Dialysis Modalities: What the Non-Nephrologist Needs to Know

Brian S. Rifkin, MD
Ursula C. Brewster, MD

Dialysis has been used as a life-saving technique for decades but has been universally available as a chronic therapy for only approximately 30 years. In the United States, there are currently more than 300,000 patients undergoing dialysis, and the prevalence of end-stage renal disease (ESRD) is growing yearly.[1] Diabetes and hypertension, which are growing to epidemic status in some areas of the United States, account for more than 50% of new ESRD patients.

For eligible patients, kidney transplantation is the best treatment for ESRD.[2] Rarely, some patients are able to obtain a preemptive transplant and never need to start dialysis. However, most patients who start dialysis will need it for the rest of their lives or until they undergo kidney transplantation. For others, dialysis is needed acutely while waiting for renal function to recover from a specific injury.

Physicians in all specialties should have a working knowledge of dialysis. Primary care physicians play a critical role in identifying patients at risk for ESRD. In addition, as more patients live longer on dialysis, physicians in all specialties need to be familiar with the basic elements of dialysis to assist in their care. Surgeons who are to operate on ESRD patients need to be familiar with dialysis to understand the importance of scheduling surgery around dialysis as well as the volume and electrolyte control options available postoperatively.

This article will review dialysis modalities for patients on chronic therapy and briefly address modalities used in the acute setting. The modalities that are currently available to patients with ESRD are hemodialysis and peritoneal dialysis. A basic knowledge of the workings of each type of dialysis will help physicians guide patients to the most appropriate form of renal replacement therapy. A brief glossary of common dialysis terms is provided in **Table 1**.

TAKE HOME POINTS

- Primary care physicians play a critical role in preparing patients both medically and emotionally for chronic dialysis.
- Most patients require the initiation of dialysis once their creatinine clearance is less than 10 mL/min, or in patients with symptoms or diabetes, less than 15 mL/min.
- Formulas are available to quickly and easily calculate estimated glomerular filtration rate from routine laboratory test results, making collecting 24-hour urine samples often unnecessary.
- Arteriovenous fistulas are the preferred access for hemodialysis patients; patients should be referred to a vascular access surgeon once their creatinine clearance is 20 mL/min or less.
- Peritoneal dialysis allows patients more autonomy and independence than hemodialysis.
- Continuous renal replacement therapy is done in acutely ill intensive care unit patients and requires special dialysate fluid and trained nurses.

ROLE OF THE PRIMARY CARE PHYSICIAN

Primary care physicians can help improve the care of patients with chronic kidney disease (CKD) and assist in the transition to dialysis with timely referral to a specialist and patient preparation. In patients with CKD, alterations in physiology take place long before the need for dialysis. These changes include anemia; derangements of calcium, phosphorus, and parathyroid hormone homeostasis; and spontaneous decreases in protein intake. Although these changes are patient-dependent, they have been described to occur when creatinine clearance is 30 to 40 mL/min/1.73 m^2. Early referral to a nephrologist is necessary not only to initiate treatment for these complications of CKD but to also allow for a smooth transition to dialysis. Patients who require dialysis within 3 months of referral to a

Dr. Rifkin is a fellow in nephrology, and Dr. Brewster is an assistant professor of medicine, Section of Nephrology, Yale University School of Medicine, New Haven, CT.

Table 1. Common Definitions in Renal Replacement Therapy

Dialysis	The clearance of small molecules and toxins using diffusion across a native membrane (peritoneal) or a synthetic semipermeable membrane (hemodialysis)
Ultrafiltration	Fluid removal across a semipermeable membrane during dialysis by convection
Hemodialysis	Dialysis utilizing a synthetic semipermeable membrane in which diffusion and ultrafiltration lead to clearance from blood
Hemofiltration	Continuous dialysis therapy in which large amounts of fluid are removed from blood by convection with concurrent reinfusion of an electrolytic solution
Hemodiafiltration	The combination of hemodialysis and hemofiltration
Peritoneal dialysis	Dialysis using the patient's own peritoneum as a semipermeable membrane across which solutes diffuse. A prepared electrolyte solution with dextrose is used as the osmotic agent that induces ultrafiltration.
Fistula	Hemodialysis access made by sewing native artery to native vein
Graft	Hemodialysis access made by interposing a piece of synthetic material between native artery and native vein

nephrologist have an increased risk of morbidity and mortality compared with those under long-term care of a specialist.[3]

