Peritoneal Dialysis International, Vol. 34, pp. 494–517
doi: 10.3747/pdi.2013.00222
0896-8608/14 $3.00 + .00

ISPD GUIDELINES/RECOMMENDATIONS

PERITONEAL DIALYSIS FOR ACUTE KIDNEY INJURY

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Peritoneal dialysis (PD) was initially used in the 1920s to treat acute kidney injury (AKI), but it was not until 1946 that it was first described to save the life of a patient (1). Dialysis solutions initially produced hyperchloremia and overhydration, but refinements such as the addition of sodium lactate or bicarbonate rather than sodium chloride, as well as the use of gelatin or dextrose to increase tonicity, led to better outcomes (2). As solutions and peritoneal dialysis catheters improved, so did outcomes, with a resulting increase in PD utilization. Peritoneal dialysis for AKI has, however, more recently become sidelined by newer, more technologically advanced treatments such as hemofiltration and hemodialysis (HD) (3,4). In a recent review on the dose of dialysis in AKI, PD was not even mentioned as a potential modality (5). This is despite studies demonstrating that it is at least as effective as daily HD and possibly hemofiltration (6,7). Gaiao *et al.*'s survey, amongst delegates at 3 major dialysis congresses, found that 36% felt PD was suitable for AKI in the intensive care unit (ICU); however, only 15% actually practiced it. When it came to treating AKI in the wards, more than 50% felt it was suitable. In the

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Received 20 August 2013; accepted 24 February 2014.
Supplemental material available at www.pdiconnect.com

same study, acute PD was far more likely to be practiced by physicians from Asia compared to those from Europe and North America (8). The reasons for this are not certain, but likely include the fact that PD is a modality now most often used in the developing world, where cost and available resources are major issues. In these countries, it offers significant cost and infrastructural benefits over HD/hemofiltration because it does not require electricity nor does it use expensive machinery or consumables (6,9). Kilonzo *et al.* showed that it costs approximately $370 to save the life of one patient with AKI with PD and George *et al.* noted that acute PD costs half that of hemofiltration (6,9).

As PD for AKI is predominantly practiced in developing countries where the infrastructure for quality research is often lacking, the result has been limited evidence on which to base clinical decisions in areas such as dosing, volumes etc. There is also a lack of standardized treatment regimes. For example, in published studies, weekly Kt/V's have ranged between 1.8 and 5.6 and fluid volumes have varied from 13 – 70 L per day (6,7,10,11). Gaiao *et al.*'s survey also noted variability in the PD modalities used and there is considerable ambiguity about the appropriate PD dose for AKI. Indeed, 66 – 70% of practitioners professed uncertainty regarding the appropriate PD dose. Even among those who did use PD for AKI, 37 – 52% were uncertain of the appropriate dose (8). This is likely related, at least in part, to a lack of definitive data and/or consensus guidelines.

METHODS

These guidelines have been developed under the auspices of the International Society of Peritoneal Dialysis to help standardize practice, based on the available evidence, and enable those practicing PD for AKI to achieve optimal results. It is hoped that this will facilitate increased access to renal replacement therapy (RRT) in developing countries, and by standardizing practice, act as a platform for future research. The committee has been carefully selected to include adult and pediatric nephrologists as well as intensive care specialists from around the world with a bias towards including practitioners from those countries where PD for AKI is practiced as a routine. Each section was written by at least two authors who performed a review of the literature in that area. The section was reviewed by the co-chairs (BC, FF) and finally the recommendations and their grading were made by consensus. The final guidelines were then subsequently reviewed by all authors. The authors of each section can be found in online supplementary material. The recommendations are based on the GRADE system, a well validated structure which matches the strength of the recommendation to the level of evidence (12), where Grade 1 is a strong and 2 is a weak recommendation. The letters (A–D) indicate the level of evidence used to make the recommendations. Where no evidence exists, but there is enough clinical experience for the committee to make a recommendation, this will be categorized as opinion (level D).

These guidelines have been developed for practitioners working in very different conditions. In some cases what is felt to be optimal care may not be practical due to resource limitations. It is, therefore, important to define a minimum standard which needs to be achieved to ensure that the benefits of PD treatment for AKI outweigh the risks; this minimum standard may not, however, be deemed optimal treatment. There will, therefore, be recommendations made for "minimum standard" or "optimum," but practitioners should always strive to achieve the latter. There is no validated method of defining these two standards, and they are based on consensus by the authors, using the best available evidence.

These are guidelines and as such should be used to direct practice patterns. It is important to keep in mind, however, that the guidelines may not be applicable to all clinical situations; clinicians should use the information to offer the best care to patients, understanding that deviation from the guidelines may be necessary.

ADULT GUIDELINES

GUIDELINE A1: Suitability of peritoneal dialysis for AKI in adults

A1.1 Peritoneal dialysis should be considered as a suitable method of continuous renal replacement therapy in patients with acute kidney injury (1B).

RATIONALE

Guideline A1.1: Peritoneal dialysis has many potential advantages over extracorporeal RRT (13). It is technically simple, with minimal infrastructure requirements, and, therefore, lower cost. It may be the preferred option for the patient with difficult vascular access or those at risk of bleeding as there is no need for anticoagulation. Solute removal is gradual, with less potential for disequilibrium syndrome and intracranial fluid shifts, making it perhaps a better modality among patients at risk of increased intracranial pressure. Since no extracorporeal circulation is required, there is relatively good hemodynamic tolerance, and local renal hemodynamics may be better preserved. It has also been postulated that PD may be more physiologic and less inflammatory than

extracorporeal therapies which involve the exposure of blood to synthetic membranes. These factors together could potentially contribute to earlier recovery of renal function (7). In sepsis there is considerable interest in the use of high cut-off membranes for hemofiltration to allow removal of toxic cytokines. These have been shown to reduce the need for vasopressors (14). As the peritoneal membrane has pores large enough to allow clearance of these molecules, PD may provide a significant advantage over conventional HD and filtration.

There are nevertheless important concerns regarding PD in AKI, primarily involving the risk of peritonitis, potentially unpredictable fluid removal rates and possible inadequate solute clearances, particularly in hypercatabolic patients or those with splanchnic hypoperfusion or who are on vasopressors. In contrast, modern HD and continuous veno-venous hemofiltration (CVVH) machines have precise volumetric systems that guide fluid removal and many have online solute clearance monitoring, conferring clear advantages and likely contributing to increased physician "comfort" with HD and CVVH as compared to PD. Other potential PD-specific problems include glucose absorption and hyperglycemia from glucose-containing dialysate, ongoing exposure to glucose degradation products and advanced glycosylation end-products from glucose-containing peritoneal dialysate exposure, and excessive protein loss through the peritoneal membrane. An additional concern, particularly in mechanically ventilated patients, is impaired diaphragmatic movement resulting in reduced functional residual capacity. Gokbel *et al.*, however, showed that in healthy continuous ambulatory PD patients, although there was a reduction in pulmonary expiratory reserve volume and functional residual capacity, inspiratory capacity increased when the abdomen was full; therefore the effects of PD on ventilation need to be studied further (15).

Overall, good data on PD in AKI are limited, and these were summarized in a recent systematic review (16). Thirteen studies described patients treated with PD only, while 11 studies compared PD and continuous or intermittent extracorporeal RRT. Of the 11 studies comparing PD and extracorporeal RRT, 4 were randomized controlled trials (RCT). Overall, there was no difference in mortality between PD and extracorporeal RRT in both the observational studies (odds ratio (OR), 0.96; 95% confidence interval (CI), 0.53–1.71) and the 4 RCTs (OR, 1.50; 95% CI, 0.46–4.86). Three of the RCTs were conducted primarily among septic or critically ill patients (77–100% of cases). Gabriel *et al.*'s randomized trial was well conducted; however, it has been criticized for flaws in randomization, inclusion criteria, and not being powered to detect a mortality difference (7). The other 2 studies were stopped early and were of suboptimal methodological quality, with unclear randomization process, lack of intention-to-treat analysis, modest sample sizes, and single-center design. Peritoneal dialysis techniques also varied among these 3 studies. Two of these studies compared continuous PD with continuous RRT (6,17), while the third compared PD with daily intermittent HD (7). The fourth RCT randomized 40 acute or chronic renal failure patients to either intermittent PD or HD; only 8 (4 PD, 4 HD, 7/8 sepsis) had AKI (18). In the 7 cohort studies, there was no difference in mortality between PD and extracorporeal RRT (OR 0.96; 95% CI, 0.53–1.71). Although pooled results of the 4 RCTs also suggested no difference in mortality (OR 1.50; 95% CI, 0.46–4.86), the results were heterogeneous.

Peritoneal dialysis was significantly inferior to CVVH in the study by Phu *et al.* (17). In this study, which was stopped early, the PD technique was less than ideal, with the use of rigid catheters, manual exchanges and open drainage. Indeed, cloudy dialysate was observed in 42%, potentially representing peritonitis episodes, which may have contributed to poor outcomes in the PD group. The CVVH group also had a surprisingly low mortality (15%) for the disease severity, conflicting with results from larger studies of AKI in sepsis where mortality ranges from 45 – 60%, suggesting a type 1 error (3,19). Furthermore, the leading cause of AKI in this study was severe falciparum malaria (68% of cases), in contrast to sepsis in the other 3 studies. It has been postulated that the erythrocytic phase of malaria parasites was accelerated due to high splanchnic-blood glucose levels resulting from glucose-based peritoneal dialysate. The results of this study have, however, been questioned by a retrospective study from India showing no difference in survival between patients treated with PD vs daily HD despite higher numbers in the PD cohort having cerebral malaria and shock (20).

In the other 3 studies, mortality rates were comparable between PD and extracorporeal therapies (6,7,18). George *et al.* compared PD with continuous veno-venous hemodiafiltration (CVVHDF) looking primarily at solute control (correction of uremia, electrolyte and acid-base disorders), as well as correction of fluid overload (6). Urea and creatinine clearances, as well as control of fluid overload, were significantly better with CVVHDF than PD; however, correction of acidosis was better with PD. Peritoneal dialysis and CVVHDF were comparable with respect to correction of hyperkalemia and hemodynamic disturbance. In the study by Arogundade *et al.*, all 8 AKI patients, of whom 4 were treated with manual

intermittent PD, survived (18). Gabriel *et al.* were the only investigators who used a cycler, allowing higher exchange volumes compared to the other trials (7).

