 An assessment of school progress, both in the hospital and locally, should be made annually.

7.13 Blood pressure should be maintained within the age appropriate normal range.

8. Access to and withdrawal from dialysis

8.1 All children with chronic kidney disease should be considered for renal replacement therapy by stage 4 CKD. CKD should be suspected in children with: bilateral renal anomalies on antenatal scans (many children with CKD are now diagnosed antenatally); a creatinine above the normal age appropriate range; bilateral renal defects on scans e.g. for UTI; a family history of CKD; persistent proteinuria; or after an episode of acute renal failure. All such children should be referred to a paediatric nephrologist.

Early referral provides the opportunity for delaying the progression of CKD by treating hypertension and proteinuria, for optimising growth and preventing renal bone disease. Importantly, it also allows for timely forward planning for renal replacement therapy.

8.2 If there is no medical contraindication the choice of initial dialysis modality should be based on patient choice. *However, although patient choice is paramount, guidance from unit staff is necessary: venous access can be difficult to achieve and maintain in those less than 5 years of age, and needling of a fistula can be particularly difficult in an uncooperative patient. For these reasons, as well as social ones, PD is recommended in young children.*

8.3 After full education and counselling a small proportion of families 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.

8.4 Renal replacement therapy should commence when a patient with an eGFR < 15ml/min/1.73m^2 has symptoms or signs of uraemia, fluid overload, malnutrition *and/or growth failure* in spite of medical therapy <u>or</u> before an asymptomatic patient has an eGFR < 6ml/min/1.73m^2.

8.5 Any decision to discontinue dialysis should be made jointly by the patient (when age appropriate) and their carers and the responsible consultant nephrologist and renal team and the family practitioner. 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.

9. Summary of the most important paediatric clinical practice guidelines

Paediatric standard 1
PD for children should take place in specialised paediatric centres able to provide multidisciplinary support (good practice)

Paediatric standard 2
A transfer process for adolescents must be in place and agreed by referring and receiving units (good practice)

Paediatric standard 3
Peritoneal dialysis catheter insertion should be undertaken by appropriately trained and skilled staff (good practice)

Paediatric standard 4
A Kt/Vurea of 1.7/week and creatinine clearance 50L/week/1.73m^2 should be the minimum for children (good practice)

Paediatric standard 5
All units should collect and audit data on the incidence of exit site infection (good practice)

Paediatric standard 6
All units should collect and audit data on the incidence of peritonitis (good practice)

Paediatric standard 7
Growth and development should be measured regularly as part of the assessment of dialysis adequacy (good practice)

Paediatric standard 8
Dry weight needs regular reassessment in the growing child (good practice)

Summary of Audit Measures for Peritoneal Dialysis

1. *Adequacy of staffing levels (medical, surgical, radiological, anaesthetic, nursing, dietetic, play therapists, psychosocial, pharmacy, and schooling)*
2. *Presence of a transfer process for adolescents that is agreed by referring and receiving units*
3. Availability of modality choice
4. Monitoring of modality switching
5. Systems in place to check medical equipment
6. Systems in place to ensure purchase of dialysis fluid fulfil legal requirements
7. Use of non-standard systems with documentation of clinical indication
8. Use of biocompatible solutions and indication for use
9. Audit of care pathway for dialysis preparation to include information given, when and who delivers it.
10. Audit of care pathway for catheter insertion to include timeliness and need for temporary haemodialysis
11. Catheter complications and their resolution
12. Frequency of solute clearance (residual and peritoneal) estimation
13. Cumulative frequency curves for the total solute clearance
14. Frequency of measurement of membrane function, residual urine and peritoneal ultrafiltration volume
15. Identify patients with fluid reabsorption in long dwell
16. Routine annual audit of infection prevention strategies
17. Routine annual audit of infection outcomes (exit site and peritonitis rates)
18. Cumulative frequency curves of plasma bicarbonate
19. Processes in place to increase awareness of interference of assays by icodextrin metabolites
20. *Cumulative frequency curves of pre-dialysis serum calcium, phosphate calcium x phosphate product and PTH concentration*
21. *Cumulative frequency curves of pre-dialysis haemoglobin concentration*
22. *Height, weight, head circumference and pubertal progression*
23. *School attendance*
24. *Cumulative frequency curves of BP predialysis*

Rationale for clinical practice guidelines for paediatric patients on peritoneal dialysis

Introduction

In the UK peritoneal dialysis is usually the first choice dialysis modality because it interferes less with the child's day-to-day life, particularly in those who may live a long way from their paediatric renal unit. The ratio of children on peritoneal dialysis compared to haemodialysis is approximately 2:1; of the 173 children who received dialysis in the UK in 2003, 62% were on peritoneal dialysis (Report of the Paediatric Renal Registry, Seventh Annual Report of the UK Renal Registry, December 2004).

The National Service Framework Part 1: Dialysis and Transplantation is a document that is applicable to both adult and paediatric services (1). It stresses the importance of a family-centred approach to the care of children. It also stresses the importance of the team needed to provide such services i.e. medical, surgical, anaesthesiology, radiology, nursing, dietetic, play therapy, psychological, social work and pharmacists, all of whom need the special skills necessary to treat such children. However, this document was not designed to set standards for clinical care.
Owing to the small numbers of children with CKD stage 5, and, in particular, the very small numbers on dialysis, there are very few analyses to help in the management of paediatric patients, and paediatric nephrologists have to rely on extrapolation of data from adult studies. Clinical practice guidelines for adults on peritoneal dialysis have been developed in Australasia, Canada, Europe and the USA as well as the UK (2-11). Guidelines for children on peritoneal dialysis have also been published (12-17).

These guidelines serve to identify and promote best practice in the delivery of haemodialysis and have set clinical standards to allow comparative audit of the key aspects of the haemodialysis 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 haemodialysis (2-4).

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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)
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9. 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)
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1. Equipment and Resources

1.1 Peritoneal Dialysis should be delivered in the context of a comprehensive and integrated service for renal replacement therapies, including haemodialysis (including temporary backup facilities), transplantation and conservative care. Both continuous ambulatory peritoneal dialysis (CAPD) and automated peritoneal dialysis (APD), in all its forms should be available. Dedicated PD nursing staff (1 W.T.E. per 20 patients) should be part of the multidisciplinary team (Good Practice)

Evidence from observational studies or registry data, with all its limitations, indicates that peritoneal dialysis (PD) used in the context of an integrated dialysis programme is associated with good clinical outcomes, certainly comparable to haemodialysis in the medium term (HD) (1-5). The only randomised study (NECOSAD), comparing HD to PD as a first treatment showed no differences in 2 year quality adjusted life years or 5 year mortality, but the number randomised was insufficient to generalize this observation; notably, most patients in this national study had sufficient life-style preferences related to one modality to decline randomisation (6). PD has a significant technique failure rate however, so patients need to be able to switch treatment modality (to either temporary or permanent HD) in a timely manner, which has implications for HD capacity.

PD modalities (CAPD v. APD) have a different impact on life-style; one randomised study found that APD creates more time for the patient to spend with family or continue employment but is associated with reduced quality of sleep (7). APD is the preferred modality for children. There are medical indications for APD (see sections 2, 3 and 4), but generally modality choice is a lifestyle issue.

The success of a PD programme is dependent upon specialized nurses with appropriate skills in assessing and training patients for PD, monitoring of treatment and with sufficient resources to provide continued care in the community. A recent randomised trial of more intensive training has shown that this reduces peritonitis risk (8) (see section 5). Several studies have documented the benefits of home visits in identifying new problems, reducing peritonitis and non-compliance (9-11). It is usually possible for a WTE PD nurse to deliver this quality of care with a case load of 20 PD patients (see recommendations of the National Renal Workforce Planning Group, 2002).

Audit measure 1 Adequacy of staffing levels (medical, surgical, radiological, anaesthetic, nursing, dietetic, play therapists, psychosocial, pharmacy, and schooling)

Audit measure 2 Presence of a transfer process for adolescents that is agreed by referring and receiving units

Audit measure 3 Availability of modality choice
Audit measure 4 Monitoring of modality switching

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1.2 All equipment used in the delivery and monitoring of therapies should comply with the relevant standards for medical electrical equipment [BS-EN 60601-2-39:1999, BS5724-2-39:1998, IEC 60601-2-39:1998, Particular requirements for the safety – specification for peritoneal dialysis equipment]. Tubing sets and catheters should carry the "CE" mark to indicate that the item conforms to the essential requirements of the Medical Devices Directive (93/42/EEC) and that its conformity has been assessed in accordance with the directive.