Patients with CKD should be actively prepared for the initiation of dialysis as renal function declines. Ideally, dialysis education, screening tests, and modality selection should take place approximately 1 year before the anticipated initiation of dialysis (**Figure 1**). During this time, ongoing discussion between the patient, the primary care physician, and the nephrologist should occur at regular intervals to decrease anxiety and increase compliance. Once dialysis therapy is initiated, patients need the expertise of a primary care physician as well as the support and continuity of care that such a person provides. The timing of procedures, the scheduling of medical appointments, and medication schedules must all be coordinated with awareness of the patient's modality of dialysis and its schedule.

INITIATION OF DIALYSIS

The main goals of dialysis are to remove nitrogenous wastes and other molecules and replenish buffers such as bicarbonate. For patients with CKD who progress in a predictable way and are under regular medical care for their condition, dialysis can be initiated in a careful, scheduled manner. For others, dialysis is initiated urgently in the hospital as a result of acute renal failure or because of a lack of previous CKD care or preparation.

Clinical Indications for Urgent Initiation of Dialysis

Several life-threatening situations warrant rapid communication with a nephrologist and initiation of dialysis as a life-saving intervention (**Table 2**). The classic indication for dialysis is uremia, a syndrome that results from the toxic effects of elevated serum concentrations of nitrogenous wastes and other as yet undefined substances in the blood. Symptoms of uremia are nonspecific and may involve multiple organ systems. Gastrointestinal symptoms often predominate, with nausea, vomiting, and anorexia being common presentations. In addition, central nervous system manifestations, including fatigue, confusion, tremors, and even coma, may occur. Finally, uremic patients have a prolonged bleeding time and increased risk of hemorrhage. Classic physical examination findings of a pericardial friction rub, asterixis, and a wrist or foot drop signal the need for urgent dialysis in the setting of renal failure; however, these findings only occur very late in the syndrome.

Laboratory Indications for Planned Initiation of Dialysis

In the setting of chronic renal failure, dialysis ideally is initiated in anticipation of uremia. Most patients will develop symptoms of uremia and need to initiate dialysis when their creatinine clearance drops below 10 mL/min/1.73 m^2. Diabetic patients appear to be more susceptible to the deleterious effects of uremia and frequently require the initiation of dialysis when the creatinine clearance falls below 15 mL/min.[4] There is no level of azotemia or creatinine clearance that absolutely necessitates the initiation of dialysis. Rather, it is a clinical decision wherein these absolute values are interpreted in a patient-specific context.

Because clinical laboratories do not report glomerular filtration rate (GFR) or creatinine clearance directly, clinicians need to calculate these values from available data. Serum creatinine concentration is affected by patient nutrition and muscle mass and therefore should not be relied upon to estimate GFR. Equations that accurately predict GFR based on routinely available serum chemistry values are readily available online and in most PDA medical calculation programs. The 2 most commonly used are the Cockcroft-Gault formula and the Modification of Diet in Renal Disease (MDRD) equation (**Table 3**). Both should be used only when a patient's creatinine is in steady state, as

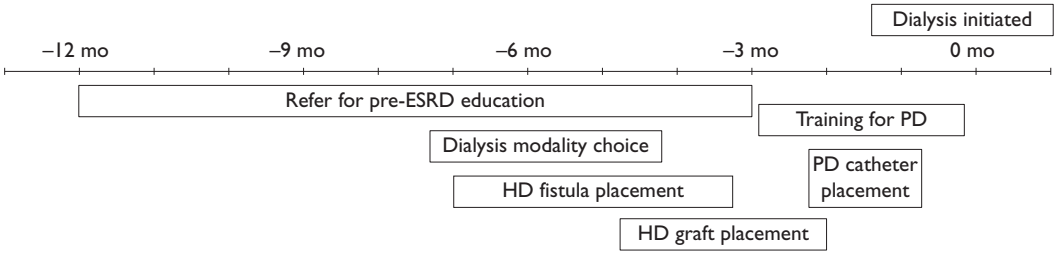

Figure 1. A timeline of important events leading up to the initiation of dialysis. ESRD = end-stage renal disease; HD = hemodialysis; PD = peritoneal dialysis.

acute renal failure with rapidly changing creatinine values renders these equations useless.

