Technology of Peritoneal Dialysis

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Seth B. Furgeson and Isaac Teitelbaum

8.1 Introduction

Peritoneal dialysis (PD) is a home dialysis modality that provides patients with flexibility and control over their dialysis treatments and often the freedom to continue employment. In addition, for reasons that are incompletely understood—perhaps related to greater hemodynamic stability—peritoneal dialysis is associated with a slower decline in residual renal function. On the other hand, patients performing home dialysis must assume the responsibility for administering and monitoring the therapy. In contrast to home hemodialysis , PD can be performed as a continuous therapy without the need for vascular access. However, in order for PD to be successful, numerous technical details of the therapy need to be optimized. This chapter will describe the best practices regarding peritoneal catheter placement, PD solutions, and efforts to maintain a healthy peritoneal membrane.

8.2 Peritoneal Dialysis Catheter

A well-functioning PD catheter is crucial for the long-term success of PD. Catheters that have migrated or have been trapped in omentum may not drain appropriately leading to fluid retention and inadequate solute clearance. Dialysate leaks at the catheter exit site can impair ultrafiltration and adversely affect patients' quality of life. Finally, since peritonitis and catheter infections are leading causes of PD technique failure, catheter designs and implantation practices that minimize infection risk may also improve technique survival.

S. B. Furgeson (✉)
University of Colorado-Anschutz Medical Campus, Aurora, CO, USA
e-mail: seth.furgeson@ucdenver.edu

I. Teitelbaum
Department of Medicine, University of Colorado Hospital, Aurora, CO, USA

Table 8.1 Modifiable components of peritoneal dialysis (PD) catheters

Silicone or polyurethane composition
Coiled or straight intraperitoneal segment
Single or double cuffed catheter
Curved (swan-neck) or straight catheter
Abdominal exit site or extender for presternal exit site

8.2.1 Catheter Characteristics

PD catheters have many potential modifications (Table 8.1). Catheters are made from polyurethane or silicone rubber. The intra-abdominal portion of the catheter can be coiled or straight and the portion within the anterior abdominal wall can have one or two cuffs. Furthermore, there are many modifications that can be made in the subcutaneous portion of the catheter to guide the catheter exit from the abdominal wall. Since the catheter possesses "memory," they tend to revert to their initial conformation. Swan-neck catheters possess a preformed bend that promotes a downward-directed exit from the abdominal wall exit site as well as a downward direction of the intraperitoneal portion of the catheter thereby preventing catheter migration. Other catheters have a straight segment between two cuffs to promote a lateral exit. Some of the above modifications have been compared in randomized trials; however, many of the trials have significant methodological limitations that limit the conclusions.

As compared to catheters made of silicone rubber, polyurethane catheters have greater tensile strength with a thinner wall and larger internal diameter. Those characteristics are desirable as they will positively influence dialysate flow rate. However, polyurethane is prone to damage with numerous antimicrobial solutions. Mupirocin ointment (containing polyethylene glycol) and alcohol have both been reported to cause damage to the catheter wall. Spontaneous rupture of the PD catheter has been reported with mupirocin ointment [1]. Therefore, most catheters used today are made of silicone rubber.

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Catheters with a coiled intraperitoneal segment offer some potential advantages over straight catheters. Coiled catheters were designed to create better separation between loops of bowel and contain numerous side ports. Since a smaller amount of dialysate moves through each side port, coiled catheters may reduce infusion pain. However, clear benefits of coiled catheters have not been seen in most studies. Comparisons between coiled and straight catheters have been the subject of numerous trials [2]. Most of the early randomized trials were small (fewer than 50 total patients) and reached different conclusions regarding the superiority of either catheter. Furthermore, some of the earlier studies had very high rates of catheter dysfunction raising questions about the generalizability of the results. The two most recent randomized studies of straight versus coiled catheters have also been the largest, enrolling 80 and 132 patients, respectively. The smaller study found that catheter migration occurred more commonly with coiled catheters [3]. The study by Johnson et al. demonstrated better catheter survival with straight catheters, an effect thought to be related to improved small solute clearance [4]. Given small sample sizes from all studies, firm recommendations from the trials are not possible. It should also be noted that the surgical implantation techniques and exit site management may differ significantly between the study sites and other PD centers.