Audit Measure 5: Systems in place to check medical equipment

This is a legal requirement

1.3 Fluids for peritoneal dialysis are required to satisfy the current European quality standards as indicated in the European good manufacturing practice and the European Pharmacopoeia Monograph "Solutions for Peritoneal Dialysis". Manufacturing facilities are required to meet the relevant standards (ISO 9001/2 and EN 46001/2). Product registration files must be submitted to and product approval given by the Medicines Control Agency.

Audit Measure 6: Systems in place to ensure purchase of dialysis fluid fulfil legal requirements.

1.4 The use of disconnect systems should be standard unless clinically contraindicated (evidence).

Audit Measure 7: Use of non-standard systems with documentation of clinical indication

Disconnect systems have been shown through randomised trials to be associated with a lower peritonitis risk, especially in infections due to touch contamination (1)

1. 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(5):1-166.

1.5 Biocompatible PD solutions (normal pH, low concentrations of glucose degradation products) should be used in patients experiencing infusion pain (evidence). Otherwise they should be considered in patients who are likely to remain on PD more than 4 years

Audit Measure 8: Use of biocompatible solutions and indication for use

A minority of patients commencing PD will experience infusion pain, often severe enough to consider discontinuing the therapy. A double blind randomised study demonstrated that pain could be prevented by using a normal pH, bicarbonate-lactate buffered dialysis fluid (Physioneal) (1). Subsequent clinical experience has found that the benefit of this more biocompatible solution on infusion pain results in immediate and sustained benefit, and is probably applicable to other biocompatible solutions.

The evidence of clinical benefit from the routine use of biocompatible solutions is more controversial. Standard solutions are clearly bio-incompatible, with low pH (~5.2), lactate rather than bicarbonate buffer, high osmolality and high concentrations of glucose which also result in high concentrations of glucose degradation products (GDPs). Many *in vitro* and *ex vivo* studies have demonstrated the relative toxicity of these solutions, with all of the biocompatible features playing their part (2-7). There is also strong observational evidence that (a) detrimental functional changes to the membrane occur with time on treatment, which are more exaggerated in patients using solutions with high glucose concentration early in their time on therapy (8, 9) and (b) morphological changes occur that are related to time on treatment which include membrane thickening and vascular scarring (10). Time on treatment is also the greatest risk factor for encapsulating peritoneal sclerosis (EPS) (11, 12).

These observations have led all the main dialysis companies to develop and market 'biocompatible' solutions, with normalization of pH, reduction of

GDPs and a variable approach to buffering. In randomised clinical trials these solutions have been shown to improve the dialysate concentrations of biomarkers considered to be indicators of mesothelial cell and possibly membrane health (13-16). Systemic benefits possibly include reduced circulating advanced glycation end-products (16) and better glycaemic control in diabetics (17). Data is currently lacking on hard clinical endpoints such as technique failure, functional membrane change or patient survival. One non-randomised study has found an improved patient but not technique survival; patients in this study using biocompatible solutions were younger, suggesting a selection bias that may not be fully adjusted for, so caution should be exercised in the interpretation of this study (18).

Currently there is insufficient evidence to recommend that all patients should be treated with biocompatible solutions, especially as this may have a significant cost implication. A selective approach to their use should be considered. Working on the assumption that the primary benefit of biocompatible solutions is membrane protection then there is evidence indicating that function membrane changes become more significant at 4 years of treatment, even in patients commencing PD with good residual renal function and low use of hypertonic exchanges (9). Likewise the incidence of SEP is rare before this period of time on treatment. This issue remains controversial at this stage and further studies are required.

An area of difference between paediatric and adult PD is that fill volumes vary with size. Surface area is preferable to body weight, which may underestimate the optimal fill volume in younger children, and should be between 1200 and 1400ml dialysate/m2 body surface area (19).

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12. Lee HY, Kim BS, Choi HY, et al. Sclerosing encapsulating peritonitis as a complication of long-term continuous ambulatory peritoneal dialysis in Korea. *Nephrology (Carlton).* 2003;8(Suppl):S33-9.
13. Rippe B, Wieslander A, Musi B. Long-term results with low glucose degradation product content in peritoneal dialysis fluids. *Contrib Nephrol* 2003(140):47-55.
14. Jones S, Holmes CJ, Krediet RT, et al. Bicarbonate/lactate-based peritoneal dialysis solution increases cancer antigen 125 and decreases hyaluronic acid levels. *Kidney Int* 2001;59(4):1529-38.
15. Jones S, Holmes CJ, Mackenzie RK, et al. Continuous dialysis with bicarbonate/lactate-buffered peritoneal dialysis fluids results in a long-term improvement in ex vivo peritoneal macrophage function. *J Am Soc Nephrol* 2002;13(Suppl 1):S97-103.
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17. Marshall J, Jennings P, Scott A, Fluck RJ, McIntyre CW. Glycemic control in diabetic CAPD patients assessed by continuous glucose monitoring system (CGMS). *Kidney Int* 2003;64(4):1480-6.
18. Lee HY, Park HC, Seo BJ, et al. Superior patient survival for continuous ambulatory peritoneal dialysis patients treated with a peritoneal dialysis fluid with neutral pH and low glucose degradation product concentration (Balance). *Perit Dial Int*. 2005;25(3):248-55.
19. White CT, Gowrishankar M, Feber J, Yiu V; Canadian Association of Pediatric Nephrologists (CAPN); Peritoneal Dialysis Working Group. Clinical practice guidelines for pediatric peritoneal dialysis. Pediatr Nephrol. 2006 Aug;21(8):1059-66

2. Preparation for Peritoneal Dialysis

2.1 All patients should, where possible, be adequately prepared for renal replacement therapy and this should include receiving information and education about PD treatment, delivered by an experienced member of the MDT. Patients commencing RRF in an unplanned fashion for whatever reason should receive this information once appropriate. (Good practice)

Audit Measure 9: Audit of care pathway for dialysis preparation to include information given, when and who delivers it

The arguments and rationale for this guideline relate to the National Service Framework for Renal Services, Part 1. The reader is referred to standard 2, Preparation and Choice pp. 21-23.

2.2 Where possible, timing of PD catheter insertion should be planned to accommodate patient convenience, commencement of training between 10 days and 6 weeks, (unless using the Moncrief catheter) and before RRT is essential to enable correction of early catheter-related problems without the need for temporary haemodialysis. (Good practice)

Audit Measure 10: Audit of care pathway for catheter insertion to include timeliness and need for temporary haemodialysis

The arguments and rationale for this guideline relate to the National Service Framework for Renal Services, Part 1. The reader is referred to standard 3, Elective Dialysis Access Surgery, pp. 24-26. The Moncrief catheter is buried subcutaneously and is designed to be left in this position, where it can remain for many months, until required (1). *If the catheter needs to be used within 7 days of insertion, fill volumes should start at 500ml/body surface area in order to reduce the chances of dialysate leak, with its associated risk of tunnel and peritoneal infection.*

1. Gokal R, Alexander S, Ash S, et al. Peritoneal catheters and exit-site practices toward optimum peritoneal access: 1998 update. (Official report from the International Society for Peritoneal Dialysis). *Perit Dial Int* 1998;18(1):11-33.
2. White CT, Gowrishankar M, Feber J, Yiu V; Canadian Association of Pediatric Nephrologists (CAPN); Peritoneal Dialysis Working Group. Clinical practice guidelines for pediatric peritoneal dialysis. Pediatr Nephrol. 2006 Aug;21(8):1059-66

2.3 Dialysis centres should have a dedicated team approach to catheter insertion. This is more important than the type of catheter or the implantation technique used. (Good practice)

An experienced team approach to catheter insertion is recommended by all available guidelines; in the case of the European guidelines this is given a level A evidence although no randomised trial has been published comparing *ad hoc* arrangements with those of a dedicated experienced team (1). This approach should be combined with regular audit of outcomes. Several randomised trials have been performed comparing different catheter designs and insertion techniques. These are fully reviewed elsewhere (1-4). Whilst there are theoretical advantages in choosing different catheters, e.g. double *v.* single cuff to reduce leakage, coiled *v.* straight to reduce catheter migration, when put to the test in randomised trials no significant benefit of one over another has been demonstrated. Equally, there may be clear logistic benefits of one approach to catheter insertion over another, e.g. laparoscopic *v.* open surgical *v.* Seldinger that reflect local expertise and facilities but no studies have demonstrated a clear benefit. Evidence would suggest that a downwards-directed exit site is associated with less infection and a caudally directed angle of the catheter in the deep tunnel, especially if this is made through the rectus muscle, is associated with reduced likelihood of catheter migration (5).