In terms of recovery of renal function, results are also conflicting. One study (7) demonstrated shorter time to renal recovery with PD compared with daily HD. Two other studies noted that patients on PD required more or longer dialysis sessions which, although not specifically reported, may indicate a longer time to recover function (6,17).

Overall there is enough evidence to base the recommendation that PD is a suitable method of renal replacement therapy in AKI.

GUIDELINE A2: Access and fluid delivery for acute PD in adults

A2.1 Flexible peritoneal catheters should be used for acute PD where resources and expertise exist (1C) (Optimal). It may be necessary to use rigid stylet catheters or improvised catheters in resource-poor environments where they may still be lifesaving (2D) (Minimum standard).

A2.2 We recommend catheters should be tunneled in order to reduce peritonitis and peri-catheter leaks (1D).

A2.3 No method of insertion of PD catheter is superior to any other overall. We recommend that the method of implantation should be based on patient factors and local availability of skills, equipment, and consumables (1D).

A2.4 Peritoneal dialysis catheter insertion by nephrologists is safe and functional results equate to those inserted surgically (1B).

A2.5 We recommend that nephrologists receive training and be permitted to insert these catheters to ensure timely dialysis in the emergency setting (1B).

A2.6 Insertion of the Tenckhoff catheter should take place in the most sterile environment available, using sterile technique with the operator using gloves, gown and mask (1D).

A2.7 We recommend the use of prophylactic antibiotics prior to insertion of the Tenckhoff Catheter (1C).

A2.8 A closed fluid delivery system with a Y connection should be used (1A) (Optimal). In resource-poor areas spiking of bags and makeshift connections may be necessary (2D) (Minimum standard). It is imperative that strict asepsis be maintained throughout.

RATIONALE

Guideline A2.1 – Catheter Type:

Flexible Catheter: The Tenckhoff catheter remains the gold standard for PD access and is the most widely used in chronic dialysis (21). These catheters are preferable to those mentioned below as they have a larger diameter lumen and side holes resulting in better dialysate flow rates and less obstruction which is imperative in acute PD to achieve adequate clearances. They are also less prone to leakage and have a lower incidence of peritonitis (22). If the patient does not recover renal function, the catheter may be used for chronic dialysis without the need for a new access procedure.

These catheters can be inserted under local anesthesia at the bedside or in a surgical theatre. The bedside insertion utilizes a modified Seldinger approach using a guidewire and peel-away sheath. This is a blind procedure and therefore contraindicated in those who have a midline surgical scar or history to suggest intra-abdominal adhesions. Where death from kidney failure is imminent and no options for direct visualization exist, this could be considered a relative contraindication. (Step-by-step insertion guidelines will be published on the ISPD website later this year.)

Rigid Catheter: These catheters are inserted using a sharp trochar device directed toward the iliac fossae. They are easy to insert; however, they tend to be associated with less efficient dialysis. Possible complications with this catheter design include bleeding, bowel or bladder perforation, obstruction due to the small side holes and lumen, and leakage of dialysate. The incidence of peritonitis increases with the time the catheter is left in the abdomen (23).

Improvised Catheters – Nasogastric Tube, Rubber Catheter and Intercostal Drainage Catheter: These improvised catheters have been used for access in resource-poor settings. They need to be surgically implanted and have the disadvantages of few side holes and are less suitable for tunneling, with a resultant higher risk of dialysate leakage. They may be lifesaving, though, and therefore may be used when no other alternative is available.

A comparison of flexible Tenckhoff catheters and rigid stylet catheters in 64 children who underwent acute PD

reported fewer complications with Tenckhoff catheters and significantly longer catheter survival (22).

In conclusion, although there is little published evidence that flexible catheters are superior to these other catheters apart from a small study in children, it is the authors' experience and opinion that better flow rates and fewer complications occur when using a flexible catheter. This is the basis for this recommendation. The advantages and disadvantages of each are summarized in Table 1.

Guidelines A2.2 – A2.6 – Method of Insertion: The key to effective PD is a catheter which allows rapid inflow and outflow of fluid to maximize the dialysate dwell time and contact of the dialysate with the peritoneal membrane. This is predominantly dependent on the catheter used (see above), but will be influenced by the position of the catheter and any interference from the omentum or adhesions. Leakage of fluid through the surgical wound necessitates reduction in fill volumes or even stopping PD for a number of days; therefore any technique which reduces this problem is preferable.

Rigid catheters are inserted using a blind trochar technique; however, the optimal method of catheter insertion involves placement of a flexible catheter using a variety of techniques, including the percutaneous ("blind" modified Seldinger technique with a peel-away sheath), laparoscopic and open surgical approaches. The potential risks and benefits of each of these methods are shown in Table 2. Most studies compare these approaches in chronic PD patients, which may influence the results as the patients may have a bowel preparation pre-operatively and there is often a delay in starting dialysis for up to 2 weeks prior to initiation of PD. This reduces the risk of catheter displacement and leak of dialysate; but this is not feasible in most patients with AKI. Nevertheless, these studies offer insight into the risks and benefits of each method and will be discussed briefly. Henderson *et al.* compared 283 percutaneous with 104 surgically inserted catheters. The incidence of leak (6% vs 10% $p = 0.18$) and poor drainage (21% vs 23% non significant) were similar between both methods. However, peritonitis within the first month was significantly higher in the surgical group (4% vs 13% $p = 0.009$) (24). Perakis *et al.* reported 170 PD catheter insertions (86 percutaneous) where a higher incidence of leak occurred in the percutaneous group (10% vs 2%). However, infectious complications were higher in the surgical group (25). A trial from Iran randomized 64 patients to surgical or percutaneous insertion and found a higher incidence of outflow failure and hemoperitoneum in the surgical group. However, the number of events was low and results should be interpreted with caution (26). An audit from the UK Renal Registry showed a higher incidence of peritonitis within the first 2 weeks as well as lower 3-month catheter malfunction in surgically implanted catheters (27). Laparoscopic insertion has been shown to have an incidence of leak of as low as 2% (28) and a meta-analysis by Strippoli *et al.* showed a trend toward reduced technique failure with laparoscopy compared to laparotomy; however, this did not reach statistical significance (relative risk [RR] 0.45 – 1.08) (29). A more recent meta-analysis by Hagen *et al.* showed better catheter survival with the laparoscopic method (30). These studies demonstrate that there is little difference in outcomes of all the various methods in chronic patients and the International Society for Peritoneal

TABLE 1
Advantages and Disadvantages of Flexible, Rigid, and Other Peritoneal Access

	Advantages	Disadvantages
Rigid stylet catheter	• Inexpensive, but not necessarily cost effective • Can be performed at bedside • Easily removed	• Catheter dysfunction • Flow-related problems • Risk of perforation of the internal organs or blood vessels
Flexible catheter	• Better inflow and outflow (5,6) • Less chance for perforation • Less leaks and infection • Can be performed at bedside	• More expensive • Requires more training than stylet catheter • Catheter tip migration
Intercostal drainage tubes, nasogastric tubes, rubber tubes, etc.	• Readily available • Inexpensive	• Flow-related problems • Infections • High risk for leaks • Difficulty with achieving reliable connections

TABLE 2
Advantages and Disadvantages Different Catheter Implantation Techniques

	Advantages	Disadvantages
Percutaneous (bedside)	• Can be performed at bedside allowing rapid initiation of dialysis • Physician or nurse can be trained to perform the procedure	• Risk of bowel or bladder injury • Not suitable in patients with previous midline surgical scars or risk of adhesions
Open surgical	• Available in most centers • Cost of consumables lower than laparoscopy	• Needs surgical scheduling, where available theatre time at a premium
Laparoscopy	• Lower incidence of leak • Ability to perform adjunctive procedures such as rectus sheath tunneling and omentopexy, etc. • Ability to place the catheter in the pelvis under vision	• Skilled personnel necessary • High cost of consumables

Dialysis (ISPD) guidelines on peritoneal access recommend that the method of insertion should depend on expertise at the center (31). In some centers this may also be influenced by the availability of catheters and laparoscopic equipment.

When comparing urgent start PD for patients with advanced renal failure, there is little evidence available as to the preferred method. Povlsen *et al.* showed an incidence of leak in their surgically placed catheters of 7.7% (using small fill volumes), which was not significantly different from their chronic patients; peritonitis rates were no different (32).

In conclusion, the method of flexible catheter placement should be that suited to the unit, balancing skills, resources, and cost effectiveness. Patients with previous midline surgical scars or high risk of peritoneal adhesions should have the catheter inserted using a technique which allows direct vision.

Guideline A2.7 – Prophylactic Antibiotics: Colonization of the Tenckhoff catheter and/or contamination at the time of insertion increases the risks of development of subsequent peritonitis, and as such needs to be avoided through strict sterile technique. The most appropriate place for insertion of the catheter will depend on the clinical setting of the patient. For example, in a patient with multi-organ failure and shock the most appropriate place may be at the bedside, whereas a stable patient should be transferred to a surgical theatre, radiology suite, or dedicated procedure room. There are no trials answering this question; however, the experience of many clinicians is that bedside insertion is safe and does not lead to increased peritonitis risk as long as strict sterile technique is adhered to.

Prophylactic antibiotics do not obviate infections if the above measures are not followed. However, when used in conjunction with sterile technique, there is a decrease in the incidence of peritonitis with the use of prophylactic antibiotics. The decision of which antibiotics to use is also dependent on local bacterial sensitivities, timing of the procedure, and availability. It is generally accepted that the most important organisms to protect against are the gram-positive organisms. However, given the small risk of bowel injury some clinicians use an agent which would also cover gram-negative bacteria.

Prophylactic antibiotics need to have adequate tissue levels prior to the initial incision. It therefore makes agents which require a long infusion time unsuitable for patients who need emergent dialysis.

