#### **REVIEW ARTICLE**

Julie R. Ingelfinger, M.D., Editor

# Peritoneal Dialysis

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N ESTIMATED 3.8 MILLION PEOPLE WORLDWIDE CURRENTLY RELY ON some form of dialysis for treatment of end-stage kidney disease (ESKD).<sup>1</sup> Although the prevalence of peritoneal dialysis varies from country to country, it accounts for approximately 11% of patients undergoing dialysis overall.<sup>2</sup> In developed countries, peritoneal dialysis is less expensive to deliver than hemodialysis.<sup>3</sup> Therefore, some national health care systems have implemented a "PD first" policy, with peritoneal dialysis as the preferred approach unless a medical contraindication is present.<sup>4</sup> There is no formal PD-first policy in the United States, although Medicare favors home dialysis over in-center dialysis.<sup>5</sup> Furthermore, implementation of the 2019 Advancing American Kidney Health executive order<sup>6</sup> may increase the use of peritoneal dialysis. Many clinicians lack knowledge of and experience in using peritoneal dialysis and may not feel comfortable managing the care of patients who are using that type of dialysis. This review aims to address the knowledge gap.

#### PERITONEAL ANATOMY

The peritoneum approximates body-surface area in size. Anatomically, it is composed of two layers: the visceral peritoneum, which covers the abdominal organs and accounts for 80% of the total surface area, and the parietal peritoneum, which lines the undersurface of the diaphragm and the interior surface of the anterior abdominal wall.<sup>7</sup> Histologically, the peritoneum consists of a single layer of mesothelial cells resting on submesothelial interstitial tissue, a gel-like matrix containing fibroblasts, adipocytes, collagen fibers, nerves, lymphatic vessels, and capillaries (Fig. 1).<sup>8</sup> The endothelium of these peritoneal capillaries functions as the filter that regulates peritoneal transport.<sup>9</sup> Thus, the peritoneum provides a suitable membrane for the performance of dialysis.

## PHYSIOLOGY OF PERITONEAL DIALYSIS

#### DIALYTIC PROCESS

In peritoneal dialysis, fluid (dialysate) is instilled in the peritoneal cavity, and solutes diffuse from the blood in the peritoneal capillaries into the dialysate, effecting an exchange analogous to that of extracorporeal hemodialysis. Similarly, imposition of a transmembrane pressure gradient creates the driving force for ultrafiltration of fluid from the capillaries into the dialysate. In contrast to hemodialysis, in which the pressure that is applied is hydrostatic, peritoneal dialysis involves osmotic pressure created by the intraperitoneal instillation of hypertonic dialysate, usually as glucose in the form of 1.5%, 2.5%, or 4.25% dextrose (glucose monohydrate). Higher concentrations of glucose exert higher osmotic pressures and effect greater degrees of ultrafiltration.

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Solute transfer across the peritoneal capillaries is bidirectional. Solutes such as urea, creatinine, and potassium diffuse from the bloodstream into the dialysate, whereas glucose diffuses from the dialysate into the peritoneal capillaries (Fig. 1). Diffusion of glucose out of the dialysate into the peritoneal capillaries results in dissipation of the osmotic gradient and progressive slowing in the rate of ultrafiltration. The rate of solute transfer across the peritoneum depends on the concentration gradient and the degree of peritoneal vascularity,<sup>10</sup> which varies from person to person.

In patients with less peritoneal vascularity, solutes diffuse slowly in both directions. Waste products accumulate in the dialysate slowly, and the glucose gradient favoring ultrafiltration dissipates slowly. Conversely, in patients with greater peritoneal vascularity, solutes diffuse more rapidly, also in both directions. Waste products accumulate in the dialysate more rapidly, and the glucose gradient favoring ultrafiltration dissipates more rapidly. Such patients have poor, sometimes even negative ultrafiltration with long "dwells." (The dwell is the time during which the dialysate remains in the abdominal cavity.) The use of a non-glucose-based fluid such as icodextrin during long dwells may be beneficial in these patients.<sup>11</sup> Icodextrin is a colloid osmotic agent that does not diffuse across the peritoneum; it effects ultrafiltration that is sustained for 12 to 16 hours.<sup>12</sup> Other types of dialysate fluids (available in some countries but not in the United States) include an amino acidbased fluid and fluids that are low in glucose degradation products. These two dialysate types decrease exposure of the peritoneal membrane to glucose, and the type that is low in glucose degradation products has been shown to help preserve residual kidney function.13

## PERITONEAL ACCESS

A single-lumen, silicone rubber catheter traversing the anterior abdominal wall is used to access the peritoneal cavity. Ideally, the catheter is positioned with the tip in the true pelvis. The catheter then passes through the rectus abdominis muscle, to which it is anchored by a Dacron cuff, and is then tunneled subcutaneously to the exit site, where it leaves the body (Fig. 2).

