Chapter 64: Hemodialysis and Peritoneal Dialysis

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KEY CONCEPTS

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1. Hemodialysis (HD) involves the perfusion of blood and dialysate on opposite sides of a semipermeable membrane. Solutes are removed from the blood by diffusion and convection. Excess plasma water is removed by ultrafiltration.

2. Native arteriovenous (AV) fistulas are the preferred access for HD because of fewer complications and a longer survival rate. Venous catheters are plagued by complications such as infection and thrombosis and often deliver low blood flow rates.

3. Adequacy of HD can be assessed by the *Kt*/*V* and urea reduction ratio (URR). The National Kidney Foundation's Kidney Disease Outcomes Quality Initiative minimum goal *Kt*/*V* is greater than 1.2 per treatment and the URR is greater than 65%.

4. During HD, patients commonly experience hypotension and cramps. Other more serious complications include infection and thrombosis of the vascular access.

5. Peritoneal dialysis (PD) involves the instillation of dialysate into the peritoneal cavity via a permanent peritoneal catheter. The peritoneal membrane lines the highly vascularized abdominal viscera and acts as the semipermeable membrane. Solutes are removed from the blood across the peritoneum via diffusion and ultrafiltration. Excess plasma water is removed via ultrafiltration created by osmotic pressure generated by various dextrose or icodextrin concentrations.

6. Patients on PD are required to instill and drain, manually or via automated systems, several liters of fresh dialysate each day. The more exchanges completed each day results in greater solute removal.

7. Peritonitis is a common complication of PD. Initial empiric therapy for peritonitis should include intraperitoneal antibiotics that are effective against both gram-positive and gram-negative organisms.

8. Nasal carriage of *Staphylococcus aureus* is associated with an increased risk of catheter-related infections and peritonitis. Prophylaxis with a topical antimicrobial agent (mupirocin 2% or polysporin triple ointment) applied to the catheter exit site after each dialysis session can reduce catheter-related infections.

BEYOND THE BOOK

BEYOND THE BOOK

Visit the National Institute of Diabetes and Digestive and Kidney Diseases Website <https://www.niddk.nih.gov/health-information/kidney-disease/kidney-failure>. Review the information provided in the "Hemodialysis" and "Peritoneal Dialysis" links. Watch the video titled "What Is Dialysis?" <https://www.youtube.com/watch?v=mi34xCfmLhw>. The video provides a brief description of hemodialysis and peritoneal dialysis. This Website and video are useful to enhance student understanding of and potential treatments for end-stage kidney disease.

INTRODUCTION

The three primary treatment options for patients with end-stage renal disease (ESRD) are hemodialysis (HD), peritoneal dialysis (PD), and kidney transplantation. The United States Renal Data System (USRDS) is the national system that "collects, analyzes, and distributes" data relating to patients with ESRD or Stage 5 chronic kidney disease (CKD) in the United States and releases these data yearly.[1] According to the 2020 USRDS, at the end of 2018, there were 785,883 patients in the United States with ESRD. Of whom, 62.7% were being treated with in-center HD, 1.6% home HD, 7.6% PD, and nearly 29.7% had a functioning kidney transplant. Each of these represents an increase in the actual number of patients in each treatment modality. In 2018, 131,636 new patients started therapy for ESRD. In 2018, the prevalence of ESRD was 3.4 times greater in Black patients than White patients. In addition, the percentage of Black patients treated with in-center HD is higher in Black people than White people.[1]

Since 1972, the cost of treating ESRD has been covered by Medicare. In 2015, Medicare fee-for-service spending for patients with ESRD was $49.2 billion, which make up approximately 7% of all Medicare claim costs. ESRD consumes a vastly disproportionate amount of resources as only 1% of Medicare patients have the disease. Although total spending for ESRD treatment continues to climb by 2.1% each year, per-patient spending (after adjusting for inflation) increased by only 1.1% in 2018.[1] The prevalence of ESRD continues to climb, reflective of reduced mortality and enhanced patient care. The two primary diagnoses and underlying etiologies of kidney disease for new patients with ESRD are diabetes and hypertension.[1] Chapter 62 provides a thorough discussion on the epidemiology of chronic kidney disease.