HEMODIALYSIS

Hemodialysis Procedure

The basic characteristics of hemodialysis and peritoneal dialysis are compared in **Table 4**. In hemodialysis, solutes diffuse across a semipermeable membrane down a concentration gradient. The rate of diffusion is highest when the concentration gradient is greatest. Heparinized blood is pumped through a synthetic dialyzer at rates of 300 to 500 mL/min, while dialysate (an electrolyte solution) flows in the opposite direction at 500 to 800 mL/min. A semipermeable membrane that permits solute and water transfer, as governed by the laws of physics, separates the blood and dialysate. Approximately 70% of blood urea nitrogen can be removed in a 3- to 4-hour hemodialysis session, depending on the surface area and permeability of the dialysis membrane.

The hemodialysis circuit consists of a heparin pump, a blood pump, an air leak detector, and arterial and venous pressure monitors (**Figure 2**). Computer-generated alarms warn dialysis staff of changes in blood pressure or heart rate, blood or air leaks, or blood clots in the system. Because 30 to 40 gallons of water are used during each hemodialysis treatment, strict water purification systems are needed (water must be free of bacteria, endotoxins, and other pollutants) and is subjected to filtration, softening, deionization, and reverse osmosis prior to being used in the rehydration of powdered dialysate. The major constituents of the dialysis solution (**Table 5**) can be adjusted in the dialysis prescription depending on serum pH and levels of potassium and calcium.

A typical hemodialysis regimen consists of a 4-hour treatment, 3 times per week, but this prescription is tailored to individual patients' needs. The length of a patient's dialysis session is based on measurements of "dialysis adequacy" to ensure that the patient is achieving sufficient clearance. Solute clearance, determined by the reduction of serum urea per treatment, is measured regularly by calculating the ratio Kt/V (where K equals the clearance coefficient, t equals time [duration] of each dialysis treatment, and V equals volume of distribution of urea), with a goal of 1.3 or greater. If a patient's Kt/V ratio falls below this level, the duration of the dialysis treatments usually needs to be increased. Hemodialysis adequacy also can be reduced by inadequate blood flow through a vascular access, a dialyzer that is too small, or skipping or early termination of dialysis sessions by patients.

Table 2. Indications for Acute Hemodialysis

Severe acidosis not responsive to bicarbonate therapy
Severe electrolyte abnormalities (hyperkalemia, hypercalcemia)
Medication overdoses/intoxication (eg, methanol, ethylene glycol, lithium, theophylline, salicylates)
Severe volume overload not responsive to diuretic therapy
Uremia (signified by nausea, vomiting, anorexia, pericardial friction rub, change in mental status in the setting of chronic renal failure)

Hemodialysis Access

Before hemodialysis can be initiated, vascular access must be obtained. Several types of hemodialysis access are possible, including central venous catheters, fistulae, and grafts. The choice of access depends on the acuity of the need for dialysis and the availability of an undamaged venous system. For immediate hemodialysis access, a large-bore intravenous line can be placed into one of the central veins, preferably the internal jugular or femoral vein. Catheters should not be placed in the subclavian vein because this placement can induce central venous stenosis, which may preclude the later use of that upper extremity for surgically created fistulae and grafts.

Central venous catheters can be placed at the bedside or in an operating suite by either a surgeon or an interventional radiologist. Catheters may be tunneled or untunneled and may have subcutaneous cuffs. Tunneling subcutaneously prior to entering the vein

Table 3. Formulas for Estimating Glomerular Filtration Rate

MDRD Equation

$$GFR\ (mL/min/1.73\ m^2) = 170 \times S_{Cr}\ (mg/dL)^{-0.999} \times age\ (years)^{-0.176} \times 0.762\ (if\ female) \times 1.80\ (if\ African\ American) \times BUN\ (mg/dL)^{-0.170} \times albumin\ (g/dL)^{0.318}$$

Cockcroft-Gault Formula

$$C_{Cr}\ (mL/min) = \frac{[140 - age\ (years)] \times IBW\ (kg)}{72 \times S_{Cr}}$$

Web site available: www.kidney.org

BUN = blood urea nitrogen; C_{Cr} = creatinine clearance; IBW = ideal body weight; MDRD = Modification of Diet in Renal Disease; S_{Cr} = serum creatinine.