Occasionally, the external portion of the cath-

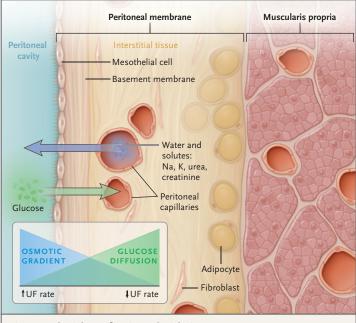


Figure 1. Physiology of Peritoneal Dialysis.

As blood in the peritoneal capillaries comes into contact with dialysate in the peritoneal cavity, solutes in the blood diffuse into the dialysate. The osmotic gradient created by glucose in the dialysate effects ultrafiltration (UF) of water from blood into the dialysate. Over time, glucose diffuses from dialysate into the peritoneal capillaries, which leads to dissipation of the osmotic gradient and slows the rate of ultrafiltration.

eter is embedded subcutaneously at the time of catheter placement and is later externalized through a small incision, which becomes the exit site.<sup>14</sup> These catheters require no special care while they are embedded and have a high like-lihood of successful functioning even if left embedded for several years before externalization.<sup>15,16</sup>

To reduce the risk of infection, the exit site should be oriented so that the catheter is directed either inferiorly or laterally but not superiorly.<sup>17,18</sup> An adapter made of plastic or titanium is placed on the distal end of the catheter, and another section of silicone rubber, called a transfer set, is attached. In case of inadvertent contamination of the distal portion of the catheter system, the transfer set can be removed and replaced, precluding the need for surgical replacement of the entire catheter (Fig. 2). Various catheter types are available: one or two cuffs to anchor the catheter, a straight intercuff segment or one with a preformed bend, and a straight or coiled intraperitoneal segment. No one catheter type has been conclusively shown to be superior

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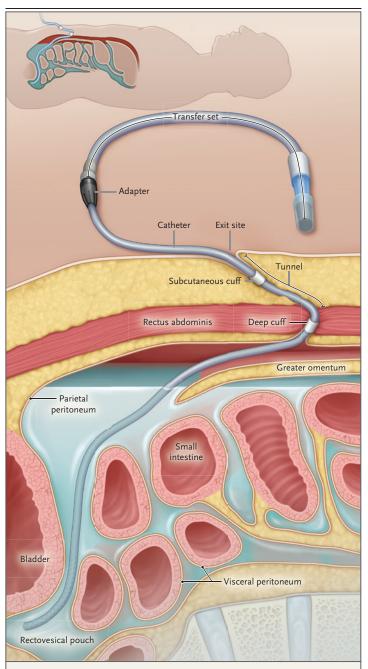


Figure 2. Peritoneal Dialysis System.

A catheter traversing the anterior abdominal wall is placed with its tip in the pelvis. Dialysate is instilled through the catheter and allowed to dwell in the abdomen, during which time solute diffusion and ultrafiltration occur. The dialysate is then drained, and the process is repeated.

to the others, but double-cuffed catheters are recommended.<sup>19</sup>

When peritoneal dialysis is being performed for treatment of acute kidney injury (AKI) (discussed below), the catheter should preferably be placed as described above. However, when the availability of catheter types is restricted by limited resources, rigid catheters and even unconventional catheters such as nasogastric tubes or Foley catheters may be used and are often lifesaving.<sup>20</sup>

The catheter can be placed surgically with the use of either an open or a laparoscopic approach. Alternatively, it may be placed percutaneously through a modified Seldinger technique, with or without fluoroscopic or ultrasound guidance. Local resources and operator experience dictate the choice of technique. However, laparoscopy is preferred, since it allows for the performance of adjunctive procedures, such as rectus sheath tunneling, omentopexy, or adhesiolysis, that reduce the risk of mechanical complications during peritoneal dialysis.<sup>19,21,22</sup>