Similarly for children, there is no evidence showing any difference in the incidence of complications and the number of cuffs. However, in young children care is necessary to avoid placement of the distal cuff too near the exit site as cuff extrusion can occur. For this reason, it is recommended that there should be at least a 2cm distance between the distal cuff and the exit site. There is also no evidence to support the use of swan necked in comparison to straight catheters or a coiled in comparison to a straight

intraperitoneal segment. However, downward or lateral pointing exit sites have been shown to be associated with a decreased incidence of peritonitis in 2 studies (6). Furthermore, there is no evidence in the paediatric literature to demonstrate any benefit of omentectomy, although there is some evidence in adults. The most important issue, therefore, is that the catheter is inserted by experienced staff who are aware of these issues.

Paediatric standard 3
Peritoneal dialysis catheter insertion should be undertaken by appropriately trained and skilled staff (good practice)

1. Dombros N, Dratwa M, Feriani M, et al. European best practice guidelines for peritoneal dialysis. 3 Peritoneal access. *Nephrol Dial Transplant*. 2005;20(Suppl 9):ix8-ix12.
2. Gokal R, Alexander S, Ash S, et al. Peritoneal catheters and exit-site practices toward optimum peritoneal access: 1998 update. (Official report from the International Society for Peritoneal Dialysis). *Perit Dial Int* 1998;18(1):11-33.
3. Canadian Guidelines for treatment wth peritoneal dialysis. *J Am Soc Nephrol* 1999;Suppl 13.
4. Flanigan M, Gokal R. Peritoneal catheters and exit-site practices toward optimum peritoneal access: a review of current developments. *Perit Dial Int*. 2005;25(2):132-9.
5. Crabtree JH, Burchette RJ, Siddiqi NA. Optimal peritoneal dialysis catheter type and exit site location: an anthropometric analysis. *ASAIO J*. 2005;51(6):743-7.
6. White CT, Gowrishankar M, Feber J, Yiu V; Canadian Association of Pediatric Nephrologists (CAPN); Peritoneal Dialysis Working Group. Clinical practice guidelines for pediatric peritoneal dialysis. Pediatr Nephrol. 2006 Aug;21(8):1059-66

2.4 Peri-operative catheter care and catheter complications (leaks, hernias, obstruction) should be managed according to the International Society of Peritoneal Dialysis guidelines, www.ispd.org (Good practice)

Audit Measure 11: Catheter complications and their resolution

For management of the catheter in the peri-operative period, for catheter related problems including leak (internal and external), poor flow, obstruction and hernias the guidelines developed by the International Society of Peritoneal Dialysis should be used, www.ispd.org (1, 2). Catheter problems due to increased intra-peritoneal pressure, especially leaks, hernias and prolapse are an important medical indication for the use of APD either temporarily or permanently; poor flow or catheter related flow pain should be treated with tidal APD.

1. Flanigan M, Gokal R. Peritoneal catheters and exit-site practices toward optimum peritoneal access: a review of current developments. *Perit Dial Int*. 2005;25(2):132-9.
2. Crabtree JH. Rescue and salvage procedures for mechanical and infectious complications of peritoneal dialysis. *Int J Artif Organs*. 2006;29(1):67-84.

3. Solute Clearance

3.1 Both residual urine and peritoneal dialysis components of small solute clearance should be measured at least six monthly or more frequently if clinically indicated. Both urea and/or creatinine clearances can be used to monitor dialysis adequacy and should be interpreted within the limits of the methods. (Good practice)

Audit Measure 12: Frequency of solute clearance (residual and peritoneal) estimation.

Small solute clearance is one of the measurements of adequate dialysis treatment. Salt and water removal and acid-base balance are considered in sections 4 and 6 respectively. There are two issues in measuring small solute clearance that need to be taken into consideration. First, the relationship to clinical outcomes of residual renal versus peritoneal small solute clearance is quantitatively different. Observational studies have shown that preserved renal clearance, in fact just urine volume, is associated with improved survival, independent of other known factors such as age and comorbidity (1, 2). Randomised controlled trials designed to replace this residual renal function with peritoneal clearance did not show a proportional survival benefit (3, 4). Second, there are two potential surrogate solutes, urea and creatinine, that can be used to measure solute clearance in PD patients. There is no clear evidence as to which is the more useful clinically, and both have their problems. Current advice, therefore, is that either or both can be used, but clinicians should be aware of their differing limitations. Urea clearances are limited by the difficulty in PD patients of estimating V accurately, whilst peritoneal creatinine clearances are affected by membrane transport characteristics (see Appendix).

1. Churchill DN, Taylor DW, Keshaviah PR. Adequacy of dialysis and nutrition in continuous peritoneal dialysis: association with clinical outcome. *J Am Soc Nephrol* 1996;7:198-207.
2. Bargman JM, Thorpe KE, Churchill DN. Relative contribution of residual renal function and peritoneal clearance to adequacy of dialysis: a reanalysis of the CANUSA study. *J Am Soc Nephrol* 2001;12(10):2158-62.
3. Paniagua R, Amato D, Vonesh E, et al. Effects of Increased Peritoneal Clearances on Mortality Rates in Peritoneal Dialysis: ADEMEX, a Prospective, Randomized, Controlled Trial. *J Am Soc Nephrol* 2002;13(5):1307-20.
4. Lo WK, Ho YW, Li CS, et al. Effect of Kt/V on survival and clinical outcome in CAPD patients in a randomized prospective study. *Kidney Int* 2003;64(2):649-56.

3.2 A combined urinary and peritoneal Kt/Vurea of 1.7/week or a creatinine clearance of 50L/week/1.73m^2 should be considered as minimal treatment doses. The dose should be increased in patients experiencing uraemic symptoms (Evidence)

Audit Measure 13: Cumulative frequency curves for the total solute clearance

Two randomised controlled trials (ADEMEX and Hong Kong) have evaluated the impact of peritoneal solute clearances on clinical endpoints (1, 2). Neither found that an increase of peritoneal Kt/V_{urea} >1.7 was associated with an improvement in survival. Only one of these studies (ADEMEX) measured creatinine clearance, which was the solute used to make decisions in this case; patients in the control group achieved an average peritoneal creatinine clearance of 46L/1.73m^2/week and a total (urine plus renal) of 54L/1.73m^2/week. In setting a recommendation for minimal peritoneal clearances, to be achieved in anuric patients, the previous Renal Association guideline of Kt/V > 1.7 and creatinine clearance >50L/1.73m^2/week is supported by both the randomised and observational data. In the Hong Kong study, patients randomised to a Kt/V <1.7, whilst their mortality was not significantly worse they had a significantly higher drop out rate, more clinical complications and worse anaemia. One observational longitudinal study demonstrated that patients develop malnutrition once the Kt/V falls below 1.7 with a three-fold increase in the death rate (3). The NECOSAD study found that a creatinine clearance of <40L/wek or a Kt/V urea <1.5 was associated with increased mortality in anuric patients (4).

The vast majority of PD patients will be able to reach these clearance targets, especially if APD is employed (5). These guidelines must however be viewed as recommendations for *minimal* overall clearance. In patients with residual renal function this renal clearance can be subtracted from the peritoneal clearance with confidence that the value of equivalent renal clearances in greater. Equally, in patients achieving these clearances but experiencing uraemic symptoms, or failing to achieve adequate acid base balance (see section 6) then the dialysis dose should be increased. Drop out due to uraemia or death associated with hyperkalaemia and acidosis was significantly more common in the control patients in the ADEMEX study (1).

Studies in children include small patient numbers and results are variable, some suggesting a ceiling above which no further improvement in growth and nutritional state occurs because of peritoneal protein losses. It is recommended that the standards for adults should be seen as a minimum for children (6).

1. Paniagua R, Amato D, Vonesh E, et al. Effects of Increased Peritoneal Clearances on Mortality Rates in Peritoneal Dialysis: ADEMEX, a Prospective, Randomized, Controlled Trial. J Am Soc Nephrol 2002;13(5):1307-20.