The largest study in chronic PD patients was performed by Gadallah *et al.*, who randomized 254 patients to receive either vancomycin, cefazolin, or no prophylaxis. The relative risk of development of peritonitis was 6.54 for cefazolin and 11 with no prophylaxis when compared to vancomycin. The vancomycin was given 12 hours before the procedure, and, as it requires an infusion for 30 to 90 minutes, it may not be suitable for patients requiring urgent acute PD (33). Wikdahl *et al.* reported a small study of 38 patients randomized to cefuroxime 1.5 g intravenous (IV) + 250 mg in PD fluid vs placebo. They showed a significant reduction in the number of cases of peritonitis; however it should be noted that in the control arm the incidence of peritonitis was unacceptably high (34). Other agents which have been used

are gentamicin and a combination of gentamicin and cefazolin (35,36). A Cochrane meta-analysis in 2004 showed that there was a significant reduction in the incidence of peritonitis with the use of prophylactic antibiotics (37).

Guideline A2.8 – Fluid Delivery: Collapsible bags of varying sizes and glucose concentrations can be used for acute PD (38). Rigid glass bottles and non-collapsible plastic containers may also be available (10,17). The collapsible bags may have integral transfer tubing which allows a closed system once connected to the patient. This is safer compared to rubber stopper bottles and bags which require spiking.

Disconnecting systems with Y-set and double bag are associated with lower peritonitis rates compared to the standard spiking system in chronic patients and there is no reason to suspect this would not be the case in acute PD (39–41). In order to use the disconnect systems, there needs to be an adequate supply of closure devices to ensure that the end of the catheter does not become contaminated between exchanges. If these are not available, it may be safer to leave the bag connected to the patient and perform a "reverse" exchange (i.e. fill the peritoneum and leave the patient connected for the dwell, then drain and disconnect, attaching the new bag prior to the next fill).

Cycler: Automated cycler PD is the term used to refer to all forms of PD that employ a mechanized device to assist in the delivery and drainage of dialysate. A volume of dialysate is prescribed as well as the therapy time and fill volume. The advantage of this system is that it can be set up by a trained staff member once per day to reduce the risk of complications. It also reduces nursing time as all cycles are automatic. There are conflicting reports of whether there is a reduction in peritonitis with cyclers but on balance there appears to be no difference compared to the manual system in chronic PD. Another benefit is that they can offer tidal PD, where a small volume of fluid is left in the abdomen at all times, which may reduce mechanical complications and may reduce pain associated with complete fluid drainage. Occasionally, though, the fixed hydraulic suction may worsen mechanical obstruction in catheters with already tenuous fluid flow. Automated cyclers have been used extensively for PD in AKI; however in a resource-poor setting, cyclers may prove too expensive (42,43). A further disadvantage of cyclers is that if there is no support after hours for inexperienced nurses using the cyclers, there is the risk of the machines being turned off during the night to avoid alarms.

We recommend that, where possible, a closed system be used. There is no evidence that automated PD is any safer than manual exchanges.

GUIDELINE A3: Peritoneal dialysis solutions for acute PD

A3.1 In patients with shock or liver failure, bicarbonate-containing solutions should be used (1B) (Optimal). Where these solutions are not available, the use of lactate-containing solutions is an alternative (1D) (Minimum standard).

A3.2 Once potassium levels in the serum fall below 4 mmol/L, potassium should be added to dialysate using sterile technique (see below) (1D).

A3.3 Potassium levels should be measured daily (1D) (Optimal). Where these facilities do not exist, we recommend assessing the patient with regular electrocardiogram (ECG) recording and, after 24 hours, consider adding potassium to dialysate (2D) (Minimum standard).

A3.4 Commercially prepared solutions should be used (1C) (Optimal). However, where resources do not permit this, then locally prepared fluids may be lifesaving (2D). There is a high potential risk of contamination when preparing fluid and every effort should be made for this to be performed by pharmacists in a sterile environment not at the bedside (1D) (Minimum standard).

RATIONALE

Guideline A3.1 – Lactate- vs Bicarbonate-Buffered Solutions: PD solutions using lactate as a buffer are the standard for use in AKI. Lactate is converted to bicarbonate mainly through liver and muscular pyruvate dehydrogenase enzymes. However, AKI occurs mostly in critically ill patients. Shock, poor tissue perfusion states, and liver failure are not uncommon in this setting, impairing the conversion of lactate to bicarbonate, which may contribute to the development of or aggravation of metabolic acidosis (44–46).

There is 1 randomized controlled trial with 20 AKI patients comparing the effectiveness of bicarbonate- vs lactate-buffered PD solutions with a dwell time of 30 minutes. The authors found no difference between bicarbonate and lactate for clinically important outcomes, such as mortality and adverse events (RR 0.50, 95% CI 0.06–3.91) (44). By cycle 12, in shock patients treated

with bicarbonate-buffered solution, there was a more rapid increase in serum bicarbonate (21.2 ± 1.8 mmol/L vs 13.4 ± 1.3 mmol/L) and blood pH (7.3 ± 0.03 vs 7.05 ± 0.04, $p < 0.05$). These improvements remained statistically significant between the 2 groups through cycle 36. Overall, lactate levels were significantly lower in the groups receiving the bicarbonate-buffered solution in both the patients with shock (3.6 ± 0.4 mmol/L vs 5.2 ± 1.3 mmol/L) and without shock (2.9 ± 0.2 mmol/L vs 3.4 ± 0.2 mmol/L). Of note, patients without shock had comparable improvements in both blood pH and serum bicarbonate with either solution. Other outcomes, such as hemodynamic stability, could not be analyzed because of the limited data available. Results of this study suggest that AKI associated with poor perfusion states should be managed with the use of bicarbonate-buffered solutions rather than lactate solutions (45,46).

Guidelines A3.2 – A3.3 – Potassium Supplementation: Standard PD solutions do not contain potassium (K), which is lost during PD by diffusion and convection. In general, after 4- to 6-hour exchanges, serum and dialysate potassium concentrations are similar (47). As a result, a significant number of chronic PD patients either develop hypokalemia (K < 3.5 mmol/L) or require potassium supplementation to maintain normal serum K levels (47,48).

Hypokalemia has been identified as a risk factor for peritonitis and death in chronic PD patients (48,49). Chuang *et al.* found a greater incidence of peritonitis in hypokalemic compared to normokalemic patients (6.9% vs 2.1%, $p < 0.001$) (49). Hypokalemia reduces gastrointestinal motility, potentially resulting in bacterial overgrowth and transmural migration of enteric organisms. It may also signify malnutrition, which may be associated with altered immune defenses within bowel loops, increasing the risk of peritonitis. Szeto *et al.* concluded that chronic PD patients with hypokalemia had significantly worse actuarial survival than those without hypokalemia after adjusting for confounding factors. They noted that serum potassium levels in these patients were associated with poorer nutritional status and increased severity of coexisting comorbid conditions (50).

Losses of potassium can be high in acute PD because each 2-L exchange has the potential to remove up to 2x the serum potassium concentration. Such removal may cause serious potassium depletion and cardiovascular instability. This might be prevented or corrected by adding potassium to the dialysis solution (4 mmol/L) (45).

In Ponce *et al.*'s and Gabriel *et al.*'s studies on PD in AKI patients, serum potassium control was obtained after a 1-day session of high-volume PD and, when serum potassium was lower than 4 mmol/L, K 3.5 to 5 mmol/L was added to dialysis solutions to avoid hypokalemia (7,11,51,52). It is important that sterile technique be maintained when potassium is added and that nurses be carefully instructed to make certain the amount added is appropriate.

Guideline A3.4 – Commercial vs Locally Mixed Solutions: Commercially produced solutions are produced to high standards with strict asepsis and careful monitoring for bacterial and endotoxin contamination. Locally prepared solutions carry the potential risks of contamination and mixing errors which may be life-threatening. Commercial solutions often have closed drainage systems to prevent accidental contamination. However, the disadvantage of commercial solutions involves the costs, which may limit utilization in low-resource settings, particularly if patients are paying for their own care. The costs include both the cost of purchasing the solutions as well as the costs of arranging transportation of solutions to sites doing the treatment, including taxes and bureaucratic assessments. The costs of peritonitis due to contaminated locally produced fluid must also be borne in mind, though, when making decisions based on financial grounds.

The ISPD recommends the following types of fluid in order of preference:

- Commercially prepared solutions
- Locally prepared fluid made in an approved and certified aseptic unit/pharmacy. These products would have a limited expiry time as approved by the manufacturing unit (see http://www.ashp.org/DocLibrary/BestPractices/PrepGdlCSP.aspx for guidelines on standards for compounding pharmaceuticals).
- Solutions prepared in a clean environment with a minimum number of punctures and the least number of steps. This fluid should be used immediately.

In situations where dialysis fluids are not available or are unaffordable, dialysis fluids can be prepared using available intravenous fluids. Table 3 below shows some examples of intravenous fluids that can be converted into dialysis fluids. Table 4 shows the composition of some commercially available fluids.

By adding glucose and/or bicarbonate to these fluids, solutions can be developed that are similar in composition to standard dialysis solutions. See Appendix 1 for examples.

The osmolality and ultrafiltration capacity of these solutions can be increased by adding further glucose to approximate that of commercial solutions.

It should be noted that in making solutions using the above approach, calcium and magnesium may not be

TABLE 3
Commercially Available Intravenous Fluids

Type of fluid	Na^+	K^+	Ca^{2+}	Mg	Cl-	HCO_3-	lactate	pH	osm.
Hartmann's solution	131	5	2.0		111		29	7.0	278
Ringer's lactate	131	5	1.8		112		28	6.5	279
Plasmalyte B	130	4	0	1.5	110	27		7.4	273
½ Normal saline	77				77			5.0	154

Na = sodium; K = potassium; Ca = calcium; Mg = magnesium; Cl = chlorine; HCO_3 = bicarbonate; osm = osmolarity.