It is recommended that 2 weeks elapse before the catheter is used; this delay allows the internal cuff to heal into place and minimizes the risk of mechanical complications. However, if a patient with ESKD and no prior planned renal replacement therapy requires dialysis, a peritoneal dialysis catheter can be placed and used before 2 weeks have elapsed, in what is called "urgent start" peritoneal dialysis.23 To avoid leakage of dialysate around the newly placed catheter, urgent-start peritoneal dialysis is performed with the patient in the supine position, which minimizes intraperitoneal pressure.<sup>24</sup> In addition, the volume of fluid infused is generally smaller than the volume in standard peritoneal dialysis and is tailored to body size. There are no data from prospective, randomized trials comparing urgent-start hemodialysis with urgentstart peritoneal dialysis. However, retrospective observational data show similar survival with the two techniques,<sup>25,26</sup> with fewer episodes of bacteremia among patients undergoing peritoneal dialysis and no increase in the incidence of peritonitis.<sup>25,27</sup> Thus, in the absence of a lifethreatening indication for immediate hemodialysis, patients presenting for the first time with ESKD should be allowed to choose between urgent initiation of hemodialysis and peritoneal dialysis.

#### DIALYTIC PROCEDURE

Peritoneal dialysis is performed by instilling fluid, called dialysate, into the peritoneal cavity. The

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Table 1. Types of Peritoneal Dialysis.	
Туре	Description
Continuous ambulatory peritoneal dialysis (CAPD)	Manual instillation and drainage of dialytic fluid several times per day
Automated peritoneal dialysis (APD)	Use of a machine (cycler) to instill and drain fluid a number of times over a pe- riod of several hours
Nocturnal intermittent peritoneal dialysis (NIPD)	APD performed at night only, with no fluid in the peritoneal cavity during the day
Continuous cycling peritoneal dialy- sis (CCPD)	APD at night plus a final installation of fluid into the peritoneal cavity, which remains there during the day; performed with or without an additional exchange of fluid during the course of the day
Incremental peritoneal dialysis	Initiation of peritoneal dialysis at a low dose, with stepwise increases as needed to compensate for loss of residual kidney function
Urgent-start peritoneal dialysis	Initiation of peritoneal dialysis within 2 wk after catheter placement in a person with end-stage kidney disease and no previously planned renal replacement therapy

fluid is allowed to dwell for a defined period, after which it is drained and fresh fluid is instilled. All exchanges are performed with the use of a sterile procedure. The volume of fluid instilled is 2 liters in most adults, although lower volumes are often used in smaller patients and higher volumes in larger patients. Volumes of up to 1.25 liters per square meter of bodysurface area are generally well tolerated.<sup>28</sup> During the dwell period, solute diffusion and ultrafiltration occur (Fig. 1); the used dialysate is then discarded, and the cycle is repeated.

Peritoneal dialysis may be performed manually, usually three or four times daily, with the dialysate dwelling in the abdominal cavity between exchanges to equilibrate; this is termed continuous ambulatory peritoneal dialysis (CAPD) (Table 1). Since patients who opt for CAPD are not tethered to a machine, they can be ambulatory at all times, if desired. Alternatively, a mechanical device, commonly referred to as a "cycler," may be used to perform a number of exchanges over a period of several hours in a procedure called automated peritoneal dialysis (APD). Some patients receiving APD, particularly those who still have substantial residual kidney function, will have sufficient solute removal and ultrafiltration to warrant dialysis only at night, which is termed nocturnal intermittent peritoneal dialysis (NIPD). When residual kidney function has deteriorated further, such patients will often need dialysis during the day as well, in a procedure known as continuous cycling peritoneal dialysis (CCPD). Other patients, usually those who are very muscular or have little or no residual kidney function, will require drainage of the fluid instilled earlier in the day, with another fluid exchange performed later in the day. This strategy of increasing the dose of dialysis as residual kidney function decreases is referred to as incremental peritoneal dialysis.<sup>29,30</sup> Even in patients with anuria (i.e., those with no residual kidney function whatsoever), peritoneal dialysis has been used successfully.<sup>31</sup>

## CONTRAINDICATIONS TO PERITONEAL DIALYSIS

There are only a few absolute contraindications to peritoneal dialysis. These include an insufficiently clean environment in which to perform exchanges, an inadequate cognitive or physical ability on the part of the patient or an assisting partner to learn and perform peritoneal dialysis, and lack of a suitable peritoneal cavity due to extensive scarring or adhesions. The degree of scarring often cannot be assessed until the peritoneal cavity is visualized laparoscopically at the time of attempted catheter placement.<sup>21</sup>

Peritoneal dialysis has been performed successfully in patients who have previously undergone liver transplantation, with rates of peritonitis and death that are similar to those in the general population of patients undergoing peritoneal dialysis and with no adverse effects on the hepatic allograft.<sup>32</sup> Other perceived barriers to peritoneal dialysis and potential solutions are listed in Table 2.