After exiting the peritoneal cavity, catheters can be anchored in the subcutaneous space with either one or two cuffs. Two cuffs may more firmly anchor the catheter in the subcutaneous space. It has been suggested that a double-cuff catheter may also provide a better barrier to bacterial spread along the catheter tunnel. The largest randomized study to test this benefit enrolled 60 patients and randomized them to either a double-cuff or single-cuff catheter [5]. The study demonstrated no benefit in peritonitis, exit site infections, or catheter infection with the double-cuff catheter. A retrospective study did demonstrate a benefit to preventing peritonitis with the use of double-cuffed catheters; however, this effect is lost in the post-2000 era [6]. Alignment of the intercuff segment of a double-cuff catheter can also improve a catheter's success. Since plastic catheters will maintain "memory" and revert to the original position, aligning the intercuff segment in the original position may help maintain the intraperitoneal segment in the pelvis.

The catheter conformation in the subcutaneous segment may either be curved (swan neck) or straight. The swan-neck conformation is designed to maintain a low, pelvic location of the intra-abdominal component as well as a downward-facing exit site. If a straight catheter has a downward-facing exit site, catheter "memory" may increase the likelihood of the intraperitoneal segment migrating to the upper abdomen. As with the other modifications, the swan-neck or straight catheters have been compared in small, randomized trials [2]. The trials have shown no difference in infection rates or migration. However, observational studies have suggested that swan-neck catheters have fewer episodes of catheter dysfunction [7].

8.2.2 Implantation Technique

The implantation procedure is as important as catheter characteristics for long-term catheter performance. The surgical technique can be performed blindly, using a laparoscopic approach, or through an open surgical approach. The blind approach (using the Seldinger technique) may be associated with more complications, such as bowel injury. A major disadvantage to this approach is the inability to simultaneously repair hernias or perform omentopexy [8]. Both surgical approaches (open and laparoscopic) are safe and allow the simultaneous repair of hernias.

Regardless of the specific implantation technique, the catheter tip should lie in the true pelvis. If the tip is located higher in the peritoneal cavity, there is a much higher risk for omental entrapment and catheter dysfunction. It is thought that placement in the left pelvis may be preferred over the right pelvis as peristalsis may continue to push the catheter in a downward direction. After catheter placement, tip migration can certainly be seen, often with constipation. If relief of constipation does not revert the catheter tip into the pelvis, surgical correction can often return the tip to the pelvis without requiring surgical placement of a new catheter.

Since omental entrapment often impairs catheter drainage, there are numerous approaches that attempt to prevent this complication. One described approach has been prophylactic removal of omentum [9]. However, this procedure significantly increases the complexity of the surgery and may be too aggressive since most patients never have omental entrapment. Another approach to manage the omentum has been described by Crabtree [8]. In this approach, the surgeon first examines the omentum to see if it will border the catheter tip in the pelvis. If the exam does suggest that there could be omental–catheter interactions in the pelvis, an omentopexy is performed. Omentopexy involves tacking the omentum to the abdominal wall and can be performed more quickly than an omentectomy. Omentopexy has been demonstrated to be a safe procedure and appears to confer good long-term outcomes for peritoneal catheters [10–12].

8.2.3 Externalization Procedure

Catheter externalization may be done immediately at the time of catheter placement. Alternatively, the catheter may be placed several weeks to months prior to the anticipated

need for dialysis (Moncrief–Popovich technique). Immediate catheter externalization is widely performed and has a number of advantages. The major advantage with externalization at the time of catheter placement is the ability to start dialysis immediately. In patients presenting with uremic symptoms or urgent dialysis needs, prompt PD catheter placement and dialysis initiation may obviate the need for a temporary hemodialysis catheter. The ability to perform urgent PD will allow patients with urgent dialysis needs to choose between hemodialysis and PD. It should be noted, however, that patients with a newly placed and immediately externalized peritoneal catheter may not tolerate large dialysate volumes as they are prone to dialysate leaks due to increased intra-abdominal pressure. Therefore, the major limitation to this approach is that dialysis is usually done in a recumbent position (overnight) with small drain volumes.

Delayed externalization offers certain advantages to the patient as well. At the time of catheter placement, after the catheter is flushed, the external portion of the catheter is buried in the subcutaneous space. Ideally, the patient will not need dialysis for at least 2 weeks and the catheter tunnel can heal in a sterile environment. For patients with chronic kidney disease (CKD) who choose PD, this proactive approach will likely preempt the need for a temporary hemodialysis catheter. When the patient develops a clinical need for dialysis, the catheter can be externalized via a small incision made under local anesthesia and full dose dialysis can be initiated. Burying PD catheters also eliminates the need for exit site care, supplies, and catheter flushes until the catheter is in use. The absence of an open exit site potentially lowers the infectious risk although that has not been clearly demonstrated in the literature. Whether or not prolonged period of embedding negatively affects catheter performance is unclear. Data from one PD center suggested that prolonged embedding does harm catheter performance, while another recent retrospective study did not show any deleterious effects from prolonged embedding [13, 14].