Table 4. Comparison of Dialysis Modalities

Characteristics	Hemodialysis	Peritoneal Dialysis
Where/when performed	In center, 3 times per week*	Daily at home by the patient or support persons
Membrane	Synthetic dialysis cartridge	Patient's own peritoneum
Access	Fistula, graft, catheter	Tenckhoff catheter
Flexibility	Limited, fixed schedule Travel arrangements must be made with local dialysis center	More flexible Supplies can be delivered to any destination
Absolute contraindications	No vascular access	Colostomy, ileostomy Intra-abdominal adhesions No space for supplies Failure of peritoneal membrane
Relative contraindications	Geographical distance from center Severe vascular disease Hypotensive heart disease Severe angina with dialysis	Morbid obesity Inability to learn technique without proper support Poor hygiene Very poor glucose control

*For some patients, at-home hemodialysis, daily hemodialysis, or nocturnal hemodialysis are options as well.

decreases the likelihood of skin bacteria translocating into the bloodstream and causing infection and allows the catheter to remain in place for months at a time. The advantage of a catheter is that it may be used for initiation of dialysis immediately following the procedure. Catheters are not, however, preferred as long-term solutions for vascular access because of their high rates of infection (approximately 2–4 episodes per 1000 patient-days) and increased patient mortality compared to fistulae or grafts.[5]

Fistulae are the best dialysis access, with grafts being the alternative. In these access types, a direct artery-to-vein connection is established to allow for the high blood flows required for hemodialysis (300–450 mL/min). Generally, patients should be referred to an experienced access surgeon when their estimated GFR declines to 20 mL/min/1.73 m^2 or when they are expected to require dialysis in the next 3 to 6 months. Surgeons often need to evaluate and image the venous system prior to placing arteriovenous access. In skilled hands, Doppler ultrasonography of the upper extremity veins allows visualization of the caliber of target vessels, which guides the surgeon in choosing the access type and location. If ultrasonography is not available or is unreliable because of inadequate technical skill or patient characteristics, upper extremity venography can give similar information. One must be cautious when performing venography to avoid a high volume of iodinated contrast, which may result in a rapid decline of already marginal kidney function. In some cases, gadolinium or carbon dioxide may be used as a contrast agent with less potential nephrotoxicity.[6]

Creation of an arteriovenous fistula by a skilled vascular surgeon is the first choice for vascular access. Creating a fistula requires the anastomosis of native artery to native vein, usually in the forearm or upper arm. This type of dialysis access often requires 6 to 12 weeks to mature before it can be used. Maturation of a fistula allows the vein to thicken and undergo arterialization under the pressures of arterial flow. Arterialization

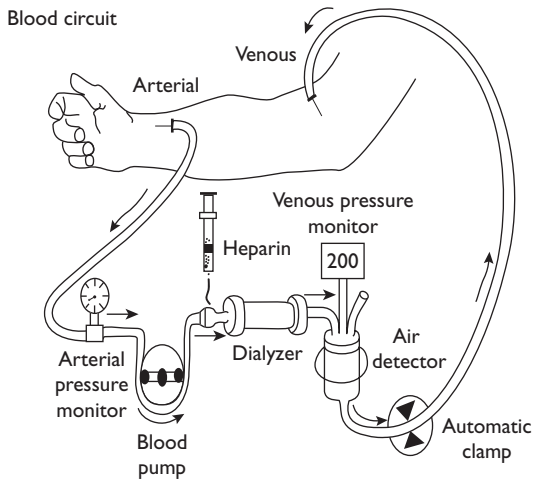

Figure 2. A schematic representation of the blood circuit for hemodialysis. Blood leaves the patient through an arterial line, cycles through the pump and dialyzer, and is returned through a venous line. (Adapted with permission from Misra M. The basics of hemodialysis equipment. Hemodial Int 2005;9:31.)

allows repeated venipuncture to be tolerated without destruction of the vein or extravasation of blood into the interstitial space, leading to venous compression and decreased blood flow. A successful fistula may last for more than a decade.