TABLE 4
Typical Composition of Commercially Available PD Fluid

Type	Na^+	K^+	Ca^{2+}	Mg	Cl-	HCO_3-	lactate	pH	osm.
Stay-safe 1.5%	132		2.5	0.5	95		40	5.5	344
Dianeal 1.5%	132		2.5	0.25	95		35	5.2	344

Na = sodium; K = potassium; Ca = calcium; Mg = magnesium; Cl = chlorine; HCO_3 = bicarbonate; osm = osmolarity.

present. In general, this is not a problem for acute PD, which is usually of short duration. If calcium or magnesium supplementation needs to be given, this can be done by giving oral or intravenous supplementation. Many of the plasma expanders contain potassium and, although after the first 24 hours this may be beneficial, it may be counter-productive initially.

General rules when preparing dialysis solutions:

- The concentrations of the well-known IV solutions may vary from country to country so check concentrations before mixing
- Maintain absolute strict sterile technique when mixing solutions
- The fewer components added to the solution, the lower the risk of infection and error
- Avoid mixing bicarbonate and calcium as they will precipitate
- In cases of severe hypernatremia, add concentrated NaCl to increase Na to within about 15 mmol of patient's sodium to allow a gradual reduction in the serum sodium.

GUIDELINE A4: Prescription of Acute PD

A4.1 Where resources permit, targeting a weekly Kt/V urea of 3.5 provides outcomes comparable to that of daily HD; targeting higher doses does not improve outcomes (1B). This dose may not be necessary for many patients with AKI and targeting a weekly Kt/V of 2.1 may be acceptable (2D).

A4.2 During the initial 24 hours of therapy, the duration of cycle times needs to be dictated by the clinical circumstances. Short cycle times (every 1 – 2 hours) may be necessary in the first 24 hours to correct hyperkalemia, fluid overload, and/or metabolic acidosis. Thereafter, the cycle time may be increased to 4 – 6 hours depending on the clinical circumstances (1D).

A4.3 Avoiding fluid overload is extremely important and ultrafiltration can be increased by raising the concentration of dextrose and/or shortening the cycle duration. When the patient is euvolemic, the dextrose concentration and cycle time should be adjusted to ensure a neutral fluid balance (1B).

A4.4 There may be enhanced clearance of medication (e.g., antibiotics) in acute PD and it is recommended that doses be adjusted accordingly and, where possible, levels should be monitored (1D).

RATIONALE

The treatment of AKI involves general supportive therapy and dialytic support when significant metabolic or fluid status derangements related to the kidney injury develop. Where resources exist to provide higher intensity protocols, PD has been shown to

provide comparable outcomes to HD in appropriately selected patients.

The dose and/or efficacy of PD is often assessed with a Kt/V urea measurement (urea clearance over time), where:

K = volume of dialysate drained multiplied by dialysate/plasma urea concentration
t = the duration of the dialysis
V = the volume of distribution of urea (Total Body Water ~ 0.5 [female] or 0.6 [male] multiplied by body weight).

The most appropriate dose for PD in the management of patients with AKI is poorly defined. This lack of clear definition has occurred because there are only a limited number of trials available to compare treatment modalities, the studies that have been done have methodological flaws, and the dose of dialysis used has varied widely. The most thorough study, by Gabriel *et al.*, compared acute PD using a cuffed catheter (delivering a Kt/V urea of 3.6) with daily HD and reported comparable outcomes (7). Some studies have shown very good outcomes with much lower doses than those used in Gabriel's study (9,10). However, these were non-randomized and the problem of a positive reporting bias needs to be kept in mind. Ponce *et al.* and Gabriel *et al.* have, however, followed up their initial report with a study comparing very high volume with lower volume acute PD and have shown no benefit from aiming for the higher target; the lower-dose group achieved a Kt/V urea of 3.43 and did as well as the higher-dose group, which achieved a Kt/V of 4.13 (11). A recent detailed review suggested that by inference from data from extracorporeal blood therapies, a targeted dose of a weekly Kt/V urea of 2.1 with PD may represent a reasonable goal as the 'minimum' dose to guide and help plan appropriate therapy (16). However, the optimal dose for individual patients remains uncertain. Higher small-solute clearances may be necessary for those patients with more complex catabolic illnesses (16).

The prescription of dialysis in AKI is hampered by our lack of understanding of the exact factors which influence survival. We know that hyperkalemia, acidosis, and massive fluid overload need to be treated. After these are corrected, the issue of whether we focus on removal of small molecules (e.g., urea, creatinine) or larger molecule clearances (e.g., cytokines, soluble receptors) is uncertain. Many intensive-care physicians believe cytokine removal is essential in septic shock. For example, it has been shown that using a high cut-off (large pore) membrane in hemofiltration reduces the need for norepinephrine in septic shock. This was felt to be due to removal of large pro-inflammatory molecules (15). If we are to concentrate on larger molecule clearance in PD, then we need to remember that the clearance of larger molecules is both time- and convection-dependent and the dialysis prescription will need to be adjusted accordingly. Another problem is that although we use AKI as a generic term, it comprises a vast array of conditions, and the dialysis clearances necessary for the catabolic, septic patient may be very different than those clearances for the patient with acute tubular necrosis secondary to a tubular toxin. We urge readers to bear this in mind when using these guidelines.

Prescribing dialysis in acute PD requires that a number of assumptions be made about peritoneal transport, as there is little data on the peritoneal transport characteristics in patients who are acutely unwell. The potential variation in rates of solute transport with different acute illnesses is not well studied. However, splanchnic blood flow rates and the presence of various cytokines could certainly impact on achieved clearances.

If, during treatment, there are a large number of cycles, then the length of time where there is diffusion of solutes into the peritoneal cavity is reduced (because of the greater percentage of time involved in inflow and outflow). The loss of dwell time with rapid cycling means that with a larger volume of fluid there is not necessarily a corresponding increase in clearance of urea and other small solutes; in fact, middle and large molecule clearance may be reduced. Thus, for example, if dialysis is performed using hourly exchanges, and we assume a 10-minute inflow and 20-minute drain time, during only half of the day is there full solute diffusion occurring with 2 liters of dialysate in the abdominal cavity. With 2 hourly exchanges, three quarters of the day will be involved in the full diffusion process.

Although much focus is directed at solute clearances, it is becoming increasingly apparent that careful attention to fluid balance is critically important in ICU patients. Therefore, the prescription of dialysis needs to pay careful attention to ultrafiltration and volume assessment in these patients (53). One must remember that a 4.25% solution can remove up to 1 liter of fluid in 4 hours and, although there is a need to be mindful of hyperglycemia, the risks of hypertonic solutions are negligible in the short term, in contrast to long-term use in patients maintained on chronic PD.

Additional attention needs to be paid to the potential adjustments of the dosing of various medications (such as antibiotics) that may need to be made depending on the peritoneal clearances achieved with acute PD, particularly with high-volume therapy (54).

The relatively good outcomes that have been reported by acute PD programs in very low resource settings have

resulted in our recommendation that acute PD can be utilized to treat AKI (6,9,18,51,55,56). A pilot study of acute PD in adults and children conducted in Tanzania between July 2009 and June 2011 included 20 patients and had good outcomes (9). Sixteen of 20 patients survived and were discharged from the hospital. Sixteen patients were adults. Technique survival was good using a closed twin-bag system with initial 2-hourly cycles in adults and 2-liter dialysate fill volumes (1 liter on the first day). Low infection rates were achieved, with peritonitis being suspected in only 2 patients (11). Chitalia *et al.* compared two modalities for treating AKI in moderately catabolic patients in a crossover study using rigid, non-cuffed catheters. Patients either received manual PD with 4-hour cycles using 2 liters of fluid over 48 hours or automated tidal PD with an initial fill of 2 liters followed by a tidal volume of 675 mL and 20-minute cycles for 12 hours. Manual PD achieved weekly Kt/V of 1.8 and tidal PD a weekly Kt/V of 2.43. The fluid volume required to achieve this in tidal automated PD (APD) was double that of the manual PD (10). Outcomes were excellent; 86 of the 87 patients recovered renal function. Phu *et al.* performed a randomized study comparing acute PD using a rigid catheter, an open drainage system, and locally made fluid with CVVH (17). The dialysis prescription was 2 liters of fluid with 30-minute dwell times. The achieved dose was not reported and the trial was stopped early due to a higher mortality in the PD group. Due to significant methodological flaws (see above) the results of this study have been excluded from this analysis.

A Brazilian study compared continuous PD (CPD) with daily hemodialysis (dHD) in patients with AKI. This study included a total of 120 patients with acute tubular necrosis (ATN) who were randomly assigned to receive CPD using an automated cycler or dHD. The primary endpoint was hospital survival and recovery of renal function. Secondary end-points included metabolic and acid-base parameters, and fluid management. The 2 groups were similar at the start of RRT with respect to age, sex, sepsis, shock, severity of ATN, and Acute Physiology and Chronic Health Evaluation (APACHE) score. When the groups were compared, the high-dose CPD provided appropriate metabolic and pH control, with a rate of survival similar to that seen with dHD and recovery of renal function significantly quicker. The limitation of this study was that the study excluded patients of very high body mass index or those who were considered highly catabolic due to the difficulties expected in controlling "uremia" in these patients. The PD treatment was prescribed as 24 hours of dialysis and Kt/V urea was targeted at 0.65 per day (prescribed weekly Kt/V – 4.5). The regimen consisted of 2-liter exchanges with a dwell time of 35 – 50 minutes; the achieved Kt/V was 3.6 (7). As noted above, however, a follow-up study by the same Brazilian group suggested that lower doses of PD achieved the same results as the higher dose of PD.

George *et al.* also compared PD and CVVHDF in a randomized trial (25 patients in each group); the outcomes were similar in the 2 groups, but the mortality rates were extremely high (84% for the CVVHDF group and 72% for the PD group) (6). The dose of PD used in this study is not clear and rigid, non-cuffed PD catheters were used.

As the only randomized controlled trial comparing PD (with an achieved weekly Kt/V of 3.5) with dHD showed comparable mortality, we have used a Kt/V of 3.5 as the optimal dose. If one extrapolates from extracorporeal studies the minimum optimal dose would be a weekly Kt/V of 2.1 (16). Until these 2 doses have been compared head to head, the former should be considered optimal but the latter is the minimum standard. The algorithm below (Figure 1) takes this into account for prescribing dialysis in both well resourced and resource-poor environments.