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Table 2. Perceived Barriers to Peritoneal Dialysis and Potential Solutions.	
Perceived Barrier	Potential Solution
Morbid obesity	Use of a presternal catheter
Polycystic kidney disease	Use of frequent low-volume exchanges (e.g., with APD)
Presence of an ostomy	Use of an extended catheter system (e.g., a presternal catheter to place the exit site far from the ostomy)
Severe cognitive or physical impairment	Performance of peritoneal dialysis by an assistant or caregiver

## OUTCOMES

Numerous studies have shown that hemodialysis and peritoneal dialysis are associated with similar survival among patients with ESKD.<sup>33-36</sup> Survival is also similar with CAPD and APD.<sup>37-39</sup> Health-related quality of life is equivalent for patients who are receiving peritoneal dialysis and those receiving hemodialysis.<sup>40,41</sup> Since APD offers a more flexible lifestyle, it is not surprising that some studies, though not all, have shown that health-related quality of life with APD is superior to that with CAPD.<sup>42-45</sup>

#### COMPLICATIONS

Complications of peritoneal dialysis are divided broadly into two categories: infectious and noninfectious complications (Table 3). The most common infectious complication is bacterial peritonitis, with gram-positive organisms predominating over gram-negative organisms.<sup>46</sup> Mycobacterial infection is a rare cause of peritoneal dialysis–related peritonitis in developed countries but is more common in underdeveloped countries.<sup>47,48</sup> The most feared peritoneal dialysis–related infection is fungal peritonitis, which necessitates catheter removal.<sup>46</sup>

The frequency of peritonitis varies among peritoneal dialysis programs. The International Society for Peritoneal Dialysis has specified, as a benchmark, that programs should have a peritonitis rate that does not exceed 0.5 episodes per patient-year.<sup>46</sup> Rates below 0.33 episodes per patient-year are common, and some programs achieve rates below 0.2 episodes per patientyear.<sup>49</sup> Although many episodes of peritoneal dialysis–related peritonitis can be treated in the outpatient setting, approximately 50% of episodes result in hospitalization.<sup>50</sup> The majority of episodes are successfully treated without removal of the peritoneal dialysis catheter.<sup>51</sup> The catheter should be removed if peritonitis fails to resolve after 5 days of treatment with appropriate antibiotics or in cases of fungal peritonitis.<sup>46</sup> Mortality from peritoneal dialysis–related peritonitis ranges from 3 to 10%.<sup>52</sup> The risk of death after an episode of peritonitis remains elevated for up to 120 days after resolution of the episode itself.<sup>53</sup>

In contrast to spontaneous bacterial peritonitis in patients with cirrhosis, which is diagnosed when the neutrophil count is 250 per  $\mu$ l or higher,54 peritoneal dialysis-related peritonitis is diagnosed with a white-cell count as low as 100 per  $\mu$ l if there are 50% or more neutrophils.<sup>46</sup> At present, the definitive diagnosis of peritonitis continues to rely on identification of an organism on culture. A dipstick designed for point-ofcare use has recently been developed; it detects the presence of immune response biomarkers in peritoneal effluent.55 With further testing and validation, use of this dipstick may result in earlier diagnosis and initiation of appropriate treatment for peritonitis. Although not all cloudy fluid is caused by infection,56 a patient presenting with cloudy fluid due to white cells should be presumed to have peritonitis and should be treated empirically, unless another cause (e.g., hemoperitoneum) is readily apparent. Delaying therapy for peritonitis has been associated with

Table 3. Complications of Peritoneal Dialysis.	
Infectious complications	
Peritonitis	
Exit-site or tunnel infections	
Noninfectious complications	
Catheter-related	
Impaired flow (unidirectional or bidirectional)	
Leak	
Pain (during infusion or drainage)	
Related to increased intraabdominal pressure	
Back pain	
Hernia	
Hydrothorax	
Metabolic	
Hypokalemia	
Metabolic syndrome	
Encapsulating peritoneal sclerosis	