This chapter serves as a primer on the principles and practice of dialysis and the complications associated with the delivery of dialysis treatments. HD and PD as the modalities most commonly employed for the management of ESRD (see Chapter 61 for a discussion of the role of renal replacement therapies in the management of acute kidney injury). The pertinent factors that should be considered before the initiation of dialysis are described. The morbidity and mortality associated with HD and PD are compared, as these considerations may influence the dialysis method chosen by patients and clinicians. The variants of HD and PD are detailed, and the multiple types of vascular and peritoneal access used with each (ie, catheters and surgical techniques) are illustrated. The concept of dialysis adequacy for each modality is briefly reviewed. Finally, the clinical presentation of common complications of both dialytic therapies is presented, along with pertinent nonpharmacologic and pharmacologic therapeutic approaches. Information resources that describe the influence of CKD on patient's quality of life, as well as the patient perspective on dialysis and dialysis-related therapies, are presented to highlight the human consequences of chronic disease.

Morbidity and Mortality in Dialysis

Morbidity in patients receiving dialysis can be assessed in a number of different ways including the number of hospitalizations per patient-year, the number of days hospitalized per patient-year, or the incidence of certain complications. The number of all-cause hospital admissions, 1.58 hospitalizations per patient-year, has fallen in recent years from greater than 1.82 hospitalizations per patient-year in 2009. Trends in hospitalization demonstrate an increase in hospitalization as a consequence of infection and cardiovascular disease and a decrease in hospitalizations as a consequence of vascular access problems. Patients with a functioning kidney transplant have a lower rate of hospitalization and shorter length of stay. Hospitalizations are more frequent in women than men, and in White people than Black people, and the frequency and duration increase with age in both dialysis modality groups.[1]

The life expectancy of US dialysis patients is markedly lower than that of healthy subjects of the same age and sex. In dialysis patients older than 75 years, the risk of dying is greater than fourfold higher when compared to all Medicare patients not receiving dialysis.[1] Adjusted all-cause mortality is greater for dialysis patients compared with age-matched individuals. Greater than 50% of deaths in dialysis patients are cardiovascular related. In fact, those with CKD are more likely to die from cardiovascular disease before they reach ESRD. Infections, usually related to the dialysis access, are the

second-most common cause of death in dialysis patients. Although mortality remains high in this patient population, the overall patient mortality rate has fallen among dialysis patients since 2009. The reductions are dependent on treatment type and are smallest for HD and greatest for transplantation. In the United States, only 58% of HD patients and 68% of PD patients are alive 3 years after ESRD diagnosis and initiation of dialysis treatment.[1]

In addition to high morbidity and mortality, a dialysis patient's quality of life is generally poor. For example, restrictions caused by thrice weekly HD and/or associated treatments have been shown to impact many areas of a patient's life. These include, but are not limited to, physical endurance, sex, employment, social life, and diet. Patients often complain of fatigue and fear of the unknown related to their disease and its progression. The PD patient or the home HD patient may have some freedom from these restrictions, but this freedom comes with its own constraints.

Indications for Dialysis

Since first published in 2002, The National Kidney Foundation's Kidney Disease Outcome Quality Initiative (KDOQI) has been the primary treatment guideline for CKD. Although the Kidney Diseases: Improving Global Outcomes (KDIGO) guidelines[2] published in 2013, the updated 2015 version of the KDOQI guidelines serves as the most up-to-date recommendations.[3] Planning for dialysis initiation should occur when a patient's kidney function declines to CKD stage 4 (estimated glomerular filtration rate [eGFR] below 30 mL/min/1.73 m^2).[3] Beginning the preparation process at this point allows adequate time for proper education of the patient and family and for the creation of a suitable vascular or peritoneal access. For patients choosing HD, a permanent arteriovenous (AV) access (preferably a fistula) should be surgically created when eGFR falls below 25 mL/min/1.73 m^2, serum creatinine is greater than 4 mg/dL (354 µmol/L), or 1 year prior to the anticipated need for dialysis.[4] The KDIGO and KDOQI guidelines provide recommendations for referral to a specialist in kidney care services and for planning for RRT. The recommendation for timely referral is for patients with progressive CKD in whom the risk of kidney failure within 1 year is greater than 10% based on validated risk prediction tools.[2]