Dialysis adequacy should be assessed regularly. There are no firm guidelines for this and although measurement of Kt/V may be ideal it will not be feasible

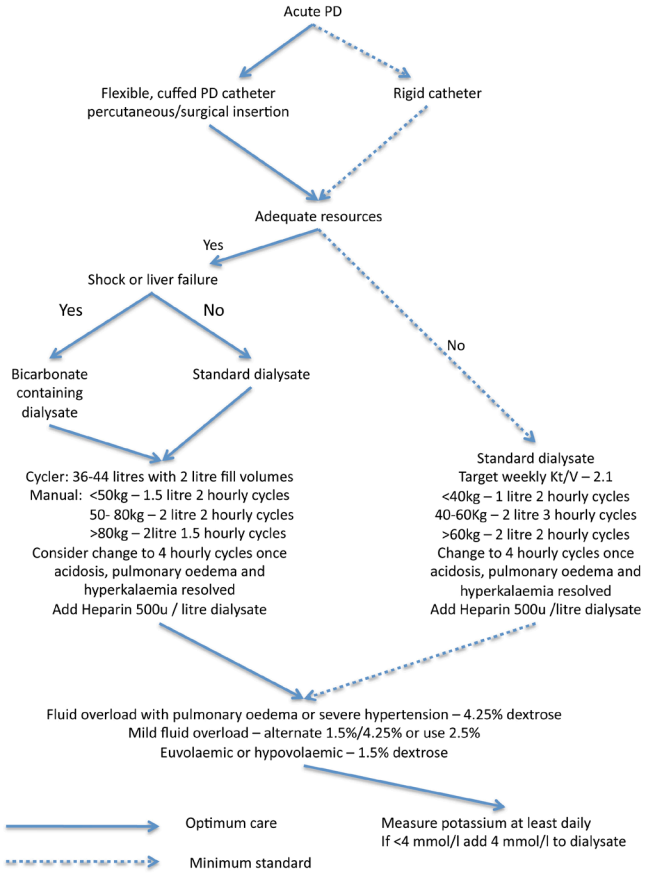

Figure 1 — Suggested dosing algorithm.

in many countries. Therefore, in these settings, adequacy will have to be assessed by clinical signs of fluid balance, normalization of potassium levels and acid base improvement.

COMPLICATIONS OF PD FOR AKI

There are a number of potential complications associated with the use of acute PD. Although an in-depth discussion of these is beyond the scope of these guidelines the following will be discussed briefly:

- Peritonitis
- Mechanical complications
- Protein loss
- Hyperglycemia

The diagnosis of peritonitis may be challenging, but should be based on the recommendations from the ISPD guidelines for infectious complications (57). The diagnosis is made based on the presence of abdominal pain, cloudy dialysate, and a leukocyte count of > 100 cells µL (or polymorphonuclear cells > 50%) after a 2-hour dwell. It is reasonable to perform a leukocyte count daily for peritonitis surveillance in patients on acute PD. In resource-limited settings this may not be feasible and an alternative method is daily use of a urine leukocyte esterase dipstick test daily which if > 2+ should prompt treatment while waiting for a confirmatory leukocyte count and cultures. This method has shown good sensitivity and specificity in small studies but other features such as abdominal pain and fever should also prompt further investigation (58,59).

Treatment of peritonitis is beyond the scope of these guidelines, and it is recommended that the ISPD infectious complication guidelines be consulted (57). It should be noted that because more rapid exchanges are generally performed with acute PD than chronic PD, antibiotics should be given intraperitoneally and with *every* exchange, as penetration into the peritoneal space from the serum is insufficient with rapid cycles to achieve therapeutic levels (60).

Another important complication is mechanical or catheter-related problems. In one study, this resulted in discontinuation of PD in over 10% of the patients randomized to the PD arm. Ponce *et al.* studied 204 patients on acute PD and found a mechanical complication rate of 7.3% with interruption of treatment in 2.6% (52). Catheter obstruction may be a result of fibrin blockage of the catheter or tubing or displacement ± omental wrapping of the catheter. In the former situation, flushing the catheter with sterile saline (using sterile technique) may dislodge the blockage. Once flow is re-established, 500 – 1000 units of heparin may be added to each liter of PD fluid.

Methods for manipulating displaced PD catheters could include the use of laxatives and guidewire (blind or flouroscopic) manipulation. If these methods fail, the catheter should be replaced using the original catheter track into the peritoneum, to reduce leakage.

Loss of protein from the peritoneum in patients on chronic PD varies in different studies from 6.2 to 12.8 g per 24 hours. However this has been known to increase to as high as 48 g during episodes of peritonitis (10,61,62). A study from Brazil measured protein loss in 31 patients on high-volume acute PD over 208 sessions. They showed that protein loss was 4.2 (± 6.1) g/24 h and there was no correlation with albumin levels. Peritonitis did however increase protein loss (63). Care should be taken to ensure that adequate protein intake occurs aiming for approximately 1.2 g/kg of protein per 24 hours. There is an association with increased mortality in those patients with a negative protein balance, but whether this is related to disease severity rather than inadequate intake is uncertain (52).

Due to the high glucose concentration in PD fluid there is a tendency toward hyperglycemia in acute PD. This decreases the osmotic gradient between PD fluid and serum and should be treated to enable optimal ultrafiltration. Maintenance of normoglycemia has also been shown to significantly improve survival in critically ill patients (64,65).

CONCLUSION

PD to treat patients with AKI provides an acceptable form of treatment. While PD is not used commonly in the developed world to treat patients with AKI, recent studies have suggested that outcomes with PD are as good as with extracorporeal RRTs. Certainly, in the developing world, there are major advantages for PD to manage patients with AKI. While the guidelines presented above focus on optimal treatment algorithms, it is important to keep in mind that treatment patterns need to be developed in accordance with individual patient needs taking into account the available resources and hospital environment. In low-resource settings, flexibility and appropriate adjustments in treatment patterns may need to be made.

PEDIATRIC GUIDELINES

Acute kidney injury has long been identified as an important risk factor for morbidity and mortality in children both in and outside the ICUs (66–70).

The etiology of AKI is different between children from developed and developing countries. Whereas ischemic/hypoxic and nephrotoxic injury secondary to prematurity, post-cardiac surgery, or bone marrow transplantation are common in the former, infection-related causes (especially malaria), gastroenteritis and primary renal diseases are common in the latter (68–70). Renal replacement therapy in the form of PD, HD or continuous renal replacement therapy (CRRT) is frequently needed and the decision to use any of these modalities should not be delayed; higher survival rates in neonates and infants have been associated with early initiation of PD (71,72).

Peritoneal dialysis was the first RRT modality used for the management of AKI in children of all ages, and remains the preferred method in younger children. However, its practice has declined in favor of the new extracorporeal blood purifying technologies (73). The results of surveys of RRT options available for children with AKI in developed and developing countries are variable and are highly dependent on the country's socioeconomic status as well as being region-specific. In a survey from India, PD was available in almost 100% of the surveyed dialysis centers and was the most common modality used, even if other modalities were available (74). This is in contrast to a survey from North America and Europe in which PD usage decreased dramatically in favor of CRRT, except as a treatment modality for young infants. In many centers, CRRT has become the modality of choice (73,75). Despite the technological advancement, refinement, and development of safety procedures for the CRRT machines, the application of this therapy in children remains expensive, complex, technology-dependent and needs experienced specialized nursing personnel, rendering it rather difficult to introduce in areas with limited resources.

Peritoneal dialysis has also undergone technological development with new machines (PD cyclers) with better safety profiles, fewer connections, and the potential for a greater variety of PD prescriptions. However, manual techniques are still more commonly used in less developed countries. In premature and small neonates for whom automated PD cycler systems are unable to deliver small enough volumes, PD can be performed manually with the new closed manual exchange systems. These manual exchange systems are inexpensive, can be applied to the smallest infant, and are readily available worldwide (76). Finally, there have been improvements in dialysate solutions with the use of low glucose degradation products (GDP), bicarbonate-buffered solutions which are associated with reduced inflow pain; unfortunately, these solutions are not available in many countries.

GUIDELINE P1: Suitability of PD for AKI in children

P1.1 Peritoneal dialysis is a suitable modality for RRT in AKI in children (1C).

RATIONALE

Guideline P1.1: There have been no randomized clinical trials comparing different RRT modalities (PD, HD and CVVH) for the treatment of children with AKI. Observational studies have shown no difference in mortality between children treated with PD and those receiving CVVH (68,77–79). However, in 1 study, CVVH was associated with better fluid control and was superior to PD in the management of hypercatabolic AKI due to sepsis (79). In another study, CVVH was associated with better ultrafiltration, solute removal and nutritional support (77). However, in none of these studies was there a survival benefit associated with the use of CVVH. In 1 study in which the 3 modalities were compared in children, it was concluded that the underlying clinical diagnosis, hemodynamic stability and the use of pressor agents were the key predictors of mortality rather than the type of RRT (68). As is characteristic of many pediatric investigations, these studies were all hampered by the small number of patients, a lack of standardization of the therapy provided, variability in terms of the modalities available, and additional variability regarding expertise and experience with the different modalities, such that the effect of bias could not be eliminated.

Much controversy exists regarding the adequacy of PD for the management of hypercatabolic pediatric patients in the ICU. No prospective studies have evaluated the effect of dialysis modality on the outcomes of children with AKI in the ICU setting (80).

GUIDELINE P2: Access and fluid delivery for acute PD in children

P2.1 We recommend a Tenckhoff catheter inserted by a surgeon in the operating theatre as the optimal choice for PD access (1B) (Optimal). If facilities do not exist then a Cook Catheter (Cook Medical Inc, Bloomington, IN, USA) (infants and neonates) or Tenckhoff catheter (older children) should be placed using the Seldinger technique in the most sterile environment available (1C). Improvised catheters may be lifesaving if nothing else is available, but are not recommended for routine use (2D) (Minimum standard).