2. Lo WK, Ho YW, Li CS, et al. Effect of Kt/V on survival and clinical outcome in CAPD patients in a randomized prospective study. Kidney Int 2003;64(2):649-56.
3. Davies SJ, Phillips L, Russell L, Naish PF, Russell GI. An analysis of the effects of increasing delivered dialysis treatment to malnourished peritoneal dialysis patients. Kidney Int 2000;57(4):1743-54.
4. Jansen MA, Termorshuizen F, Korevaar JC, Dekker FW, Boeschoten E, Krediet RT. Predictors of survival in anuric peritoneal dialysis patients. Kidney Int. 2005;68(3):1199-205.
5. Brown EA, Davies SJ, Heimburger O, et al. Adequacy targets can be met in anuric patients by automated peritoneal dialysis: baseline data from EAPOS. Perit Dial Int 2001;21(Suppl 3):S133-7.
6. Lesley Rees 1, Vanessa Shaw. Nutrition in children with CRF and on dialysis. Pediatr Nephrol. 2007 Oct;22(10):1689-702.

4. Ultrafiltration and fluid management

4.1 Peritoneal membrane function should be monitored regularly (6 weeks after commencing treatment and at least annually or when clinically indicated) using a peritoneal equilibration test (PET) or equivalent. Daily urine and peritoneal ultrafiltration volumes, with appropriate correction for overfill, should be monitored six-monthly. (Good practice)

Audit Measure 14: Frequency of measurement of membrane function, residual urine and peritoneal ultrafiltration volume

Assessment of membrane function, specifically solute transport rate and ultrafiltration capacity) is fundamental to PD prescription. (See appendix for methodological description of membrane function tests). This is for the following reasons:

1. There is considerable between-patient variability in both solute transport and ultrafiltration capacity that translates into real differences in achieved solute clearance and ultrafiltration unless they are accounted for in prescription practice (1-5)

2. Membrane function is an independent predictor of patient survival; specifically high solute transport and low ultrafiltration capacity are associated with worse outcomes (6-10)

3. Membrane function changes with time on therapy. There are early changes – usually during the first few weeks of treatment that can be avoided by performing tests 6 weeks after commencing PD. Later changes vary between patients but tend to be increasing solute transport and reduced ultrafiltration capacity; the rate of membrane change is accelerated in patients with earlier loss of residual renal function and greater requirement for hypertonic glucose solutions. (5, 11, 12)

Residual renal function, as discussed above, is one of the most important factors, along with age, comorbidity, nutritional status, plasma albumin and membrane function that predict survival in PD patients. Its rate of loss is variable and clinically significant changes can occur within 6 months. Total fluid removal is associated with patient survival, especially once anuric (9, 13, 14), ADEMEX study, data awaiting publication.

1. Twardowski ZJ, Nolph KD, Khanna R, et al. Peritoneal Equilibration Test. Perit Dial Bull 1987;7:138-47.
2. Smit W, van Dijk P, Langedijk MJ, et al. Peritoneal function and assessment of reference values using a 3.86% glucose solution. Perit Dial Int 2003;23(5):440-9.
3. Smit W, Schouten N, van den Berg N, Langedijk MJ, Struijk DG, Krediet RT. Analysis of the prevalence and causes of ultrafiltration failure during long-term peritoneal dialysis: a cross-sectional study. Perit Dial Int 2004;24(6):562-70.
4. Selgas R, Bajo MA, Cirugeda A, et al. Ultrafiltration and small solute transport at initiation of PD: questioning the paradigm of peritoneal function. Perit Dial Int. 2005;25(1):68-76.
5. Davies SJ. Longitudinal relationship between solute transport and ultrafiltration capacity in peritoneal dialysis patients. Kidney Int 2004;66:2437-45.
6. Davies SJ, Phillips L, Naish PF, Russell G. Quantifying comorbidity in Peritoneal Dialysis patients and its relationship to other predictors of survival. Nephrol Dial Transplant 2002;17(6):1085-92.
7. Churchill DN, Thorpe KE, Nolph KD, Keshaviah PR, Oreopoulos DG, Page D. Increased peritoneal membrane transport is associated with decreased patient and technique survival for continuous peritoneal dialysis patients. J Am Soc Nephrol 1998;9:1285-92.
8. Rumpsfeld M, McDonald SP, Johnson DW. Higher peritoneal transport status is associated with higher mortality and technique failure in the Australian and New Zealand peritoneal dialysis patient populations. J Am Soc Nephrol. 2006;17(1):271-8. Epub 2005 Nov 23.
9. Brown EA, Davies SJ, Rutherford P, et al. Survival of Functionally Anuric Patients on Automated Peritoneal Dialysis: The European APD Outcome Study. J Am Soc Nephrol 2003;14(11):2948-57.
10. Brimble KS, Walker M, Margetts PJ, Kundhal KK, Rabbat CG. Meta-analysis: peritoneal membrane transport, mortality, and technique failure in peritoneal dialysis. J Am Soc Nephrol. 2006;17(9):2591-8. Epub 006 Aug 2.
11. Heimburger O, Wang T, Lindholm B. Alterations in water and solute transport with time on peritoneal dialysis. Perit Dial Int 1999;19 Suppl 2:S83-90.
12. del Peso G, Fernandez-Reyes MJ, Hevia C, et al. Factors influencing peritoneal transport parameters during the first year on peritoneal dialysis: peritonitis is the main factor. Nephrol Dial Transplant. 2005;20(6):1201-6.
13. Ates K, Nergizoglu G, Keven K, et al. Effect of fluid and sodium removal on mortality in peritoneal dialysis patients. Kidney Int 2001;60(2):767-76.
14. Jansen MA, Termorshuizen F, Korevaar JC, Dekker FW, Boeschoten E, Krediet RT. Predictors of survival in anuric peritoneal dialysis patients. Kidney Int. 2005;68(3):1199-205.

4.2 Dialysis regimes resulting in fluid reabsorption should be avoided. (Good practice). Patients with high or high average solute transport, at greatest risk of this problem, should be considered for APD and icodextrin (Evidence)

Audit Measure 15: Identify patients with fluid reabsorption in long dwell

Increased solute transport has been repeatedly shown to be associated with worse survival, especially in CAPD patients (1-4). The explanation for this association is most likely to be because of its effect on ultrafiltration when this is achieved with an osmotic gradient (using glucose or amino-acid dialysis fluids). The reason is twofold: first, due to more rapid absorption of glucose, the osmotic gradient is lost earlier in the cycle resulting in reduced ultrafiltration capacity. Second, once the osmotic gradient is dissipated the rate of fluid reabsorption in high transport patients is more rapid. This will result in significant fluid absorption, contributing to a positive fluid balance, during the long exchange.

These problems associated with high transport can be avoided by using APD to shorten dwell length and by using icodextrin for the long exchange to prevent fluid reabsorption. Several randomised controlled trials have shown that icodextrin can achieve sustained ultrafiltration in the long dwell (5-9) and that this translates into a reduction in extracellular fluid volume (10, 11). Observational studies indicate that high solute transport is not associated with increased mortality or technique failure in APD patients, especially when there is also a high use of icodextrin (3, 12, 13).

1. Davies SJ, Phillips L, Naish PF, Russell G. Quantifying comorbidity in Peritoneal Dialysis patients and its relationship to other predictors of survival. Nephrol Dial Transplant 2002;17(6):1085-92.
2. Churchill DN, Thorpe KE, Nolph KD, Keshaviah PR, Oreopoulos DG, Page D. Increased peritoneal membrane transport is associated with decreased patient and technique survival for continuous peritoneal dialysis patients. J Am Soc Nephrol 1998;9:1285-92.
3. Rumpsfeld M, McDonald SP, Johnson DW. Higher peritoneal transport status is associated with higher mortality and technique failure in the Australian and New Zealand peritoneal dialysis patient populations. *J Am Soc Nephrol*. 2006;17(1):271-8. Epub 2005 Nov 23.
4. Brimble KS, Walker M, Margetts PJ, Kundhal KK, Rabbat CG. Meta-analysis: peritoneal membrane transport, mortality, and technique failure in peritoneal dialysis. *J Am Soc Nephrol*. 2006;17(9):2591-8. Epub 006 Aug 2.
5. Posthuma N, ter Wee PM, Verbrugh HA, et al. Icodextrin instead of glucose during the daytime dwell in CCPD increases ultrafiltration and 24-h dialysate creatinine clearance. *Nephrol Dial Transplant Nephrology, Dialysis, Transplantation* 1997;12(3):550-3.
6. Plum J, Gentile S, Verger C, et al. Efficacy and safety of a 7.5% icodextrin peritoneal dialysis solution in patients treated with automated peritoneal dialysis. *Am J Kidney Dis* 2002;39(4):862-71.
7. Wolfson M, Piraino B, Hamburger RJ, Morton AR. A randomized controlled trial to evaluate the efficacy and safety of icodextrin in peritoneal dialysis. *Am J Kidney Dis* 2002;40(5):1055-65.
8. Ota K, Akiba T, Nakao T, et al. Peritoneal ultrafiltration and serum icodextrin concentration during dialysis with 7.5% icodextrin solution in Japanese patients. *Perit Dial Int* 2003;23(4):356-61.