The KDIGO guidelines and commentaries addressing them agree that the primary criterion for initiation of dialysis is the patient's clinical status, rather than a specific level of kidney function.[2,5] Namely, dialysis should be initiated when one or more of the following are present: signs or symptoms of kidney failure (eg, serositis, acid-base or electrolyte abnormalities, pruritis); inability to control volume status or blood pressure; a progressive deterioration in nutritional status or cognitive impairment. The guidelines suggest that these signs and symptoms are patient specific but tend to be evident once the patient's eGFR is in the range of 5 to 10 mL/min/1.73 m^2. The guidelines specifically indicate that RRT should be initiated to manage signs and symptoms and not to treat an arbitrary kidney function measurement.[2] The advantages and disadvantages of HD and PD are depicted in Tables 64-1 and 64-2, respectively. These factors, along with the patients' concomitant diseases, personal preferences, and support environments, are the principal determinants of the dialysis mode they will receive. The timing of dialysis initiation is a compromise between maximizing patient quality of life by extending the dialysis-free period while avoiding complications that will decrease the length and quality of dialysis-assisted life.[3]

TABLE 64-1

Advantages and Disadvantages of Hemodialysis

Advantages

1. Higher solute clearance allows intermittent treatment.
2. Parameters of adequacy of dialysis are better defined and therefore underdialysis can be detected early.
3. Technique failure rate is low.
4. Even though intermittent heparinization is required, hemostasis parameters are better corrected with hemodialysis than peritoneal dialysis.
5. In-center hemodialysis enables closer monitoring of the patient.

Disadvantages

1. In-center hemodialysis requires multiple visits each week to the hemodialysis center, which translates into loss of patient independence.
2. Disequilibrium, dialysis-induced hypotension, and muscle cramps are common. May require months before the patient adjusts to hemodialysis.
3. Infections in hemodialysis patients may be related to the choice of membranes, the complement-activating membranes being more deleterious.
4. Vascular access is frequently associated with infection and thrombosis.
5. Decline of residual kidney function is more rapid compared to peritoneal dialysis.

TABLE 64-2

Advantages and Disadvantages of Peritoneal Dialysis

Advantages

1. Hemodynamic stability due to slow ultrafiltration rate.
2. Higher clearance of larger solutes, which may explain good clinical status in spite of lower urea clearance.
3. Better preservation of residual kidney function.
4. Convenient intraperitoneal route for administration of drugs such as antibiotics and insulin.
5. Suitable for elderly and young patients who may not tolerate hemodialysis well.
6. Freedom from the “machine” gives the patient a sense of independence (for continuous ambulatory peritoneal dialysis).
7. Less blood loss and iron deficiency, resulting in easier management of anemia or reduced requirements for erythropoietin and parenteral iron.
8. No systemic heparinization required.
9. Subcutaneous versus intravenous erythropoietin or darbepoetin may reduce overall doses and be more physiologic.

Disadvantages

1. Protein and amino acid losses through peritoneum and reduced appetite from continuous glucose load and sense of abdominal fullness predispose patients to malnutrition.
2. Risk of peritonitis.
3. Catheter malfunction, and exit-site and tunnel infection.
4. Inadequate ultrafiltration and solute clearance in patients with a large body size, unless large volumes and frequent exchanges are employed.
5. Patient burnout and high rate of technique failure.
6. Risk of obesity with excessive glucose absorption.
7. Mechanical problems such as hernias, dialysate leaks, hemorrhoids, or back pain are more common than HD.
8. Extensive abdominal surgery may preclude peritoneal dialysis.
9. No convenient access for intravenous iron administration.