P2.2 A closed system utilizing buretrols to measure fill and drainage volumes should be used when

performing manual PD (1C) (Optimal). In resource-limited settings, an open system with spiking of bags may be used; however, this should be designed to limit the number of potential sites for contamination (2D) (Minimum standard).

P2.3 Automated PD (APD) is suitable for management of pediatric AKI with the exception of low birth weight neonates where fill volumes are too small for currently available machines (1D).

RATIONALE

Guideline P2.1 – Catheter Design and Insertion Techniques: The provision of acute dialysis in children can be challenging due to many factors including a lack of equipment suitable for use in small children and babies including PD catheters, circuits and fluid bags, as well as the limited availability of trained staff (both nursing and medical) comfortable with dialysis in smaller patients (81,82). In particular, lack of familiarity with PD catheter insertion has remained a significant obstacle to the widespread use of PD. Placement of catheters is often perceived as technically difficult, resulting in a lack of uptake of this potentially lifesaving treatment. Contrary to this belief, insertion of PD catheters in children can be achieved safely, even by non-surgically trained clinicians. (Step-by-step insertion guidelines will be published on the ISPD website this year.)

There are a range of PD catheters with differences in the configuration of the intraperitoneal portion (straight, coiled, straight with silicone discs and T-fluted) and the subcutaneous portion. Cuffs also vary and catheters may have single, dual, or disc ball cuffs. Other short-term catheters, such as the Cook PD catheter (Cook Medical Inc, Bloomington, IN, USA) and multipurpose drainage catheter, may be appropriate for acute PD as well (83).

A surgically placed Tenckhoff catheter should be the catheter of choice when initiating acute PD in children. A study of 59 children comparing surgically placed Tenckhoff catheters and rigid catheters showed that Tenckhoff catheters were associated with longer duration of use—16.5 days vs 4.9 days ($p < 0.001$) and fewer complications (9% vs 49%) (84). The current trend is for this to be inserted laparascopically, where facilities allow, as there is less chance of leakage compared with catheter placement by laparotomy.

Access to pediatric surgeons and theatre facilities appropriate for this group of patients may be limited. For this reason, pediatricians are often called upon to insert bedside catheters without the back-up of theatre facilities. Sedation and analgesia for bedside insertion in children can be the greatest hazard in this situation and it is imperative that facilities and staff be available to administer and deal with the consequences of these agents. The procedure needs to be performed in the most sterile environment available, and operators must wear hats, masks, gowns, and gloves.

A study of 108 cases of bedside catheters inserted by pediatric nephrologists showed this to a be a safe and cost-effective method of insertion. Of particular note, there were no cases of bowel perforation despite using both blind and Seldinger techniques (85).

An alternative to the Tenckhoff catheter which can be inserted at the bedside in children of all sizes is the flexible Cook Mac-Loc (Cook Medical Inc, Bloomington, IN, USA) Multi-purpose Drainage Catheters (CMMDCs). These were used in 21 infants and children with a mean age of 6.9 months. There were only 3 complications in 2 patients precluding continuation of PD—the remainder of the patients used the catheter until recovery from AKI or non-renal death (83). Good target fluid and solute removal were achieved with no catheter-related infections. The mean complication-free days was 10.5 (range 2 – 29 days) with 90% catheter survival at 14 days. There were no significant differences between CMMDCs and historical Tenckhoff catheter usage with respect to complication-free survival and catheter-related complications ($p = 0.057$).

Cook PD catheters placed in Seldinger fashion also provide a rapid, safe procedure. In a small study, there were no cases of bleeding (0/44), a low leakage risk (1/44) and low manipulation and peritonitis rates (81). Automated cyclers can be used with these catheters to maximize clearances and permit a closed system to help prevent infection (22,86).

Rigid catheters with a stylet are used less frequently due to an increased frequency of leakage compared to Tenckhoffs (10/33 vs only 2/34, $p < 0.01$), as well as an increased risk of accidental dislodging, perforation, etc. (22). These should only be used if other Seldinger catheters are not available.

Yet additional alternatives that have been used to serve as PD catheters include double lumen adult dialysis catheters, chest drains, and nasogastric tubes placed in the subumbilical region. Whereas these devices may be lifesaving, there is little evidence to support their use in terms of safety and efficacy, and thus their routine use is not recommended.

In many cases of AKI, leakage of dialysate occurs due to the immediate use of the catheter. In the event of leakage through the catheter exit site, fibrin glue has been used successfully in children. In a small study of 8 children in which there was dialysate leakage in the

first 24 – 48 hours of dialysis, fibrin glue was applied (1 mL) to the external part of the catheter at the exit site. No recurrence of dialysate leakage was seen in any of the 8 children (86).

Guideline P2.2 – Manual PD Delivery Systems: Peritoneal dialysis for infants and children with AKI may be implemented with a manual and gravity-based system. The circuit should consist of a closed system which reduces the risk of infection (87). Strict fluid balance, which is of utmost importance in the very young, is assisted by the use of buretrols, which permit the precise measurement of in- and outflow. This technique also minimizes the number of connections and, therefore, the risk of touch contamination. Systems are now available commercially—the PD-Paed system (Fresenius Medical Care, BadHomburg, Germany) and the Dialy-Nate system/Gesco Dialy-nate (Utah Medical Products, Midvale, UT, USA). In older children, a twin-bag system (as used by chronic PD patients) can be used to ensure a closed system.

In resource-limited settings, a closed system may not be available and an open system may need to be utilized. This should be designed to minimize the potential sources of contamination at the point of the spike and connection to the catheter and drainage bag. The circuit should consist of a single dialysis fluid bag attached to a buretrol and infusion set which is then attached to the dialysis catheter through a 3-way tap. The drainage tubing can then be inserted into an empty, sterile 200 mL fluid bag or catheter bag. A buretrol is essential in neonates and infants where exact volumes need to be delivered to reduce the risk of overdistension which can result in respiratory embarrassment or leakage.

Note: for older children and/or if buretrols are not readily available, a scale may be used to weigh the PD bag while fluid flows into and out of the patient.

Guideline P2.3 – Automated PD Systems: Automated PD employing a cycler was introduced into clinical practice in the 1980s, decreasing the frequency of peritonitis and providing efficient metabolic and electrolyte control in AKI patients (88,89). Automated PD offers a wide selection of highly efficient treatment schedules obtained through the use of short dwell times, high dialysate flows, and customized intraperitoneal volumes (IPVs). Automated PD has the advantage of requiring less intensive nursing care, but comes with a financial burden.

Components of the APD system: Cycler: treatment settings, such as the amount of solution to be infused and the length of time the solution remains in the peritoneal cavity (dwell time), are programmed into the cycler. The cycler then automatically performs the treatment. As is the case with manual PD, the APD exchange has 3 phases: fill, dwell, and drain.

Components of the APD prescription:

- Type of dialysis solutions
- Total volume of dialysis solution
- Total therapy time: Total time starting with the initial drain. Maximum setting is 48 hours, minimal setting 10 minutes, and setting increments are 10 minutes
- Intraperitoneal fill volume

APD options for treatment of AKI include the following: Continuous Cycling Peritoneal Dialysis (CCPD)/ Intermittent Peritoneal Dialysis (IPD): Total volume of PD solution used for the therapy includes the total fill volume for all cycles and the last fill volume. The last fill volume has to be prescribed in this mode of APD; it is delivered at the end of the therapy and left in the abdominal cavity. The PD solution used for the "last fill volume" can have the same dextrose concentration as the solution used throughout the dialysis session, or it can be different. The total number of cycles, not including the last fill volume, and the dwell time are not prescribed per se; they are calculated by the cycler.

Tidal: In this modality, only a portion of the dialysis solution within the peritoneal cavity is drained and replaced with new solution during each therapy cycle; this leaves a residual volume of fluid in the abdomen. This is beneficial in 2 ways: a) the residual volume continues to facilitate water and solute removal even during filling and draining of the abdomen, thus increasing effective dialysis time, and b) it can be helpful when there is difficulty draining the dialysis solution or there is drainage pain, as the catheter does not directly appose the peritoneum.

For tidal PD, cycler programming needs to include:

- Tidal volume percentage (volume of fluid drained and refilled during each cycle, expressed as a percentage of the initial fill volume)
- Total Ultrafiltration (UF) (total UF expected for the entire dialysis session).
- Number of *full* peritoneal drain cycles during the dialysis session.

The cycler calculates the number of cycles, the dwell time, the tidal volume and the ultrafiltration volume per cycle.

The limiting factor for using APD equipment in infants and children is the availability of low-fill mode option for pediatric patients and the minimum accepted fill volume.

GUIDELINE P3: Peritoneal dialysis solutions for acute PD in children

P3.1 The composition of the acute PD solution should include dextrose in a concentration designed to achieve the target ultrafiltration (1D).

P3.2 Serum concentrations of electrolytes should be measured 12-hourly for the first 24 hours and daily once stable (1D) (Optimal). In resource-poor settings, sodium and potassium should be measured daily if practical (2D) (Minimum standard).

RATIONALE

Guideline P3.1: Peritoneal dialysis solutions for acute PD are generally commercially available with dextrose concentrations of 1.5%, 2.5%, and 4.25% (1.36%, 2.27% or 3.86% are equivalent if glucose is measured). Adult Guideline 3.4 (above) addresses the unique aspects of pharmacy-prepared solutions. The osmolality of the 1.5%, 2.5%, and 4.25% solutions are 346, 396, and 485 mOsmol/L, respectively and their use results in an osmotic gradient between dialysate and plasma that promotes fluid removal (90). Glucose absorption occurs across the peritoneal membrane continuously, and is enhanced by small exchange volumes that are typically used for acute PD and which result in a gradually diminished osmolar gradient and less efficient ultrafiltration. In turn, acute PD is usually initiated with a 2.5% dextrose solution in order to achieve effective ultrafiltration when fluid overload exists and the prescribed exchange volume is small to avoid dialysate leakage. Initial use of a 1.5% solution may be appropriate when euvolemia or only mild fluid overload exists. The use of a 2.5% or 4.25% solution in a PD prescription characterized by frequent exchanges can result in hyperglycemia, especially in young infants, and may necessitate insulin therapy or a modification of the dextrose concentration used. The latter can be achieved by mixing equal volumes of 1.5% and 2.5% dextrose solutions infused through two Buretrols connected via a Y-set. If insulin is to be used by placing it in the dialysis solution, the dose should be appropriate for the dialysis dextrose concentration. Typical initial doses are as follows, with adjustment based on frequent blood glucose monitoring (90): *This should only be used in the event of hyperglycemia, not routinely in all patients*.