If a vein that is suitable in length and caliber is not found during vascular surgery, a synthetic graft made of polytetrafluoroethylene (PTFE) may be interposed between native vessels. An arteriovenous graft can be used when the vascular anastomoses have healed—typically 2 to 4 weeks after placement. A synthetic PTFE graft is not as durable as an arteriovenous fistula; on average, PTFE grafts have a patency rate of 60% at 2 years.[7] Additionally, synthetic materials in the vascular system are prone to serious infections that are unlikely to be cleared by antibiotics alone and may require major surgical interventions. Maintenance of access requires diligence on the part of nephrologists, surgeons, and radiologists. Vascular access is often complicated by infections, thrombosis, stenosis from intimal hyperplasia, aneurysm formation, and distal arm ischemia. Vascular access failure and infections remain a major source of morbidity and mortality for ESRD patients. Early referral to an experienced surgeon is essential to avoid the need for catheter placement.

Hemodialysis Complications

Hypotension is the most common adverse event during hemodialysis, occurring in 25% to 55% of treatments.[8] Dialysis rapidly removes urea from the extracellular space, creating an osmolar gradient from the extracellular to the intracellular space. Fluid shifts result, causing intracellular swelling and further extracellular volume depletion. In addition, if a patient is noncompliant with fluid restrictions, removal of more than 12 lb of fluid may be required to reach a target "dry weight" in a single 3- to 4-hour dialysis session. This rapid removal of volume often results in hypotension as fluid does not have time to re-equilibrate into the intravascular space. Various strategies are used for peripheral vasoconstriction to combat episodic hypotension, including cooling the dialysate and administering medications such as midodrine (an α-agonist). Intermittent boluses of saline, albumin, or mannitol are also used when necessary to transiently increase blood pressure.

Although less common, other complications of hemodialysis include nausea, cramping, headache, chest pain, and itching. Individual patients may be plagued with these symptoms to the point of intolerance. Long-term complications of hemodialysis include vascular access failure, cardiovascular disease, anemia, and renal osteodystrophy.

Table 5. Major Components of Hemodialysate

	Concentration	
Component	**Range**	**Typical**
Sodium (mEq/L)	135–155	140
Potassium (mEq/L)	0–4	2.0
Calcium (mEq/L)	0–3.5	2.5
Bicarbonate (mEq/L)	25–40	35
Glucose (mg/dL)	200	200

PERITONEAL DIALYSIS

In peritoneal dialysis, the exchange of solutes takes place across the peritoneal membrane. It is well tolerated and is an excellent modality option for many patients. Peritoneal dialysis patients often feel that their quality of life is improved over hemodialysis because of the flexibility and control peritoneal dialysis allows. Peritoneal dialysis is the modality used in 91% of patients on dialysis in Mexico, 50% of those in England, 38% of those in Canada, and 10% of those in the United States.[9]

Peritoneal Dialysis Procedure

Peritoneal dialysis is accomplished by using the patient's own peritoneum as a semipermeable membrane through which diffusion and ultrafiltration can occur. A silastic (Tenckhoff) catheter is inserted by a surgeon into the peritoneal cavity and then tunneled