There is considerable debate in the literature regarding the mortality differences between HD and PD.[6-8] Most observational trials suggest that PD is

associated with a survival advantage early in therapy, which wanes with increased treatment time. Prospective trials have reported conflicting results relative to efficacy of one modality over another. If there is a survival advantage for PD, the consensus is that the advantage is early in therapy and may not with continued therapy. Well-designed studies are extremely difficult to conduct in this population, and thus the question of superiority of one modality over the other is controversial and continues to be debated. Differences in outcomes may be related to a wide array of confounding factors, such as the dose of dialysis, baseline patient health status, physician bias in modality selection, patient compliance with dialysis and medication therapy, or other unknown factors. For example, healthier patients tend to be directed toward PD, and factors such as age, duration of dialysis, and comorbidities play an important role in the complex relationship between patient outcomes and mortality. Without clear distinction between modalities in terms of many important outcomes, the selection of the optimal therapy for a given patient is challenging. The selection of one modality over the other should be based upon patient motivation, desire, geographic distance from an HD unit, healthcare team preference, and patient education rather than survival advantages alone.

HEMODIALYSIS

Although HD was first successfully used in 1940, the procedure was not used widely until the Korean War in 1952. Permanent dialysis access was developed in the 1960s, which allowed routine use of HD in patients with ESRD. Subsequent decades brought advances in dialysis technology, including the introduction of more efficient and biocompatible dialyzer membranes and safer techniques. HD is the most common type of renal replacement therapy for patients with ESRD.

Principles of Hemodialysis

1 Hemodialysis consists of the perfusion of blood and a physiologic solution on opposite sides of a semipermeable membrane. Multiple substances, such as water, urea, creatinine, potassium, uremic toxins, and drugs, move from the blood into the dialysate, by either passive diffusion or convection as the result of ultrafiltration. Diffusion is the movement of substances down a concentration gradient. The rate of diffusion depends on the difference between the concentration of the solute in blood and dialysate, solute characteristics, that is, size, water solubility, and charge, the dialyzer membrane composition, and blood and dialysate flow rates. Diffusive transport is rapid for small solutes but decreases with increasing molecular size. Other important diffusive solute transport factors include the membrane thickness, porosity, and the steric hindrance between the membrane pores and solute. Ultrafiltration is the movement of water across the dialyzer membrane because of hydrostatic or osmotic pressure and is the primary means for removal of excess fluid. Convection occurs when dissolved solutes move across a membrane with water transport. This occurs only if the pores in the dialyzer are large enough to allow them to pass along with water. Convection can be maximized by increasing the hydrostatic pressure gradient across the dialysis membrane or by using a dialyzer that is more permeable to water transport. Diffusion and convection can be controlled independently, and thus, a patient's HD prescription can be individualized to attain the desired degree of solute and fluid removal.[9]

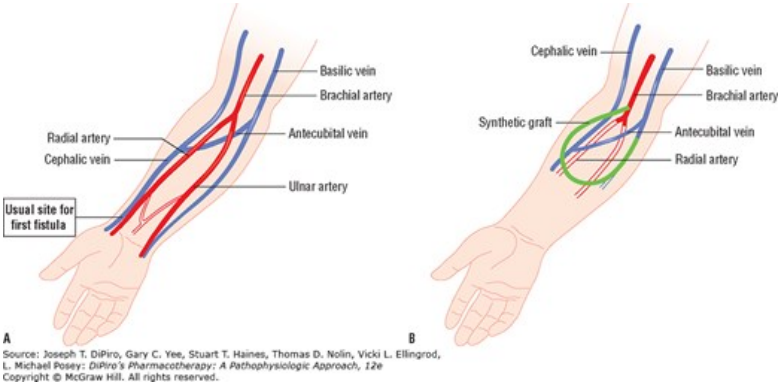
Hemodialysis Access

2 Obtaining and maintaining access to the circulation has been a challenge for long-term use and success of HD. Permanent access to the circulation may be accomplished by several techniques, including the creation of an AV fistula, an AV graft, or by venous catheters (Fig. 64-1).[10] As shown in Fig. 64-1, the native AV fistula is created by the anastomosis of a vein and artery (ie, the radial artery to the cephalic vein or the brachial artery to the cephalic vein). The native AV fistula has many advantages including providing the longest survival time of all blood-access devices and the lowest rate of complications such as infection and thrombosis. Patients with fistulas have increased survival and lower hospitalization rates compared to other HD patients. Finally, AV fistulas are the most cost-effective in terms of placement and long-term maintenance. Ideally, the most distal site (the wrist) is used to construct the first fistula; it is the easiest to create, and in the case of access failure, more proximal sites on the arm are preserved for later use. Unfortunately, fistulas require at least 1 to 2 months to mature before they can be routinely utilized for dialysis. Creation of an AV fistula, however, may be difficult in elderly patients and in patients with peripheral vascular disease, which is a particularly common comorbidity in patients with diabetes.