4 – 5 units/L for 1.5 g/dL
5 – 7 units/L for 2.5 g/dL
7 – 10 units/L for 4.25 g/dL

The inclusion of alkali in the dialysate helps to correct the acidosis that may accompany AKI. Whereas many commercially prepared solutions for acute PD are lactate based with a concentration of 35 – 40 mmol/L, more biocompatible solutions (e.g. bicarbonate- or lactate/bicarbonate-based) are available in countries other than the United States and have been used for acute PD (91–93). On occasion, infants and young children do not tolerate the lactate absorbed from the dialysis solution in the setting of hepatic dysfunction, hemodynamic instability, and persistent/worsening metabolic acidosis. In these situations, use of a commercial or pharmacy-prepared bicarbonate-based solution is preferable. If calcium is needed (see below) it must be given by a route other than in the PD solution to prevent precipitation. Serum ionized calcium levels must be closely monitored when the dialysate contains a high concentration of bicarbonate to prevent the risk of tetany. It should also be noted that bicarbonate loss from dialysate is increased in association with high ultrafiltration rates as a result of convective clearance (94).

The dialysate sodium concentration is typically 132 – 134 mmol/L. With only a small concentration gradient between dialysate and plasma, the transport of sodium is primarily by convection. As often occurs with acute PD, rapid cycling with hypertonic dialysis solutions to promote ultrafiltration can result in hypernatremia as a result of enhanced free water clearance secondary to sodium sieving and transport of water through aquaporin channels (95). The removal of free water is greatest during the initial 30 – 60 minutes of each exchange. If hypernatremia develops, consideration should be given to extending the dwell time if solute clearance allows or lowering the concentration of glucose in the dialysis solution. If rapid cycling is needed for solute removal and fluid balance is neutral or negative, a hypotonic fluid such as 0.45% saline can be infused intravenously to match the net ultrafiltration from PD.

The potassium concentration of the dialysis solution should be negligible (0–2 mmol/L) at treatment initiation as many patients will present with hyperkalemia, often accompanied by metabolic acidosis. Once a normal serum potassium concentration is achieved, as typically occurs over the initial 6 – 12 hours, the concentration of potassium in the dialysis solution can be gradually increased to a concentration of ≤ 4 mmol/L with ongoing modification dependent on factors that influence the serum potassium level (e.g. dialysate dextrose concentration, serum CO2, medications, parenteral nutrition, etc.). If no facilities exist to measure the serum potassium, consideration should be given for the empiric addition of potassium to the dialysis solution after 12 hours of continuous PD to achieve a dialysate concentration of 3 – 4 mmol/L.

GUIDELINE P4: Prescription of acute PD in pediatric patients

P4.1 The initial fill volume should be limited to 10 – 20 mL/kg to minimize the risk of dialysate leakage; a gradual increase in the volume to approximately 30 – 40 mL/kg (800 – 1,100 mL/m^2) may occur as tolerated by the patient (1D).

P4.2 The initial exchange duration, including inflow, dwell, and drain times, should generally be every 60 – 90 minutes; gradual prolongation of the dwell time can occur as fluid and solute removal targets are achieved (1D). In neonates and small infants, the cycle may need to be reduced to achieve adequate ultrafiltration.

P4.3 Close monitoring of total fluid intake and output is mandatory with a goal to achieve and maintain normotension and euvolemia (1B).

P4.4 Acute PD should be continuous throughout the full 24-hour period for days 1 – 3 (1C).

P4.5 There may be enhanced clearance of medication (e.g. antibiotics) in acute PD and it is recommended that doses be adjusted accordingly and, where possible, levels should be monitored (1D).

RATIONALE

Guideline P4.1: Small exchange volumes are generally recommended at the initiation of acute PD and soon after PD catheter placement to decrease the risk of dialysate leakage that may arise because of the PD solution-induced rise in intraperitoneal pressure (IPP). If no leakage occurs, the exchange volume can be gradually increased to enhance solute and fluid removal since larger volumes result in more prolonged maintenance of the concentration and osmolar gradients (96). In general, exchange volumes should not exceed 800 mL/m^2 in patients < 2 years because of the associated rise in IPP that can occur and the resultant reabsorption of ultrafiltrate through lymphatics (97). Exchange volumes > 40 mL/kg (1,100 mL/m^2) are rarely required if PD is prescribed using a continuous schedule, and may result in respiratory compromise in the ICU setting (96). (See Figure 2 for dosing algorithm.)

Guideline P4.2: The use of short exchange times initially aims to accomplish the desired ultrafiltration and solute removal while the gradients between serum and dialysate are preserved. Although even shorter (< 60-minute) exchange times have been used on occasion, solute removal is often compromised because of the substantial period of time that is spent filling and draining the patient (98). In general, the inflow time is 5 – 10 minutes (or less), and depends on the amount of fluid to be infused, the height of the bag of dialysis solution relative to the patient, and the resistance created by the PD catheter and the associated tubing. The dwell time, that period of the exchange when the dialysis solution remains in the peritoneal cavity, is approximately 30 – 40 minutes. The drain time is typically 10 – 20 minutes and is dependent on the volume of fluid to be drained, the resistance of the catheter and tubing, and the height difference between the patient and the drainage bag. As noted previously, frequent exchanges increase the risk for hypernatremia and mandate close monitoring for these laboratory abnormalities. Finally, the exchange duration can gradually be prolonged in association with an increasing exchange volume to a regimen comparable to what is used for chronic dialysis, dependent on the tolerance of the patient and the ability of the regimen to meet the solute and fluid removal goals.

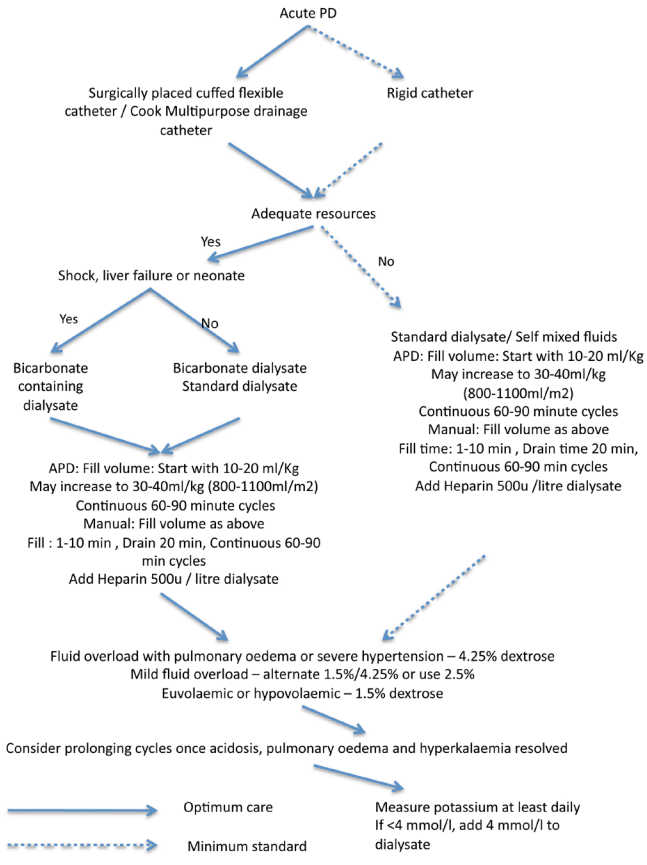

Figure 2 — Suggested pediatric dosing algorithm.

Guideline P4.3: Pediatric patients with AKI are frequently hypervolemic and substantial fluid overload has been associated with an increased risk for morbidity and mortality (99). Fluid removal is, in turn, an important treatment goal for many patients. Ideally, the successful generation of ultrafiltrate with each exchange (plus any urine output that might exist) will result in resolution of the fluid overloaded state, while permitting the fluid needs of the patient for medications, blood products, nutrition and maintenance of hemodynamic stability to be met. The ability to regularly achieve positive ultrafiltration and meet the patient's needs will often require hypertonic dialysis solutions (2.5%/4.25%) and frequent exchanges early in the course of acute PD when the exchange volumes are small; modification of the ultrafiltration needs will mandate adjustment of the dialysis prescription. Ideally, once the patient is euvolemic, the dextrose concentration of the dialysate and the frequency of exchanges can be decreased.

Frequent assessment of the patient's fluid status, and the associated intake and output of fluid is of utmost importance. Early during the course of therapy, the use of frequent exchanges of hypertonic dialysate can result in substantial fluid removal and, on occasion, intravascular volume depletion. Failure to address this issue by decreasing ultrafiltration or increasing the provision of enteral or parenteral fluid can potentially slow kidney recovery. Conversely, monitoring of all sources of intake (e.g. medications, nutrition, blood products) is equally important. A decrease in the insensible fluid loss while a child is maintained on a respirator/oscillator can substantially influence the fluid balance of the small infant. In most cases, the ability to achieve a targeted fluid goal should be reassessed no less frequently than every 2 – 3 hours initially, with subsequent modification of therapy as deemed necessary. Gradual prolongation of the time interval between assessments can occur once stability of the fluid management has been achieved.

Guideline P4.4: In most cases, the use of acute PD with frequent exchanges should be continuous during the initial period of stabilization in order to meet the patient's needs for solute and fluid removal. The frequency of exchanges should be determined by the clinical status of the patient. The small exchange volume that typically characterizes the initial prescription limits the efficacy of PD for treatment of AKI and therefore PD needs to be continued over a full 24-hour period in the acute setting to achieve adequate clearances. Reassessment of the patient's needs should occur daily. Once the immediate needs of the patient have been met, and most commonly with gradual recovery of kidney function and the achievement of solute/fluid stability, the provision of dialysis during only a portion of each 24 hours using an increased exchange volume is usually sufficient. It should be emphasized that the use of PD continuously does not inhibit the resolution of AKI.