9. Finkelstein F, Healy H, Abu-Alfa A, et al. Superiority of icodextrin compared with 4.25+ACU- dextrose for peritoneal ultrafiltration. J Am Soc Nephrol 2005;16(2):546-54.
10. Konings CJ, Kooman JP, Schonck M, et al. Effect of icodextrin on volume status, blood pressure and echocardiographic parameters: A randomized study. Kidney Int 2003;63(4):1556-63.
11. Davies SJ, Woodrow G, Donovan K, et al. Icodextrin improves the fluid status of peritoneal dialysis patients: results of a double-blind randomized controlled trial. J Am Soc Nephrol 2003;14(9):2338-44.
12. Brown EA, Davies SJ, Rutherford P, et al. Survival of Functionally Anuric Patients on Automated Peritoneal Dialysis: The European APD Outcome Study. J Am Soc Nephrol 2003;14(11):2948-57.
13. Davies SJ. Mitigating peritoneal membrane characteristics in modern PD therapy. Kidney Int 2006; 103:S76-83

4.3 Dialysis regimes resulting in routine utilisation of hypertonic (3.86%) glucose exchanges should be avoided (Good practice). Where appropriate this should be achieved by avoiding excess dietary salt intake, using diuretics or icodextrin (Evidence).

There is growing evidence that regular use of hypertonic glucose dialysis fluid (3.86%), and where possible glucose 2.27%, is to be avoided. It is associated with acceleration in the detrimental changes in membrane function that occur with time on treatment (1, 2), as well as several undesirable systemic effects including weight gain (3, 4), poor diabetic control (5), delayed gastric emptying (6), hyperinsulinaemia and adverse haemodynamic effects (7). In addition to patient education to avoid excessive salt and fluid intake, where possible the use of hypertonic glucose should be minimised by enhancing residual diureses with the use of diuretics (e.g. furosemide 250mg daily) (8). Substituting icodextrin for glucose solutions during the long exchange will result in equivalent ultrafiltration whilst avoiding the systemic effects of the glucose load (3, 5, 7, 9). Observational evidence would suggest that icodextrin is associated with less functional deterioration in the membrane in APD patients (2).

1. Davies SJ. Longitudinal relationship between solute transport and ultrafiltration capacity in peritoneal dialysis patients. Kidney Int 2004;66:2437-45.
2. Davies SJ, Brown EA, Frandsen NE, et al. Longitudinal membrane function in functionally anuric patients treated with APD: Data from EAPOS on the effects of glucose and icodextrin prescription. Kidney Int 2005;67(4):1609-15.
3. Wolfson M, Piraino B, Hamburger RJ, Morton AR. A randomized controlled trial to evaluate the efficacy and safety of icodextrin in peritoneal dialysis. Am J Kidney Dis 2002;40(5):1055-65.
4. Fernstrom A, Hylander B, Moritz A, Jacobsson H, Rossner S. Increase of intra-abdominal fat in patients treated with continuous ambulatory peritoneal dialysis. Perit Dial Int 1998;18(2):166-71.
5. Marshall J, Jennings P, Scott A, Fluck RJ, McIntyre CW. Glycemic control in diabetic CAPD patients assessed by continuous glucose monitoring system (CGMS). Kidney Int 2003;64(4):1480-6.
6. Van V, Schoonjans RS, Struijk DG, et al. Influence of dialysate on gastric emptying time in peritoneal dialysis patients. Perit Dial Int 2002;22(1):32-8.
7. Selby NM, Fonseca S, Hulme L, Fluck RJ, Taal MW, McIntyre CW. Hypertonic glucose-based peritoneal dialysate is associated with higher blood pressure and adverse haemodynamics as compared with icodextrin. Nephrol Dial Transplant 2005; 20(9):1848-53.

8. Medcalf JF, Harris KP, Walls J. Role of diuretics in the preservation of residual renal function in patients on continuous ambulatory peritoneal dialysis. Kidney Int 2001;59(3):1128-33.
9. Davies SJ, Woodrow G, Donovan K, et al. Icodextrin improves the fluid status of peritoneal dialysis patients: results of a double-blind randomized controlled trial. J Am Soc Nephrol 2003;14(9):2338-44.

4.4 Treatment strategies that favour preservation of renal function should be adopted where possible (Good practice). These include avoidance of episodes of dehydration, use of diuretics, ACEi and ARBs (Evidence)

This is the single most important parameter in PD patients, and also the one most likely to change with time. Clinically significant changes can occur within three months. Because secretion of creatinine by the kidney at low levels of function overestimates residual creatinine clearance, it is recommended to express this as the *mean* of the urea and creatinine clearances. Observational and randomised studies have shown that episodes of volume depletion, whether unintentional or in response to active fluid removal with the intent of changing blood pressure or fluid status, are associated with increased risk of loss in residual renal function (1-4). Care should be taken not to volume deplete a PD patient too rapidly or excessively. The use of diuretics to maintain urine volume is not associated with a risk to renal clearances (5). ACE inhibitors, (Ramipril 5mg) (6) and ARBs (valsartan) (7) have been shown in randomised studies to maintain residual diuresis.

1. Jansen MA, Hart AA, Korevaar JC, Dekker FW, Boeschoten EW, Krediet RT. Predictors of the rate of decline of residual renal function in incident dialysis patients. *Kidney Int* 2002;62(3):1046-53.
2. Gunal AI, Duman S, Ozkahya M, et al. Strict volume control normalizes hypertension in peritoneal dialysis patients. *Am J Kidney Dis* 2001;37(3):588-93.
3. Konings CJ, Kooman JP, Gladziwa U, van der Sande FM, Leunissen KM. A decline in residual glomerular filtration during the use of icodextrin may be due to underhydration. *Kidney Int* 2005;67(3):1190-1.
4. Konings CJ, Kooman JP, Schonck M, et al. Effect of icodextrin on volume status, blood pressure and echocardiographic parameters: A randomized study. *Kidney Int* 2003;63(4):1556-63.
5. Medcalf JF, Harris KP, Walls J. Role of diuretics in the preservation of residual renal function in patients on continuous ambulatory peritoneal dialysis. *Kidney Int* 2001;59(3):1128-33.
6. Li PK, Chow KM, Wong TY, Leung CB, Szeto CC. Effects of an angiotensin-converting enzyme inhibitor on residual renal function in patients receiving peritoneal dialysis. A randomized, controlled study. *Ann Intern Med.* 2003;139(2):105-12.
7. Suzuki H, Kanno Y, Sugahara S, Okada H, Nakamoto H. Effects of an angiotensin II receptor blocker, valsartan, on residual renal function in patients on CAPD. *Am J Kidney Dis.* 2004;43(6):1056-64.

4.5 Anuric patients who consistently achieve a daily ultrafiltration of less than 750 ml should be closely monitored and the benefits of modality switch considered (Good practice)

Audit Measure (adult only): Identify patients with a total fluid removal <750 ml per day.

Observational studies have consistently shown that reduced peritoneal ultrafiltration is associated with worse survival rates; whilst this is seen in studies with or without residual urine (1), this effect is most marked in anuric patients (2, 3). In the only prospective study to have preset an ultrafiltration target (750 ml/day), patients who remained below this had higher mortality after correcting for age, time on dialysis, comorbidity and nutritional status. It is likely this association is multifactorial, but failure to prescribe sufficient glucose or icodextrin and a lower ultrafiltration capacity of the membrane were factors in this study and should be considered (2, 4). The European guidelines have suggested a 1 litre minimal daily ultrafiltration target;(5) there is insufficient evidence to say that such a target must be met at this stage. Blood pressure, salt (and fluid) intake, nutritional and fluid status should be taken into account. Nevertheless patients with less than 750 ml ultrafiltration once anuric should be very closely monitored and the potential benefits of modality switch considered.