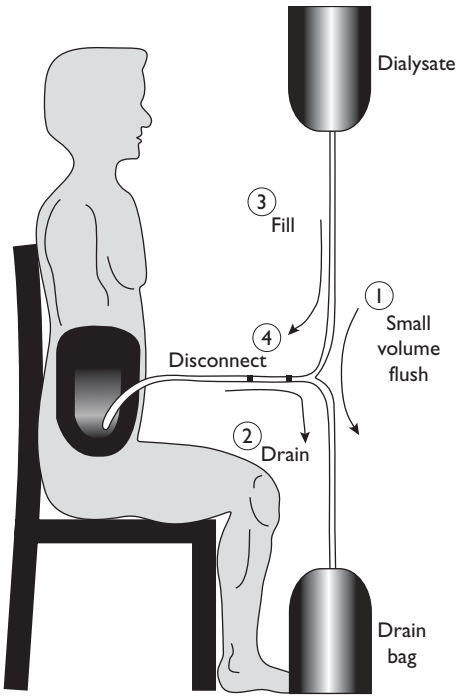

Figure 3. Diagram of continuous ambulatory peritoneal dialysis exchange. After a flush of the tubing with dialysate, residual fluid is drained from the patient's abdomen. New dialysate is then instilled by gravity and dwells for a prescribed period of time. That fluid is subsequently drained, and the cycle continues. (Adapted from Greenberg A, editor. Primer on kidney disease. 2nd ed. San Diego [CA]: Academic Press; 1998:417. Copyright © 1998, with permission from Elsevier.)

beneath the skin to exit on the anterior abdominal wall. It takes approximately 2 weeks for the catheter to heal and become anchored in the subcutaneous tissue. The catheter can then be used without fear of leaking or dislodging.

The basic continuous ambulatory peritoneal dialysis (CAPD) system consists of a bag of dialysis solution, a transfer set that serves as a conduit for fluid, and an indwelling silastic catheter (**Figure 3**). Dialysis solutions for peritoneal dialysis contain physiologic concentrations of sodium, magnesium, and calcium, with lactate usually included as a buffer. Dextrose is added to the dialysate as the primary osmotic agent, and standard solutions of 1.5%, 2.5%, or 4.25% are used to pull fluid into the peritoneal cavity.

In CAPD, solutes and fluid are exchanged between the peritoneal capillary blood supply and the dialysis solution. The blood vessel wall, interstitium, and peritoneal mesothelium make up the semipermeable membrane. A volume of fluid (typically 2 L) is infused through the catheter into the peritoneal cavity and allowed to dwell for a prescribed number of hours (usually 3–4 hours). The volume of fluid varies by patient comfort and body habitus. The number of hours the fluid is allowed to dwell depends on the innate characteristics of the patient's peritoneal membrane to either rapidly or slowly transfer solutes and fluid. Patients on CAPD will typically do 4 to 5 exchanges per day. Often, fluid will dwell longer at night, to allow for more restful sleep. Experienced patients can do an exchange (emptying their belly of the fluid and instilling new fluid) in approximately ½ hour. Fluid that is drained can be emptied down the household drain as it is simply an electrolyte solution and there is no blood involved in this type of dialysis.

Fluid removal is controlled by the type of solution used. Dialysate solutions containing more dextrose generate greater osmotic gradients and remove greater volumes of ultrafiltrate. However, high-dextrose infusions increase the production of advanced glycosylation end products, which cause oxidation and tissue damage. In diabetic patients, higher dextrose–containing solutions can result in increased serum glucose concentrations and poor glycemic control. Over time, this may lead to failure of the peritoneal membrane to adequately transfer solutes and eventually the failure of peritoneal dialysis as a modality option. Dialysis adequacy is measured by combining the clearance from the dialysate and the patient's own residual renal function. Patients collect all the fluid that drains out of their abdomen for a 24-hour period, and the amounts of urea and creatinine are measured and a Kt/V calculated.

Automated peritoneal dialysis (APD) has become an acceptable, and often preferable, alternative to conventional CAPD. Instead of the patient manually exchanging peritoneal dialysis solutions into and out of the abdomen several times daily, a machine is employed. The peritoneal dialysis cycler, which has both a scale and a warmer, rapidly infuses and drains peritoneal fluid, usually at night while the patient is sleeping. The length of time each exchange dwells in the peritoneal cavity is often shorter than for CAPD, but the total volume of fluid infused is much greater. The idea is that the same amount of solute clearance can be accomplished over a shorter period of time while the patient sleeps comfortably. Although each prescription is tailored to an individual patient's needs, most patients are on the cycler for approximately 10 hours. The main disadvantages of APD are the greater cost compared to CAPD and the need to store larger amounts of dialysate in the home. In addition, many patients still need to perform at least 1 daytime exchange in addition to the nocturnal exchanges. However, most

patients prefer APD to CAPD because of the increased freedom during daytime hours.