Guideline P4.5: Clearance of many drugs may be altered once the patient transitions between AKI with oliguria to PD. This may result in inadequate serum levels especially with agents such as antibiotics and anticonvulsants and dosing should be adjusted accordingly.

GUIDELINE P5: Continuous flow peritoneal dialysis (CFPD)

P5.1 Continuous flow peritoneal dialysis could be considered as a PD treatment option when an increase in solute clearance and ultrafiltration is desired but cannot be achieved with standard acute PD. Therapy with this technique should be considered experimental since experience with the therapy is limited (Ungraded).

P5.2 Continuous flow peritoneal dialysis could be considered for dialysis therapy in children with AKI when the use of only very small exchange volumes is preferred (e.g. children with high ventilator pressures) (Ungraded).

RATIONALE

Continuous flow peritoneal dialysis has been shown in chronic adult PD patients to increase the clearance of small solutes 3- to 8-fold and to significantly increase ultrafiltration compared to conventional PD (100–102). In one of the few studies of this dialysis technique in patients with AKI, Ponce *et al*. used CFPD in two adult AKI patients and achieved a clearance similar to that reported with extracorporeal blood purification methods and an ultrafiltration rate of 200 – 500 mL/h (45). A study of 6 children with AKI secondary to various causes and prescribed CFPD showed a 5-fold increase in clearance and a 9-fold increase in ultrafiltration compared to conventional PD (103). In another study in children, successful ultrafiltration was achieved in fluid-overloaded children with acute respiratory distress syndrome (ARDS) using CFPD. Whereas these children could not tolerate high intraperitoneal volumes, CFPD was conducted without a fixed fill volume and with a relatively low peritoneal flow rate (104).

In most adult studies of CFPD, a standard fill volume of approximately 2 liters has been used with a peritoneal flow

rate of between 100 – 300 mL/min and a glucose concentration of 1.5%. With this prescription, greatly improved ultrafiltration and clearances were obtained (100–103). However, these studies were conducted with stable chronic PD patients. As noted in section P5.1, it is customary to initially prescribe small fill volumes (10 – 20 mL/kg) in children on acute PD because of concerns regarding raised IPP and its effect on ventilation (80). Raaijmakers *et al.* were able to achieve greatly enhanced small-solute clearance and ultrafiltration with CFPD using a fill volume of 20 mL/kg, a peritoneal flow rate of 100 mL/1.73m^2/min and a dialysate glucose concentration of mostly 1.5% (105). Thus, CFPD could be useful in situations where standard acute PD does not achieve adequate clearance or ultrafiltration because of the requirement for small fill volumes. As is the case with all approaches to acute PD, careful and frequent monitoring of the patient is essential and ultrafiltration rates need to be closely tracked.

Practically, CFPD can be set up in the following manner (see Figure 3). A second catheter should be placed in the peritoneal cavity for adequate flow rates. Raaijmakers *et al.* used one catheter below the umbilicus and the second a point mid-way between the superior iliac crest and the umbilicus in their case series (105). Tubing from the dialysis fluid runs through an inflow pump. After this (or before), the fluid should run through a heater and then into the patient through one of the catheters. Preferably, a bubble trap and a pressure transducer should be built into this part of the circuit which should alarm if the inflow pressure becomes too high (> 10 mm Hg above baseline). Tubing from the outflow catheter should also run through a pump which is set at a slightly faster rate (2.5 mL/1.73m^2/min) than the inflow pump. A transducer should preferably be connected to this circuit which is set to alarm if the outflow pressure becomes excessive (101,102).

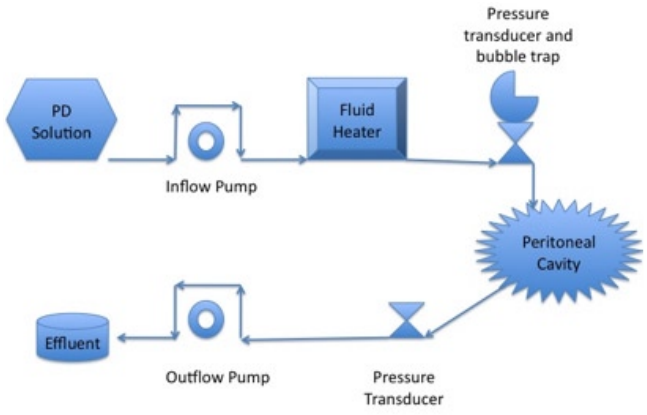

Figure 3 — Example of a continuous flow PD circuit.

Single-pass CFPD circuits have been described in adult patients using only an inflow pump and partially occluding outflow to maintain satisfactory flow (102,103). Purely gravity-assisted CFPD has also been described in children, but without a fixed intraperitoneal volume (104). Single-pass CFPD is the use of dialysate which is discarded and not regenerated after it has passed through the abdomen. As such small volumes of fluid are used in pediatric patients, this is felt to be reasonable. It is important to note that experience with CFPD is limited and although the technique is potentially useful, its use should be considered experimental.

Dialysis Prescription for CFPD:

- Fill volume of 10 – 20 mL/kg
- Dialysate flow rate of 100 mL/1.73m^2/min
- Ultrafiltration flow: This can initially be set at 2.5 mL/1.73m^2/min, but may have to be adjusted according to actual ultrafiltration.
- Dialysis solution: Adequate ultrafiltration can usually be achieved using 1.5% dialysis solution; however, on occasion, an increased dialysis dextrose concentration may be necessary.
- Dialysis time: A dialysis session of 6 – 8 hours can initially be prescribed, with modification as needed following re-evaluation of the patient.
- Once the serum potassium falls below 4 mmol/L, potassium (4 mmol/L) should be added to the dialysate solution.

Safety:

- Safety measures should be taken to ensure that the inflow of fluid does not continue if there is obstruction to outflow. Transducers or careful observation of fluid pumps with alarms can facilitate monitoring.
- Monitoring for excessive ultrafiltration and resultant raised intra-abdominal pressure is recommended. This should be conducted with a combination of hourly measurements of abdominal circumference, monitoring for changes in ventilation, perfusion and blood pressure and, if the patient is in the ICU, assessment of intra-abdominal pressure using a bladder catheter.
- Because of the efficiency of CFPD, frequent assessment of serum potassium levels is important. The frequency of measurements will depend on the baseline values and the dialysate flow rates.

CONCLUSION

Peritoneal dialysis is a safe and effective method of blood purification and fluid removal for the management

of AKI in children. It has the significant advantage of not requiring vascular access, so often difficult in acutely ill infants and small children. In developing countries, where access to qualified pediatric HD staff and equipment is often limited or in most cases non-existent, PD offers a relatively inexpensive, safe and effective lifesaving treatment. The guidelines above are designed for clinicians in both developed and developing countries and as such, there are differences between optimal practice and minimum standards. Therefore, the guidelines should be read in the context of the local resource availability and clinician skill set, but always striving to achieve the best practice available and the best patient outcomes possible.

Abbreviations:

AKI	Acute Kidney Injury
APD	Automated Peritoneal Dialysis
ARDS	Acute Respiratory Distress Syndrome
ATN	Acute Tubular Necrosis
CAPD	Continuous Ambulatory Peritoneal Dialysis
CFPD	Continuous Flow Peritoneal Dialysis
CPD	Continuous Peritoneal Dialysis
CRRT	Continuous Renal Replacement Therapy
CVVH	Continuous Veno-Venous Hemofiltration
CVVHDF	Continuous Veno-Veno Hemodiafiltration
dHD	Daily Hemodialysis
ICU	Intensive Care Unit
IPP	Intraperitoneal Pressure
PD	Peritoneal Dialysis
RCT	Randomized Controlled Trial
SLED	Sustained Low Eficiency Dialysis
UF	Ultrafiltration

DISCLOSURES

BC has received speaker fees from Baxter Healthcare, Adcock Ingram Critical Care and Fresenius Medical. RPF has received speaker fees from Baxter Healthcare and research grants from Baxter Healthcare and Fresenius Medical. KY has received speakers fees from Amgen and Otsuka Pharmaceuticals. BW is an advisor for and received research grants from Baxter Healthcare. FOF recieved speaker fees from Baxter Healthcare and research support from Fresenius Medical. The remaining authors have no competing financial interests to declare.

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APPENDIX 1:
Local Preparation of Solutions

Type of fluid	Na^+	K^+	Ca^{2+}	Mg	Cl-	HCO_3-	lactate	pH	osm.
Hartmann's solution	131	5	2.0		111		29	7.0	278
Ringer's lactate	131	5	1.8		112		28	6.5	279
Plasmalyte B	130	4	0	1.5	110	27		7.4	273
½ Normal saline	77				77			5.0	154

Na = sodium; K = potassium; Ca = calcium; Mg = magnesium; Cl = chlorine; HCO_3 = bicarbonate; osm = osmolarity.
Preparation of dialysis solutions using the above intravenous solutions:

- 1 L Plasmalyte + 30 mL 50% dextrose (15 g) will generate a solution with the following concentrations: glucose 1.45%, Na 126 mmol/L, HCO_3- 2 7mmol/L, K 3.8 mmol/L, Mg 1.45 mmol/L, osmo = 342
  This is very similar to some of the bicarbonate-based solutions sold by industry.
- 1 L Ringers lactate + 30 mL 50% dextrose (15 g) will generate a solution with the following concentrations: Na 127 mmol/L, lactate 27 mmol/L, Ca 1.36 mmol/L, K 3.8 mmol/L, glucose 1.45 %, osmo = 346
  This is similar to lactate-based PD solutions.

NOTE: The above solutions both contain potassium

- 1 L ½ normal saline + 40 mL 8.5% Na Bic (40 mmol) + 40mL 50% dextrose (20 g) + 60 mL 3% NaCl (30 mmol) will generate a solution with approximately the following concentrations: Na ± 130 mmol/L, Bicarb 35 mmol/L, glucose 1.7%, osmo = 340