1. Ates K, Nergizoglu G, Keven K, et al. Effect of fluid and sodium removal on mortality in peritoneal dialysis patients. *Kidney Int* 2001;60(2):767-76.
2. Brown EA, Davies SJ, Rutherford P, et al. Survival of Functionally Anuric Patients on Automated Peritoneal Dialysis: The European APD Outcome Study. *J Am Soc Nephrol* 2003;14(11):2948-57.
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4. Davies SJ, Brown E, Riegel W, et al. What is the link between poor ultrafiltration and increased mortality in anuric APD patients? Analysis of data from EAPOS. *Perit Dial Int* 2006;26(4):458-65.
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5. Infectious complications

5.1 Prevention Strategies

5.1.1 PD units should undertake regular audit of their peritonitis and exit-site infection rates, including causative organism, treatment and outcomes. They should enter into active dialogue with their microbiology department and infection control team to develop optimal local treatment and prevention protocols (Good practice)

5.1.2 Flush-before-fill dialysis delivery systems should be used (Evidence)

5.1.3 Patients should undergo regular (annually or more frequently if indicated) revision of their technique and receive intensified training if this is below standard (Evidence)

5.1.4 Initial catheter insertion should be accompanied by antibiotic prophylaxis (Evidence)

5.1.5 Invasive procedures should be accompanied by antibiotic prophylaxis and emptying the abdomen of dialysis fluid for a period commensurate with the procedure (Good practice)

5.1.6 Topical antibiotic administration should be used to reduce the frequency of *Staph. aureus* and Gram negative exit-site infection and peritonitis (Evidence)

Audit Measure 16: Routine annual audit of infection prevention strategies

The rationale underpinning the guidelines in this section is laid out in a series of documents published by the International Society of Peritoneal Dialysis, available on their web-site: www.ispd.org

Prevention strategies: Both the ISPD 2005 guidelines (1) and the NSF Part 1 place increasing emphasis on prevention strategies. Regular audit is essential to this progress and the following standards should be considered as minimal:

1. Peritonitis rates of less than 1 episode per 18 months in adults and 12 months in children (see NSF part 1)
2. A primary cure rate of 80%
3. A culture negative rate of < 20%

Approaches that have been shown to reduce infection rates in randomised studies include increased intensity of training (2), use of flush before fill systems,(3) antibiotic prophylaxis to cover catheter insertion and prevention of exit-site infections (1). Several studies have addressed the

latter issue; following demonstration that the risk of *Staph aureus* exit site infection (the organism responsible in 90% of cases) is associated with pre-existing skin carriage, several randomised studies demonstrated that clinical exit-sire infection and associated peritonitis could be reduced by either nasal or exit-site application of mupirocin. This has led to the practice of applying mupirocin to all patients(4, 5); this approach should be discussed with the local microbiology and infection control team. A more recent study, comparing mupirocin with gentamicin cream, found that the latter prevented both *Staph aureus* and *Pseudomonas* exit-site infections and peritonitis episodes (6). This approach should be strongly considered in patients with a known history of *Pseudomonas* infections; again the policy should be discussed and agreed with the local microbiology team.

1. Piraino B, Bailie GR, Bernardini J, et al. Peritoneal dialysis-related infections recommendations: 2005 update. Perit Dial Int. 2005;25(2):107-31.
2. Hall G, Bogan A, Dreis S, et al. New directions in peritoneal dialysis patient training. Nephrol Nurs J. 2004;31(2):149-54, 59-63.
3. 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(5):1-166.
4. Bernardini J, Piraino B, Holley J, Johnston JR, Lutes R. A randomized trial of Staphylococcus aureus prophylaxis in peritoneal dialysis patients: mupirocin calcium ointment 2% applied to the exit site versus cyclic oral rifampin. Am J Kidney Dis 1996;27(5):695-700.
5. Piraino B. Staphylococcus aureus infections in dialysis patients: focus on prevention. Asaio J 2000;46(6):S13-7.
6. Bernardini J, Bender F, Florio T, et al. Randomized, double-blind trial of antibiotic exit site cream for prevention of exit site infection in peritoneal dialysis patients. J Am Soc Nephrol. 2005;16(2):539-45. Epub 2004 Dec 29.

5.2 Treatment

5.2.1 Exit site infection is suggested by pain, swelling, crusting, erythema and serous discharge; purulent discharge always indicates infection. Swabs should be taken for culture and initial empiric therapy should be with oral antibiotics that will cover *S. aureus and P. aeruginosa* (Good practice)

5.2.2 Methicillin resistant organisms (MRSA) will require systemic treatment (e.g vancomycin) and will need to comply with local infection control policies. (Good practice)

5.2.3 Initial treatment regimes for peritonitis should include cover for bacterial Gram positive and Gram negative organisms until result of culture and antibiotic sensitivities are obtained. (Good practice)

Audit Measure 17: Routine annual audit of infection outcomes (exit site and peritonitis rates

The ISPD has developed a simple scoring system for exit site signs and symptoms which is easy to use and gives guidance on when to treat immediately rather than waiting for a swab result. Purulent discharge is an absolute indicator for antibiotic treatment (1). The ISPD has become less dogmatic about the initial choice of antibiotic treatment for peritonitis, provided that gram positive and negative infections are covered. It is recognised that patterns of resistance vary considerably and thus a local policy must be developed.

1. Piraino B, Bailie GR, Bernardini J, et al. Peritoneal dialysis-related infections recommendations: 2005 update. *Perit Dial Int*. 2005;25(2):107-31.

6. Metabolic Factors

6.1 Standard strategies to optimise diabetic control should be used; these should be complemented by dialysis prescription regimens that minimise glucose, including glucose free solutions (icodextrin and amino-acids), where possible. (Good practice)

Glycaemic control can be made worse by glucose absorption across the peritoneal membrane. Dialysis regimes that incorporate less glucose and more glucose free (amino acid, icodextrin) solutions have been shown to improve glycaemic control (1), Paniagua (in press).

1. Marshall J, Jennings P, Scott A, Fluck RJ, McIntyre CW. Glycemic control in diabetic CAPD patients assessed by continuous glucose monitoring system (CGMS). *Kidney Int* 2003;64(4):1480-6.

6.2 Plasma bicarbonate should be maintained within the normal range; this can be achieved in the vast majority of patients by adjusting the dialysis dose and/or dialysate buffer concentration. Occasionally bicarbonate buffered solutions will be required (Good practice).

Audit measure 18: Cumulative frequency curves of plasma bicarbonate

Two randomised controlled trials have suggested that clinical outcomes, including gaining lean body mass and reduced hospital admissions are achieved if the plasma bicarbonate is kept within the upper half of the normal range.(1, 2) Generally this can be achieved by using dialysis fluids with a 40 mmol buffer capacity (lactate or bicarbonate results in similar plasma bicarbonate levels(3)) and ensuring that the dialysis dose is adequate (see section 3 (b), above) (4). However, for solutions with a lower buffering capacity, when patients are switched from an all lactate (35 mmol/l) to a 25 mmol bicarbonate: 10 mmol lactate mix, there is a significant improvement in plasma bicarbonate (24.4 to 26.1 mmol/l), such that a higher proportion of patients will fall within the normal range (5). Whilst bicarbonate solutions may have a role in biocompatibility (see

section 1(e), above), they are generally not required to achieve satisfactory acid-base balance. The main reason for using a 35 mmol buffer capacity solution (25:10 bicarbonate:lactate mix) is to avoid excessive alkalinisation (6).

Control of acidosis is especially important in malnourished patients who may benefit from the glucose available in dialysis solutions as a calories source. Amino acid solutions were developed in an attempt to address protein calorie malnutrition and several randomised studies have been conducted. In using amino acid solutions it is essential to ensure that acidosis does not develop and to use the solution at the same time as there is a significant intake of carbohydrate (7). Despite demonstration that amino acids delivered in dialysis fluids are incorporated into tissue protein, the randomised trials have failed to show benefit in terms of hard clinical endpoints (8, 9).