There has been one prospective study comparing the two externalization techniques. Danielsson et al. randomized patients at two centers to immediate catheter externalization or delayed externalization [15]. Sixty patients were enrolled in the study and infectious complications were compared. After 2 years of follow-up, there was no significant difference in exit site infections or peritonitis between the two groups. Rates of catheter dysfunction were not specifically quantified in the study.

8.2.4 Exit Site Characteristics

Creation of a good exit site will also improve the likelihood of success for a peritoneal catheter. After the catheter is externalized, providers should employ appropriate measures to maintain a sterile exit site. Sutures should be avoided at the exit site due to the risk of foreign body reaction; rather, Steri-Strips should be used. The exit site should be directed downwardly or laterally and away from the belt line or skin folds [7, 16]. Since patients will be responsible for caring for the exit site, it is crucial that the patients can see and reach the exit site.

For many patients, a presternal catheter is an appropriate choice. Presternal exit sites are created by connecting an extender catheter to the PD catheter and creating a presternal exit site. The catheter should not cross the sternum in case the patient will need cardiac surgery. Patients with morbid obesity are potential candidates for presternal catheters due to greater ease of catheter care. Other conditions that may warrant presternal catheters are the presence of abdominal stomas or urinary and fecal incontinence. Observational studies have shown that abdominal and presternal catheters have similar infection rates and overall survival [17, 18].

8.3 Dialysis Solutions

8.3.1 Dextrose-Based Solutions

Dextrose-containing solutions have been the most widely used dialysate solutions for decades. The electrolyte composition of the commonly used solutions is shown in Table 8.2. A high dextrose concentration provides an osmotic gradient favoring water movement into the peritoneal space. Lactate is used as the buffer since bicarbonate will precipitate with dialysate calcium. The pH of the solutions is acidic (5.0) to minimize production of glucose degradation products (GDPs) during sterilization.

The degree of solute and water removal with dextrose solutions depends on the characteristics of the individual patient's peritoneal membrane. These characteristics have been quantified using the peritoneal equilibration test (PET) [19]. During a standard PET, 2.5% dextrose dialysate is instilled into peritoneal cavity for a 4-h period. The dialysate glucose concentration at 4 h is compared to the dialysate glucose concentration at the beginning of the dwell (D/D_0 glucose). The concentration of dialysate urea and creatinine are compared to their relative plasma concentration (D/P_{urea} and

Table 8.2 Composition of dextrose-based peritoneal dialysate solutions

Component	Concentration
Dextrose	1.5%, 2.5%, 4.25%
Sodium	132 mEq/L
Calcium	2.5 or 3.5 mEq/L
Magnesium	0.5 mEq/L
Chloride	96 mEq/L
Lactate	40 mEq/L

$D/P_{creatinine}$). Patients designated as rapid transporters have rapid systemic absorption of dialysate glucose and quick equilibration of urea and creatinine. Most patients on PD are high- or low-average transporters [20]. In this patient population, approximately 40% of dialysate glucose is absorbed after 4 h. Since urea is a small molecule, dialysate urea is roughly 90% of plasma urea by 4 h, while dialysate creatinine is approximately 65% of plasma creatinine.

Ultrafiltration with the use of dextrose solutions occurs by water transport down an osmotic gradient. Some water transport occurs concurrently with solute transport via the small pores in peritoneal capillaries. Another component of water transport is mediated by aquaporin-1 water channels and is independent of solute transport. In low- or high-average transporters, water will continue to enter the peritoneal cavity for more than 6 h after instillation of 2.5% dextrose dwell. However, since there is a constant rate of lymphatic absorption of peritoneal dialysate, dextrose solutions may lead to net fluid reabsorption if an individual dwell remains in the peritoneal cavity for a prolonged period [21].

Both local and systemic adverse effects can be seen with dextrose-containing solutions. In some patients, infusion of the dextrose solutions can lead to pain, possibly as a result of the non-physiologic pH. The solutions can also be associated with adverse metabolic consequences. Systemic absorption of dextrose can increase the daily caloric load, potentially leading to hypertriglyceridemia and worsening control of diabetes mellitus. The increase in calories from dextrose may worsen obesity or, alternatively, may paradoxically lead to malnutrition by decreasing appetite and protein intake.