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an increased likelihood of treatment failure.<sup>57</sup> Therefore, if the fluid cell count is not readily available, consideration should be given to initiation of empirical therapy even in its absence. Empirical treatment should provide coverage for both gram-positive and gram-negative organisms. Unless the patient has signs of systemic sepsis, intraperitoneal administration of antibiotics is preferred because it delivers the highest concentration of drug directly to the infected site.<sup>46</sup> This treatment can be administered either by a trained dialysis nurse or at home by the patient or caregiver. Other infections occasionally complicating peritoneal dialysis involve the exit site, the catheter tunnel, or both.<sup>58</sup>

Common noninfectious complications of peritoneal dialysis include catheter-related issues such as catheter malfunction, problems with increased intraabdominal pressure, and metabolic consequences of the glucose-rich peritoneal dialysate.59 Mechanical complications include flow dysfunction, fluid leaks, and pain on infusion or draining of dialysate. Flow dysfunction is usually limited to poor outflow and is most commonly due to constipation, in which distended bowel loops impinge on the catheter. Therefore, careful attention to a bowel regimen is important for patients treated with peritoneal dialysis. Less commonly, bladder distention is the cause of poor outflow. Occasionally, omentum, epiploic appendixes, or fallopian tube fimbriae impinge on the side holes of the catheter, necessitating laparoscopic repair. Bidirectional obstruction to catheter flow is relatively uncommon, but it may be caused by kinking of the intramural portion of the catheter or intraluminal obstruction (e.g., by a fibrin clot).<sup>19</sup> Leakage of fluid around the catheter, through a hernia or other defect in the abdominal wall, or leakage into the pleural space may occur.

Metabolic complications include development of metabolic syndrome,<sup>60</sup> with concern regarding the attendant weight gain, which may prevent or delay kidney transplantation. It is important to recognize, however, that the average weight gain after 1 year of peritoneal dialysis is reported to be only 1.3 kg<sup>61</sup> or 2.3 kg.<sup>62</sup> Some of this weight gain presumably reflects reversal of uremic anorexia and is therefore physiologically appropriate. Furthermore, in a large, propensitymatched cohort study of weight gain in patients treated with peritoneal dialysis as compared with those receiving hemodialysis, weight gain was lower in the peritoneal dialysis group.<sup>63</sup> In addition, patients in the peritoneal dialysis group were more likely to undergo transplantation than those in the hemodialysis group and had equivalent survival. Thus, the concern about excessive weight gain and delay of transplantation appears to be unfounded.

Hypokalemia is another common metabolic complication of peritoneal dialysis. Since peritoneal dialysate contains no potassium, patients treated with peritoneal dialysis, particularly continuous dialysis, are prone to hypokalemia, much more so than to hyperkalemia (which is more common in patients treated with hemodialysis). Consequently, it is important to recognize that patients receiving peritoneal dialysis are generally permitted to consume a more potassiumrich diet than patients receiving hemodialysis. In fact, potassium supplementation may occasionally be required to maintain a normal plasma potassium level in a patient undergoing peritoneal dialysis. Finally, encapsulating peritoneal sclerosis is a severe but rare complication of longterm peritoneal dialysis (almost always occurring in patients treated for more than 5 years)<sup>64</sup> that is associated with substantial morbidity and mortality. This disorder leads to progressive peritoneal fibrosis, culminating in "cocooning" of the bowel, with resultant symptoms of bowel obstruction and malnutrition.

## PERITONEAL DIALYSIS IN PATIENTS WITH ACUTE KIDNEY INJURY

Use of peritoneal dialysis as therapy for AKI has increased in recent years, particularly in lowresource settings.<sup>20</sup> This increase is due, in large measure, to the efforts of the International Society of Nephrology Saving Young Lives project, which has brought peritoneal dialysis treatment for AKI to underserved regions around the world.65,66 A systematic review of studies involving patients with AKI compared outcomes of those who were treated with extracorporeal therapies, continuous or intermittent, with outcomes of those treated with peritoneal dialysis; the review showed no significant difference in survival between the groups.67 Peritoneal dialysis successfully treats the acidosis and most cases of hyperkalemia that occur in AKI in a manner equivalent to that of intermittent hemodialysis.68

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Life-threatening hyperkalemia is successfully treated more rapidly with extracorporeal therapies than with peritoneal dialysis. However, peritoneal dialysis can be initiated much more quickly than placement of a catheter for emergency hemodialysis. Therefore, if a patient with ESKD and a peritoneal dialysis catheter but no vascular access presents with life-threatening hyperkalemia, peritoneal dialysis should be initiated immediately, with the possible need for other therapies reassessed frequently. Although volume removal cannot be as finely regulated with peritoneal dialysis as it can with extracorporeal therapies, frequent hypertonic exchanges can successfully address pulmonary edema. In this regard, it is important to recognize that concern about the potential adverse effects of intraperitoneal fluid on respiratory mechanics have not been borne out on careful study.69