1. Stein A, Moorhouse J, Iles-Smith H, et al. Role of an improvement in acid-base status and nutrition in CAPD patients. Kidney Int 1997;52(4):1089-95.
2. Szeto CC, Wong TY, Chow KM, Leung CB, Li PK. Oral sodium bicarbonate for the treatment of metabolic acidosis in peritoneal dialysis patients: a randomized placebo-control trial. J Am Soc Nephrol 2003;14(8):2119-26.
3. Coles GA, Gokal R, Ogg C, et al. A randomized controlled trial of a bicarbonate- and a bicarbonate/lactate-containing dialysis solution in CAPD. Perit Dial Int 1997;17(1):48-51.
4. Mujais S. Acid base profile in patients on PD. Kidney Int 2003;Suppl. 83(Deb):in press.
5. Otte K, Gonzalez MT, Bajo MA, et al. Clinical experience with a new bicarbonate (25 mmol/L)/lactate (10 mmol/L) peritoneal dialysis solution. Perit Dial Int 2003;23(2):138-45.
6. Dratwa M, Wilkie M, Ryckelynck JP, et al. Clinical experience with two physiologic bicarbonate/lactate peritoneal dialysis solutions in automated peritoneal dialysis. Kidney Int 2003;88:S105-13.
7. Kopple JD, Bernard D, Messana J, et al. Treatment of malnourished CAPD patients with an amino acid based dialysate. Kidney Int 1995;47(4):1148-57.
8. Li FK, Chan LY, Woo JC, et al. A 3-year, prospective, randomized, controlled study on amino acid dialysate in patients on CAPD. Am J Kidney Dis 2003;42(1):173-83.
9. Jones M, Hagen T, Boyle CA, et al. Treatment of malnutrition with 1.1% amino acid peritoneal dialysis solution: results of a multicenter outpatient study. Am J Kidney Dis 1998;32(5):761-9.

6.3 Central obesity can worsen or develop in some PD patients. The risk of this problem, and associated metabolic complications, notably increased atherogenicity of lipid profiles and insulin resistance, can be reduced by avoiding excessive glucose prescription and using icodextrin. (Good practice)

Weight gain, or regain, is common after starting peritoneal dialysis and this is associated with a worsening in the lipid profile (1). Randomised studies comparing glucose 2.27% with icodextrin in the long exchange have shown that the latter prevents weight gain, which in body composition studies is at least in part fat weight (2, 3). Recommendations on how to treat dyslipidaemia are published by the ISPD and include the use of statins (4). There is no currently available trial data on the benefit of statins in PD patients with a hard clinical endpoint; the 4D study did not include PD

patients and there are good reasons for believing that the PD patient population may be different.

1. Little J, Phillips L, Russell L, Griffiths A, Russell GI, Davies SJ. Longitudinal lipid profiles on CAPD: their relationship to weight gain, comorbidity, and dialysis factors. *J Am Soc Nephrol* 1998;9(10):1931-9.
2. Wolfson M, Piraino B, Hamburger RJ, Morton AR. A randomized controlled trial to evaluate the efficacy and safety of icodextrin in peritoneal dialysis. *Am J Kidney Dis* 2002;40(5):1055-65.
3. Davies SJ, Woodrow G, Donovan K, et al. Icodextrin improves the fluid status of peritoneal dialysis patients: results of a double-blind randomized controlled trial. *J Am Soc Nephrol* 2003;14(9):2338-44.
4. Fried L, Hutchison A, Stegmayr B, Prichard S, Bargman JM. Recommendations for the treatment of lipid disorders in patients on peritoneal dialysis. ISPD guidelines/recommendations. International Society for Peritoneal Dialysis. *Perit Dial Int* 1999;19(1):7-16.

6.4 Awareness of the effects of Icodextrin on assays for estimation of amylase and glucose (using glucose dehydrogenase) should be disseminated to patients, relatives, laboratory and clinical staff.

Audit Measure 19: Processes in place to increase awareness of interference of assays by icodextrin metabolites

Use of icodextrin is associated with circulating levels of metabolites that can interfere with laboratory assays for amylase (or actually suppress amylase activity) (1-4) and for glucose when finger-prick tests that utilise glucose dehydrogenase as their substrate are employed (manufactured by Boehringer Mannheim) (5-8). In the case of amylase, the measured level will be reduced by 90%, leading to the potential failure in the diagnosis of pancreatitis. No adverse events have been reported, but clinicians should be aware of this possibility. If clinical concern remains then plasma lipase can be used. In the case of glucose measurements, the methods using glucose dehydrogenase will *over*-estimate blood glucose levels, leading to a failure to diagnose hypoglycaemia. This has been reported on several occasions in the literature and has contributed to at least one death. Typically these errors occur in places and circumstances in which staff not familiar with peritoneal dialysis work, for example emergency rooms and non-renal wards. A number of solutions to this problem are under active review (e.g. use of alarm bracelets) but it is also the responsibility of health-care professionals to ensure that clinical environments in which their patients using icodextrin may find themselves are notified of this issue on a routine basis.

1. Schoenicke G, Grabensee B, Plum J. Dialysis with icodextrin interferes with measurement of serum alpha-amylase activity. *Nephrol Dial Transplant* 2002;17(11):1988-92.
2. Wang R, Leesch V, Turner P, Moberly JB, Martis L. Kinetic analysis of icodextrin interference with serum amylase assays. *Adv Perit Dial* 2002;18:96-9.
3. Anderstam B, Garcia-Lopez E, Heimburger O, Lindholm B. Determination of alpha-amylase activity in serum and dialysate from patients using icodextrin-based peritoneal dialysis fluid. *Perit Dial Int* 2003;23(2):146-50.

4. Garcia-Lopez E, Anderstam B, Heimburger O, Amici G, Werynski A, Lindholm B. Determination of high and low molecular weight molecules of icodextrin in plasma and dialysate, using gel filtration chromatography, in peritoneal dialysis patients. *Perit Dial Int* 2005;25(2):181-91.
5. Wens R, Taminne M, Devriendt J, et al. A previously undescribed side effect of icodextrin: overestimation of glycemia by glucose analyzer. *Perit Dial Int* 1998;18(6):603-9.
6. Oyibo SO, Pritchard GM, McLay L, et al. Blood glucose overestimation in diabetic patients on continuous ambulatory peritoneal dialysis for end-stage renal disease. *Diabet Med* 2002;19(8):693-6.
7. Mehmet S, Quan G, Thomas S, Goldsmith D. Important causes of hypoglycaemia in patients with diabetes on peritoneal dialysis. *Diabet Med* 2001;18(8):679-82.
8. Janssen W, Harff G, Caers M, Schellekens A. Positive interference of icodextrin metabolites in some enzymatic glucose methods. *Clin Chem* 1998;44(11):2379-80.

7. Laboratory and clinical indices

7.1 Monitoring of biochemical and haematological parameters should be performed monthly or at each clinic visit (Good practice).

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).

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

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

The main causal factors of metabolic acidosis are inadequate dialysis delivery, *ongoing renal losses*, excessive animal protein (sulphur containing amino acid) intake and high interdialytic 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. 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.

1. *Mioni R, Gropuzzo M, Messa M et al. Acid production and base balance in patients in chronic hemodialysis. Cli Sci 201;101:329-37*
2. *Lowrie EG, Lew NL. Death risk in hemodialysis 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 hemodialysis 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 hemodialysis 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 hemodialysis 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 hemodialysis patients: a prospective study. Nephrol Dial Transplant 1998;13:1719-22*

7.3 Serum potassium should be between 3.5 and 6.5 mmol/l (Good practice)

The risk of developing hyperkalaemia is inversely related to renal function. 3-5% of deaths in dialysis patients have been attributed to hyperkalaemia (1). Non-compliance with the PD 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.

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 (2). 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 .

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
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)

7.4 Serum phosphate should be within, and preferably nearer to the 50th centile for age. (Good practice) (The normal range for phosphate declines from birth to adult levels by the age of 3 years)

7.5 Serum calcium, adjusted for serum albumin, should be within the age appropriate normal range. (Good practice)

7.6 Serum albumin corrected calcium x phosphate product should be less than 4.8 $mmol^2/l^2$ (Good practice)

7.7 The optimal range for PTH is controversial. There is emerging evidence that levels should be maintained at less than twice the upper limit of normal for the intact PTH assay used. (Good practice)

Audit measure 21 - Cumulative frequency curves of serum calcium, phosphate calcium x phosphate product and PTH concentrations

7.8 Haemoglobin concentration should be greater greater than the lower limit of the age appropriate normal range. (Evidence) The target haemoglobin concentration should be 1g/dl higher, to allow for the normal distribution around the mean haemoglobin value of the patient population and intra individual variation of laboratory measurements and hydration status.

