Clinical Practice Guidelines : 3b - Peritoneal Dialysis

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Renal Association Audit and Standards Committee

Clinical Practice Guidelines: Peritoneal Dialysis
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RATIONALE FOR CLINICAL PRACTICE GUIDELINES FOR PERITONEAL DIALYSIS

1. Equipment and Resources (Guidelines 1.1-1.5)
2. Preparation for Peritoneal Dialysis (Guidelines 2.1-2.4)
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Summary of Clinical Practice Guidelines for Peritoneal Dialysis

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

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.

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.

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

1.5 Biocompatible PD solutions (normal pH, low concentrations of glucose degradation products) should be used in patients experiencing infusion pain.

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.

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.

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/V_{urea} 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

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, use of diuretics, ACEi and ARBs

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

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

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 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.

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.

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.

DETAILED RATIONALE AND AUDIT MEASURES

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, indicate 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 caseload of 20 PD patients (see recommendations of the National Renal Workforce Planning Group, 2002).

Audit Measure 1: Availability of modality choice
Audit Measure 2: Monitoring of modality switching
Audit Measure 3: Patient to peritoneal dialysis nursing staff ratio

1. Fenton SSA, Schaubel DE, Desmeules M, et al. Hemodialysis versus peritoneal dialysis: a comparison of adjusted mortality rates. *American Journal of Kidney Diseases* 1997;30(3):334-42.
2. Vonesh EF, Snyder JJ, Foley RN, Collins AJ. The differential impact of risk factors on mortality in hemodialysis and peritoneal dialysis. *Kidney Int.* 2004;66(6):2389-401.
3. Heaf JG, Lokkegaard H, Madsen M. Initial survival advantage of peritoneal dialysis relative to haemodialysis. *Nephrol Dial Transplant* 2002;17(1):112-7.
4. Termorshuizen F, Korevaar JC, Dekker FW, Van Manen JG, Boeschoten EW, Krediet RT. Hemodialysis and peritoneal dialysis: comparison of adjusted mortality rates according to the duration of dialysis: analysis of the Netherlands cooperative study on the adequacy of dialysis 2. *J Am Soc Nephrol* 2003;14(11):2851-60.
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7. Bro S, Bjorner JB, Tofte-Jensen P, et al. A prospective, randomized multicenter study comparing APD and CAPD treatment. *Perit Dial Int* 1999;19(6):526-33.
8. 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.
9. Lewis NM, Pickering KR. Establishment of a formalized CAPD retraining program. *Perit Dial Int* 1995;15:S58.
10. Bernardini J, Piraino B. Compliance in CAPD and CCPD patients as measured by supply inventories during home visits. *Am J Kidney Dis* 1998;31(1):101-7.
11. Ponferrada L, Prowant BF, Schmidt LM, Burrows LM, Satalowich RJ, Bartelt C. Home visit effectiveness for peritoneal dialysis patients. *Anna J* 1993;20(3):333-6.

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 4: 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 5: 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 6: 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).

Audit Measure 7: 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 (Dianeal) (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 EPS is rare before this period of time on treatment. This issue remains controversial at this stage and further studies are required.

1. Mactier RA, Sprosen TS, Gokal R, et al. Bicarbonate and bicarbonate/lactate peritoneal dialysis solutions for the treatment of infusion pain. *Kidney Int* 1998;53(4):1061-7.
2. Liberek T, Topley N, Jorres A, et al. Peritoneal dialysis fluid inhibition of polymorphonuclear leukocyte respiratory burst activation is related to the lowering of intracellular pH. *Nephron* 1993;65(2):260-5.
3. Jorres A, Bender TO, Finn A, et al. Biocompatibility and buffers: effect of bicarbonate-buffered peritoneal dialysis fluids on peritoneal cell function. *Kidney Int* 1998;54(6):2184-93.
4. Jörres A, Topley N, Steenweg L, Müller C, Köttgen E, Gahl GM. Inhibition of cytokine synthesis by peritoneal dialysate persists throughout the CAPD cycle. *Am J Nephrol* 1992;12(1-2):80-5.
5. McGregor SJ, Brock JH, Briggs JD, Junor BJ. Longitudinal study of peritoneal defence mechanisms in patients on continuous ambulatory peritoneal dialysis (CAPD). *Perit Dial Int*
Peritoneal Dialysis International 1989;9:115-9.
6. Topley N. Membrane longevity in peritoneal dialysis: impact of infection and bio- incompatible solutions. *Adv Ren Replace Ther* 1998;5(3):179-84.

7. Topley N, Alobaidi HM, Davies M, Coles GA, Williams JD, Lloyd D. The effect of dialysate on peritoneal phagocyte oxidative metabolism. *Kidney Int* 1988;34(3):404-11.
8. Davies SJ, Phillips L, Naish PF, Russell GI. Peritoneal glucose exposure and changes in membrane solute transport with time on Peritoneal Dialysis. *J Am Soc Nephrol* 2001;12(5):1046-51.
9. Davies SJ. Longitudinal relationship between solute transport and ultrafiltration capacity in peritoneal dialysis patients. *Kidney Int* 2004;66:2437-45.
10. Williams JD, Craig KJ, Topley N, et al. Morphologic changes in the peritoneal membrane of patients with renal disease. *J Am Soc Nephrol* 2002;13(2):470-9.
11. Rigby RJ, Hawley CM. Sclerosing peritonitis: the experience in Australia. *Nephrol Dial Transplant.* 1998;13(1):154-9.
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.
16. Williams JD, Topley N, Craig KJ, et al. The Euro-Balance Trial: the effect of a new biocompatible peritoneal dialysis fluid (balance) on the peritoneal membrane. *Kidney Int* 2004;66(1):408-18.
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.

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 8: 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 9: 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).

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.

2.3 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).

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.

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 10: 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 11: 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). The recommendation to measure solute clearance six-monthly is driven primarily by the residual renal function component; indeed if dialysis dose has not been changed the peritoneal component will not be different and it would be acceptable just to measure the residual renal function. Indeed RRF can fall rapidly in some patients, certainly within a few weeks, and if there are clinical concerns this should be undertaken more frequently. 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 one or both can be used, ensuring that minimal clearances are achieved for at least one, 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 and/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 (Evidence)

Audit Measure 12: 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/week 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 is greater. Equally, in a patient 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).

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.
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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 13: 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:

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

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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.
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4.2 Dialysis regimens 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 14: 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.
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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.
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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.
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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;in press.

4.3 Dialysis regimens 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. frusemide 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).

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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.

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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 15: 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.

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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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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.
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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 regimens 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

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 regimens 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.
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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.

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 regimens, 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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