Peritoneal dialysis is ideal for patients who require more flexibility in scheduling. Children are often treated with peritoneal dialysis because the large extracorporeal blood volume required by the hemodialysis tubing and dialyzers can be hemodynamically prohibitive. Patients with severe cardiovascular disease with a reduced ejection fraction also tend to tolerate the more gentle daily ultrafiltration achieved with peritoneal dialysis. Survival on peritoneal and hemodialysis, although still debated and studied, appears similar for both modalities.

Peritoneal Dialysis Complications

Peritonitis, which occurs an average of once for every 15 to 20 months of dialysis,[10] is the most serious complication of peritoneal dialysis. Patients with peritonitis develop abdominal pain and often note cloudy dialysate effluent. Samples of such dialysate typically demonstrates more than 100 white blood cells/μL, with more than 50% polymorphonuclear cells. The most common organisms are gram-positive bacteria.

Nearly 80% of peritonitis episodes may be managed at home with the addition of antibiotics to the dialysate under the direction of a nephrologist.[11] Fungal peritonitis is devastating and usually requires the removal of the peritoneal catheter and conversion to hemodialysis for several months. Complete abandonment of peritoneal dialysis in favor or hemodialysis is often necessary.

Other complications of peritoneal dialysis include malnutrition from loss of albumin and amino acids in draining dialysate.[12] In addition, patients may need to switch to hemodialysis because of loss of peritoneal membrane function due to infection or advanced glycosylation damage. Patients with diabetes frequently struggle with weight gain and glucose control because of the high volume of dextrose-containing solutions passing through their abdomen.

ACUTE DIALYSIS

Acute dialysis is initiated in the setting of acute renal failure for many of the same signs and symptoms that necessitate the initiation of chronic dialysis (Table 4). These patients are often critically ill with multi-organ failure, but some have isolated kidney disease, which may occur with acute interstitial nephritis, acute tubular necrosis, or a necrotizing glomerulonephritis. For patients who are otherwise stable, intermittent hemodialysis (IHD) 3 to 4 times per week will suffice. This procedure is similar to chronic hemodialysis. The most important difference is that in the acute setting, clinicians need to monitor carefully for signs of renal recovery and stop dialysis when it is no longer needed. Serum creatinine concentration, serum electrolyte levels, urine output, and volume status are all critical to making this decision. For those patients who are critically ill and cannot tolerate IHD, other modalities are available.

Acute Hemodialysis in Critically Ill Patients

Continuous renal replacement therapy (CRRT) modalities are used in critically ill patients unable to tolerate the large fluid shifts and hypotension that frequently accompany IHD. CRRT is now the standard dialytic therapy to achieve acid-base, fluid, and electrolyte balance in hypotensive patients in the intensive care unit. CRRT allows slow and isotonic fluid removal, resulting in excellent hemodynamic tolerance, even in patients with shock or severe fluid overload. In addition, because the therapy is continuous, volume removal and correction of metabolic abnormalities can be modified at any time, allowing for rapid adjustments in critically ill patients.[13] Parenteral nutrition, which often requires a large volume of fluid in catabolic patients, can also be compensated for, allowing for better nutrition without concerns for volume overload.

Several CRRT modalities are currently in use. The most common is continuous venovenous hemodiafiltration, which combines convective and diffusive clearance through a dialyzer with reinfusion of electrolyte-rich solutions. It requires commercially available replacement solutions, a special dialysis machine with volumetric pumps, and scales to control the replacement rate of ultrafiltration. Other modalities include sustained low-efficiency dialysis and extended daily dialysis. All of these modalities require a double-lumen catheter, a blood pump with safety devices similar to those used in IHD, and a dialysis membrane. All forms of CRRT must be performed in an intensive care unit setting with properly trained staff.