In addition to the clinical effects listed above, some research suggests that dextrose-containing solutions may negatively affect the health of the peritoneal membrane. Longitudinal studies have established that the peritoneal membrane thickens over years of PD with increased angiogenesis and vessel density [22, 23]. Studies have supported the hypothesis that the non-physiologic pH of the solutions as well as GDPs and advanced glycosylated end products (AGEs) may promote peritoneal thickening. In vitro and animal studies have demonstrated negative effects of dextrose solutions on mesothelial cells [24, 25]. Establishing a causal relationship between dialysate solutions and peritoneal membrane pathology is more difficult. Most studies have reported effluent levels of cancer antigen 125 (CA-125), vascular endothelial growth factor (VEGF), and interleukin-6 (IL-6) as surrogate markers of peritoneal health. CA-125 is used as marker for mesothelial cell mass although the relationship between mesothelial cell mass and effluent CA-125 has not been rigorously tested. Similarly, VEGF levels are assumed to be a proxy for angiogenesis and IL-6 is reported to measure inflammation. In some studies, there is discordance between the markers. Nonetheless, based on the above studies, the hypothesis that chronic use of dextrose solutions negatively affects membrane health seems probable.

In vitro studies have also suggested that the high GDP levels negatively affect the function of peritoneal immune cells and potentially increase the risk of peritonitis. High GDP levels and low pH decrease survival of peritoneal leukocytes [26, 27]. Retrospective, observational studies have detected an increase in peritonitis rates. However, the data from RCTs published to date has not consistently demonstrated that alternative dialysis solutions lead to an improvement in peritonitis rates.

8.3.2 Icodextrin

A solution with 7.5% icodextrin is approved for use a single daily dwell (daytime dwell in patients on automated PD and nighttime dwell for patients performing continuous ambulatory PD). Icodextrin is an iso-osmolar solution of large molecular weight starch molecules. It is slowly metabolized to maltose, a monosaccharide that is subsequently absorbed. The electrolyte composition in an icodextrin solution matches that of the standard dextrose solutions.

Since icodextrin is a large molecule and is slowly absorbed, it provides for sustained peritoneal ultrafiltration. For the first 2–4 h of a dwell, icodextrin solutions provide similar ultrafiltration to 2.5% dextrose solutions. While 4.25% dextrose solutions deliver more rapid ultrafiltration than icodextrin, the latter solution allows for more ultrafiltration over a 12–14-h period. Furthermore, the amount of carbohydrate absorbed from icodextrin is less than that of a 4.25% dextrose solution. Icodextrin solution also has fewer GDPs although the clinical significance of this difference is unknown. Clinical studies have shown that icodextrin provides equivalent ultrafiltration to 4.25% dextrose solutions over 8–12 h, reduces glucose and hemoglobin A_{1C} levels, and possibly serum triglycerides [28–30].

In patients with rapid transporter status, icodextrin solutions offer a significant advantage over dextrose solutions [31–34]. In this patient population, dextrose is rapidly absorbed and fluid overload can be seen with long dwells; icodextrin can provide improved ultrafiltration with long dwells. A randomized, controlled trial in automated peritoneal dialysis (APD) patients with high-average or high transporter status demonstrated superior ultrafiltration, improved small solute clearance, and reduced carbohydrate absorption with icodextrin [31].

Patients with other transport characteristics may also benefit from icodextrin instillation during long dwells. Icodextrin can improve ultrafiltration and small solute clearance in low-average transporters although that has not been a universal finding [31, 32]. A small minority of PD patients exhibit a low transport status. Since dialysate glucose is absorbed slowly in low transporters, icodextrin would not be predicted to have a significant beneficial effect. In clinical trials, icodextrin has not demonstrated improved ultrafiltration in low transporters; however, no study has enrolled a large number of patients with low transporter status [31, 32, 35].

Although most studies evaluating icodextrin have been short-term studies, there is evidence that a sustained ultrafiltration benefit is maintained for up to 2 years. At 1 year, there is improved weight loss in patients on ultrafiltration. Patients treated with icodextrin for 1 year appear to have fewer episodes of volume overload [29, 35]. In one study, icodextrin improved technique survival by decreasing episodes of volume overload [35]. Most studies involving icodextrin have been short-term studies and were unable to study technique survival. In summary, the bulk of data from randomized controlled trials validates the hypothesis that icodextrin improves ultrafiltration and volume status in patients on PD, although this effect is most robust in high-average or high transporters.

While icodextrin is well tolerated in clinical studies, there are adverse effects associated with icodextrin. Icodextrin degradation products such as maltose are absorbed and serum amylase levels are reduced probably as an artifact of measurement methods. Whether either consequence directly causes harm is unknown but both do have implications for patients. There is a significant safety precaution that must be taken in patients with diabetes mellitus. Many glucometers used for home glucose monitoring do not differentiate between glucose and maltose, placing patients at risk for hypoglycemia if insulin doses are inappropriately raised [36]. It is therefore crucial that providers ensure that each diabetic patient receiving icodextrin has a glucometer compatible with this therapy. The incorrect levels of amylase suggest that a low serum amylase alone cannot exclude pancreatitis in patients for whom there is clinical suspicion [37]. Icodextrin has also been linked to an exfoliative rash on palms and soles [33]; patients with this complication should have icodextrin temporarily stopped.