Audit measure 22 - Cumulative frequency curves of haemoglobin concentration

7.9 Ferritin levels should be between 100 and 800 mcg/l

***7.10** Growth, wellbeing and school attendance are very important indicators of dialysis adequacy and should be assessed at least monthly in those under two years of age (length, weight and head circumference) and at least 3 monthly in older children (height, weight and pubertal stage, school attendance). Assessment of dry weight may be difficult in the growing child and also needs checking with at least the same frequency, with close collaboration with a paediatric renal dietician.*

Audit measure 22 Height, weight, head circumference and pubertal progression

***7.10** An assessment of school progress, both in hospital and locally, can be used as an assessment of well-being, and should be made annually*

Audit measure 23 – School attendance

***7.11** Blood pressure should be maintained within the age appropriate normal range*

Audit measure 24 - Cumulative frequency curves of BP pre-dialysis

8. Access to and withdrawal from dialysis

RATIONALE

***8.1** All children with CKD should be considered for renal replacement therapy by stage 4 (Good practice)*

CKD should be suspected in children with: bilateral renal anomalies on antenatal scans (many children with CKD are now diagnosed antenatally); a creatinine above the normal age appropriate range; bilateral renal defects on scans e.g. for UTI; a family history of CKD; persistent proteinuria; or after an episode of acute renal failure. All such children should be referred to a paediatric nephrologist. Early referral provides the opportunity for delaying the progression of CKD by treating hypertension and proteinuria, for optimising growth and preventing renal bone disease. Importantly, it also allows for timely forward planning for renal replacement therapy.

In adults, 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).

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

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

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). 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).

However, although patient choice is paramount, guidance from unit staff is necessary: venous access can be difficult to achieve and maintain in those less than 5 years of age, and needling of a fistula can be particularly difficult in an uncooperative patient. For these reasons, as well as social ones already discussed, PD is recommended in young children.

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 hemodialysis 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)

8.3 After full education and counselling a small proportion of families 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)

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). 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 (e.g. 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), and the family. The family will need to be fully informed throughout, and to be aware of the options. 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 and family'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). Certain patients who are severely ill, often with conditions affecting several organs, may have a concurrent acute deterioration of their chronic renal failure. 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.

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

8.4 Renal replacement therapy should commence when a patient with an eGFR < 15ml/min/1.73m^2 has symptoms or signs of uraemia, fluid overload or malnutrition in spite of medical therapy <u>or</u> before an asymptomatic patient has an eGFR < 6ml/min/1.73m^2. (Good practice)

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/1.73m^2 or 5-7ml/min/1.73m^2 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/1.73m^2 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/1.73m^2 (8).

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

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
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8.5 Any decision to discontinue haemodialysis should be made jointly by the patient (when age appropriate) and their carers and the responsible consultant nephrologist and the renal team and the family practitioner. The decision and reasons for it should be recorded in the patient's notes. Renal units should develop guidelines for palliative care of such patients, including liaison with community services. (Good practice)

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 case notes (7). Renal units should develop guidelines for withdrawal of dialysis that include liaison with palliative care and community services.

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APPENDIX

Assessment of Membrane Function

(a) A number of methods to assess peritoneal membrane have been developed, the most commonly used, supported by clinical observation being the Peritoneal Equilibration Test (PET). This test measures two aspects of membrane function, low molecular weight solute transport (expressed as the dialysate:plasma ratio of creatinine at four hours), and the ultrafiltration capacity of the membrane. In the PET as originally described, ultrafiltration capacity is the net volume of ultrafiltration achieved at four hours using a 2.27% glucose exchange (1, 2). In the simplified Standard Permeability Analysis (SPA) test, it is the net volume of ultrafiltration using a 3.86% exchange (3, 4)

(b) Using a standard PET, an ultrafiltration capacity of < 200 mls (includes overfill) is associated with a 50% risk of achieving < 1000 mls ultrafiltration in anuric patients . Using a SPA test, an ultrafiltration capacity of < 400 mls indicates ultrafiltration failure .

(c) The methods of performing PET and SPA tests are well described in the literature, The following points should be remembered in the interpretation of results:

- High concentrations of glucose interfere with many assays for creatinine. It is important to work with the local biochemists to ensure that the appropriate correction for measurement of creatinine in dialysate has been taken into account.
- Remember that dialysis bags are overfilled, mainly due to the additional fluid volume required to perform the 'flush before fill' procedure. Dialysis manufacturers are being encouraged to publish overfill volumes which differ significantly. The typical volume is 100-200ml. The value of 200 ml UF capacity defining ultrafiltration failure quoted above *includes* the flush volume as this is easier for patients to perform (the alternative is weighing before and after flush which is time consuming and difficult).
- The patient should follow their usual dialysate regime, draining out as completely as possible before the test dwell. Large residual volume of dialysate will affect the results.
- Intra-patient variability of the ultrafiltration capacity (~ 20%) is greater than for the solute transport (<10%). Results of the PET/SPA, in particular the ultrafiltration capacity, should always be interpreted in the light of additional exchanges performed during the

same 24-48 hour period (usually collected to assess solute clearance – see below).

- The PET/SPA are not surrogates for measuring solute clearance.

Measurement of Solute Clearance

In measuring solute clearance and planning changes to the dialysis regime, three clinical parameters are essential: Estimates of (1) *patient size*, (2) peritoneal *solute transport* and (3) *RRF*. In each case, the choice of surrogate "toxin", urea or creatinine, interacts with each of these parameters in different ways. At present, there is no clear evidence from the literature that one surrogate is superior to another. Where possible, clinicians should measure both, attempt to reach at least one of the targets, and understand why there appears to be a discrepancy. A number of commercial computer programs exist that are designed to aid dialysis prescription. Whilst some have been validated, good practice dictates that a change in dialysis prescription is checked for efficacy by repeating clearance studies.

(1) Patient Size

In calculating urea clearances, patient size is expressed as an estimate of the total body water (volume of distribution of urea). It is recommended that the Watson formula is used for this (5):

Males: V = 2.447 – 0.09156 * age (years) + 0.1074 * height (cm) + 0.3362 * weight kg)

Females: V = -2.097 + 0.1069 * age (years) + 0.2466 * weight (kg)

Alternatively 58% of body weight (kg) may be used; this is less precise, and will give lower values for Kt/V, especially in obese patients. Creatinine clearances should be corrected for body surface area, normalising to 1.73 m^2.

(2) Peritoneal Solute Transport

Solute transport rates have an important influence on peritoneal creatinine clearance, but not on urea clearance. This means that it is easier to achieve creatinine clearance targets in high transport patients. It should be remembered, however, that these patients might have less satisfactory ultrafiltration. In designing optimum dialysis regimes, patients with low solute transport will require equally spaced medium length dwells, such as are achieved with CAPD and single extra night exchanges (e.g. 5 x 2.5 litre exchanges). Those with high transport are more like to achieve targets with short dwells (APD) plus polyglucose solutions (e.g. 4 x 2.5 litre exchanges

overnight, 1 x 2.5 litre evening exchange and 1 x 2.5 litre daytime icodextrin).

(3) Residual Renal Function (RRF)

This is the single most important parameter in PD patients, and also the one most likely to change with time. Clinically significant changes can occur within three months. Because secretion of creatinine by the kidney at low levels of function overestimates residual creatinine clearance, it is recommended to express this as the *mean* of the urea and creatinine clearances.

Estimating Total Ultrafiltration

The total achieved ultrafiltration is best measured from the 24-hour dialysate collections used to calculate solute clearance. For APD patients this is simple as machines now calculate the ultrafiltration volumes precisely. Furthemore, many models store this information over several weeks so that an average value can be obtained. In CAPD patients it is important to remember that each bag is overfilled to achieve flush before fill; the total dialysate drain volume must be measured and sampled from to calculate solute clearance accurately, but the overfill must then be subtracted to calculate the net ultrafiltration. If this is not done then over a 24-hour period the overestimate of ultrafiltration may be anything from 200 to 800 ml depending on manufacturer.(6, 7)

Peritoneal sodium losses are largely determined by convection and are thus proportional to the ultrafiltration volume. Typically 1 litre of ultrafiltration results in 100 mmol of sodium loss in CAPD patients and 70-80 mmol in APD patients.

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