Despite its demonstrated efficacy, peritoneal dialysis for AKI is not often used in developed countries because extracorporeal therapies are used preferentially. However, during the coronavirus disease 2019 (Covid-19) pandemic, even developed countries have discovered that they are relatively resource-poor and have successfully used peritoneal dialysis when dialysis machines for extracorporeal therapies were in short supply.<sup>70,71</sup> It remains to be seen whether this trend will continue when the pandemic abates.<sup>72</sup>

## USE OF PERITONEAL DIALYSIS IN THE PERIOPERATIVE SETTING

Many hospitals lack personnel with experience in the performance of peritoneal dialysis. As a result, sometimes a central venous catheter is placed and hemodialysis is performed when it is not actually required. In addition, many surgeons believe that patients treated with peritoneal dialysis who are undergoing surgery must be switched to hemodialysis during the postoperative period, often for many weeks, if not permanently. Concerns cited include leakage of dialysate through an abdominal incision, delayed wound healing, and the risk of peritonitis with possible subsequent infection of foreign materials (e.g., surgical mesh or aortic grafts).73,74 However, study data and anecdotal experiences do not support such concerns. In patients undergoing hernia repair or a variety of laparoscopic

procedures, peritoneal dialysis can often be resumed within 48 hours after surgery by performing small-volume exchanges with the patient in the supine position, thereby minimizing intraabdominal pressure.74,75 The same is true for surgeries associated with relatively small upper abdominal incisions (e.g., cholecystectomy). When such procedures are planned, it is often helpful to intensify peritoneal dialysis for several days before surgery, thereby allowing for a safe delay in resuming peritoneal dialysis postoperatively.75,76 Patients undergoing bowel procedures that involve large anterior abdominal incisions should probably have a 2-to-3-week hiatus from peritoneal dialysis. However, if the abdomen is not infected, the peritoneal dialysis catheter does not need to be removed at the time of surgery.

Patients with ESKD may require cardiac surgery: coronary-artery bypass grafting, valve replacement, or a combination of the two procedures. Studies have shown that, after cardiothoracic surgery, both early complications and long-term survival are similar for patients treated with hemodialysis and those treated with peritoneal dialysis.<sup>77,78</sup> Thus, patients with a peritoneal dialysis catheter in place who undergo cardiothoracic surgery do not automatically require conversion to extracorporeal renal replacement therapy.

In considering the continued use of peritoneal dialysis after cardiothoracic surgery, advanced planning is advised. It is important to have a preoperative discussion with the surgeon to ensure that the integrity of the diaphragm is maintained. If possible, the surgical incision itself and all drains, chest tubes, and other devices should be placed so as to avoid penetrating the diaphragm. Failure to maintain the integrity of the diaphragm may result in dialysate leakage, precluding the use of peritoneal dialysis in the postoperative period.79 After major cardiac surgery, the frequency of AKI that requires dialysis is estimated at 5 to 8%. In adults, it is commonly treated with extracorporeal therapies. In the pediatric population, however, peritoneal dialysis is often preferred and has been shown to provide excellent outcomes.80,81

The patient who is receiving a prosthetic aortic graft deserves specific mention. In a number of case series, peritoneal dialysis was used successfully in such patients, both in the immediate postoperative period<sup>82,83</sup> and later.<sup>84,85</sup> Although

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peritonitis did develop in 6 of 41 patients, it did not result in graft infection in any of them. Finally, although continuous extracorporeal therapy is the dialytic approach of choice in people with AKI or ESKD who require neurosurgery, peritoneal dialysis should be considered if continuous extracorporeal therapy is not available. Peritoneal dialysis offers several advantages over intermittent hemodialysis in these circumstances: hemodynamic fluctuations are minimal, there is no need for anticoagulant therapy, and peritoneal dialysis has no acute effects on plasma osmolality, which might cause or exacerbate cerebral edema.<sup>86</sup>

## SUMMARY

Peritoneal dialysis is a valuable therapeutic approach for patients with AKI or ESKD. Clinicians caring for such patients should have a basic understanding of peritoneal dialysis and its use.

Disclosure forms provided by the author are available with the full text of this article at NEJM.org.

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