8.3.3 Amino Acid Solutions

A 1.1 % amino acid (AA) solution is approved for exchanges in PD patients in Europe but not in the USA. AA solutions provide similar ultrafitration and small solute clearance to 1.5 % dextrose solutions but contain no dextrose. The pH of the AA solutions is higher than standard dextrose solutions and, given the lack of dextrose, the solutions contain no GDPs. Given the relatively high rate of protein-calorie malnutrition in patients on dialysis and the daily loss of AAs in dialysate, AA solutions were designed to prevent protein loss and improve measures of malnutrition.

There is limited data from controlled trials regarding outcomes with AA solutions. Substituting a dwell of dextrose dialysate with AA dialysate does not significantly change ultrafiltration or dialysis adequacy [38]. Short-term studies do demonstrate an improvement in surrogate markers of muscle anabolism, such as an increase in serum insulin-like growth factor-1 (IGF-1), serum albumin, and serum pre-albumin [39, 40]. Whether or not AA solutions can significantly modify endpoints such as technique survival or mortality has not been tested in adequately powered studies. Given the increase in AA and nitrogen absorption, AA solutions have the potential to provoke uremic symptoms in a dose-dependent manner [41].

8.3.4 Biocompatible Dextrose-Based Solutions

Since standard dextrose solutions contain low pH and GDPs, it has been hypothesized that, after use for long periods of time, these solutions can harm the peritoneal membrane and peritoneal immune function. Recently, many different "biocompatible" solutions characterized by normal pH and low GDPs have been studied. Some solutions have lactate buffer while others employ a dual chamber system with bicarbonate-based buffer. Recently, studies have been published using a low glucose-icodextrin hybrid solution [42].

As with most studies evaluating dialysate solutions, clinical trials with biocompatible solutions have been relatively small and short. A summary of large trials with low-GDP solutions is presented in Table 8.3 [43–49]. The biocompatible solutions appear to improve urine volume but have no significant effect on glomerular filtration rate [50]. However, the solutions also lead to lower ultrafiltration. The change in urine volume may not be due to a lower rate of GDP absorption but may be secondary to volume overload. Long-term studies have not demonstrated an improvement in volume status or left ventricular hypertrophy nor has there been reproducible data demonstrating an improvement in technique survival or the incidence of peritonitis.

Table 8.3 Selected trials studying low-GDP and neutral pH dialysate solutions

Reference	Experimental solution	Patient number/ duration (mos)	Outcomes
Choi et al. [43]	Lactate buffered, pH 7, low GDP (Fresenius, Balance)	104/12	Low-GDP solution with improved ultrafiltration and urea clearance. No change in residual kidney function (RKF)
Haag–Weber et al. (DIUREST) [44]	Lactate buffered, normal pH, multicompartment, low GDP (Gambro, Gambrosol Trio)	80/18	Low-GDP with improved urine volume and increased CA-125. Trend towards decreased UF with low-GDP solution
Johnson et al. (balANZ) [45]	Lactate buffered, pH 7, low GDP (Fresenius, Balance)	185/24	Experimental group with longer time to anuria, fewer episodes of peritonitis, and reduced ultrafiltration
Williams et al. (Euro-Balance) [46]	Lactate buffered, pH 7, low GDP (Fresenius, Balance)	86/3	Experimental group with increased effluent CA-125 and decreased hyaluronic acid
Kim et al. [47]	Lactate buffered, pH 7, low GDP (Fresenius, Balance)	91/12	Experimental group with higher glomerular filtration rate (GFR) and effluent CA-125 but lower peritoneal ultrafiltration
Rippe et al. [48]	Lactate based, multicompartment solution	80/24	Experimental group with increased CA-125 and decreased hyaluronic acid
Fan et al. [49]	Different bicarbonate-based solutions	93/12	No change in peritoneal solute transport. No change in solute clearance, urine volume, or peritoneal ultrafiltration
Li et al. (IMPENDIA and EDEN) [42]	Low glucose, icodextrin, amino acid solutions	251/6	Intervention group with improved glycated hemoglobin and triglycerides but increased volume overload and death

GDP glucose degradation products, *CA-125* cancer antigen 125, *UF* ultrafiltration

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