The major advantages of CRRT are improved cardiovascular stability, maintenance of cerebral perfusion, and adequate control of volume, electrolytes, and nutrition. Patients with acute renal failure combined with hemodynamic instability, cerebral edema, hypercatabolism, and severe fluid overload stand to benefit the most from this therapy. It is the dialysis modality of choice in patients with liver disease and hepatic encephalopathy.[14]

There are some theoretical advantages to CRRT over IHD. Some nephrologists believe that CRRT may have advantages in renal recovery in patients with acute renal failure. It has been hypothesized that acute renal failure is associated with a loss of renal blood flow

autoregulation, resulting in pressure-dependent renal perfusion.[13] Improved hemodynamic stability achieved with CRRT may lead to more rapid recovery of renal function.[15] There has also been speculation that CRRT may accomplish the extracorporeal removal of inflammatory mediators. However, current data do not support this hypothesis. In 2 controlled clinical trials, concentrations of clinically significant mediators, including tumor necrosis factor and interleukin-6, were not significantly altered in the plasma of patients receiving CRRT.[16,17] Currently, CRRT is not indicated in septic patients independent of renal failure.

The main complications of CRRT include embolization, arteriovenous fistula formation, hemorrhage, and infection from catheter access. Other complications include electrolyte imbalances, hypotension, and air embolism. As with IHD, the optimal dose of CRRT therapy has not been determined. Patients on a continuous dialysis modality should be assessed daily to determine when they will be able to tolerate conventional hemodialysis, and they should be converted over when possible.

Acute Peritoneal Dialysis

Peritoneal dialysis can also be very effective in the intensive care setting. Rapid exchanges (1–2 hr dwell time) with a highly concentrated dextrose dialysate solution can lead to rapid ultrafiltration. It is perhaps best used in patients who already have a catheter in place but also can be performed acutely, provided the patient remains recumbent to minimize intra-abdominal pressures on a newly placed catheter. With the availability of CRRT modalities, peritoneal dialysis in the acute setting has largely fallen out of favor.

THE FUTURE OF RENAL REPLACEMENT THERAPY

Despite all the advances in dialysis technology in the past 4 decades, mortality rates of patients on dialysis remain high. For all persons on dialysis, first-year mortality rates on dialysis are nearly 25%, primarily related to cardiovascular disease.[18] Five-year mortality on dialysis reaches approximately 70%. Survival on dialysis in the United States ranks between that of colon cancer (7 years) and lung cancer (3 years), and there is much room for improvement in the quality and quantity of life.[19]

Advances in dialysis and renal replacement therapy will be led by the further development of microelectronics and molecular biology. Technological advances in miniaturization of dialysis equipment may facilitate daily hemodialysis, which has been shown to be more physiologic than standard hemodialysis and may improve mortality.[20] It is conceivable that a wearable hollow-fiber membrane with a reconstitutable fluid balance system will be developed. Microtechnology developed at Oregon State University is being used to develop a portable dialysis machine, and the company that is developing the machine claims to have reduced the size of a dialysis machine from that of a refrigerator to that of a piece of carry-on luggage.[21] Researchers believe that this technology, known as multiscale materials and devices, could eventually lead to an implantable artificial kidney device. These advances could lead to a more personalized dialysis prescription with the ability to adjust the level of dialysis for the level of patient activity and consumption.

The addition of renal tubular cells to dialyzer membranes to form a bioartificial kidney has met with some success in animal studies.[22] The idea behind the technology, known as a renal tubular assist device (RAD), is that the kidney has evolved to not only eliminate toxins but also to retain certain biologically important constituents that may be lost by conventional filters. In addition, the placement of tubular cells within the dialysis circuit may help modulate metabolic and endocrine functions not adequately replaced by other methods. The ability of the renal tubular cells to metabolize and synthesize critical compounds (cytokines, glutathione, free radical scavenger enzymes, active vitamin D) may have substantial clinical benefits in acute and chronic renal failure. Experimental RADs first used tubular cells extracted from pigs; however, RADs with porcine cells have fallen out of favor due to reports of porcine retroviruses that have been shown to infect human cells in vitro. RADs with human renal tubular cells have begun phase I/II trials in animals with acute renal failure.[23] Further development is needed before these devices can be used clinically.

In the realm of gene therapy, prokaryotic and eukaryotic organisms modified to process urea and perform other tasks for the treatment of uremia are under investigation. Such organisms might be introduced into the gut to create a symbiotic relationship and clear the body of nitrogenous wastes while generating useful substances. Similarly, other organisms might be introduced that carry genes for erythropoietin or vitamin D. This work is far from being practical currently but does give a glimpse of what the future of renal replacement therapy might hold. **HP**

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