FIGURE 64-1

The predominant types of vascular access for chronic dialysis patients are (*A*) the arteriovenous fistula and (*B*) the synthetic arteriovenous forearm graft. The first primary arteriovenous fistula is usually created by the surgical anastomosis of the cephalic vein with the radial artery. The flow of blood from the higher-pressure arterial system results in hypertrophy of the vein. The most common AV graft (depicted in green) is between the brachial artery and the basilic or cephalic vein. The flow of blood may be diminished in the radial and ulnar arteries since it preferentially flows into the low-

pressure graft.



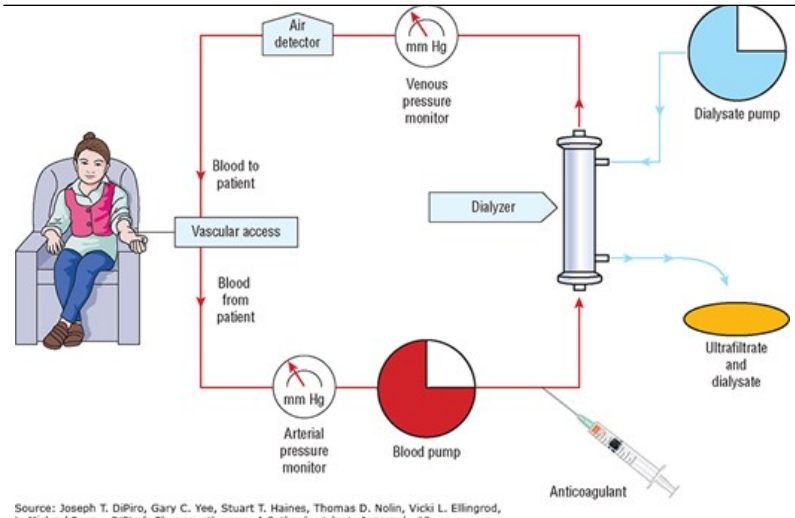
Synthetic AV grafts, usually made of polytetrafluoroethylene, are another permanent AV access option. These grafts require 2 to 3 weeks before they can be routinely used. Their primary disadvantages are shorter survival of the graft, and higher rates of infection and thrombosis. The least-desirable and least permanent HD access option involves the placement of a central venous catheter. Venous catheters can be placed in the femoral, subclavian, or internal jugular veins. Their main advantage is that they can be used immediately, and they are often used in small children, diabetic patients with severe vascular disease, the morbidly obese, and patients who have no viable sites for permanent AV access. Late referrals to a nephrology specialist for HD initiation and delayed placement of a more appropriate long-term access contribute to the use of venous catheters in chronic HD patients. The major problem with all venous catheters is that they have shorter survival and are more prone to infection and thrombosis than either AV grafts or fistulas. Furthermore, some catheters are not able to provide adequate blood flow rates, which may limit the deliverable dose of dialysis.[10,11] Regardless, tunneled dialysis catheters are used frequently because of the ease of insertion, pain-free dialysis needle placement and availability for immediate use. They are, however, associated with increased morbidity, mortality, and cost.

Hemodialysis Procedures

The HD system consists of an external vascular circuit through which the patient's blood is transferred in sterile tubing to the dialyzer via a mechanical pump (Fig. 64-2).[10] The patient's blood then passes through the dialyzer on one side of the semipermeable membrane and is returned to the patient. The dialysate solution, which consists of purified water and electrolytes, is pumped through the dialyzer countercurrent to the flow of blood on the opposite side of the semipermeable membrane. In most cases, systemic anticoagulation (usually unfractionated heparin in the United States) is used to prevent blood clotting in the HD circuit tubing. The process of dialysis results in the removal of metabolic waste products, medications, and water and replenishment of body buffers, such as acetate and bicarbonate.

FIGURE 64-2

In hemodialysis, the patient's blood is pumped to the dialyzer at a rate of 300 to 600 mL/min. An anticoagulant is administered to prevent clotting in the dialyzer. The dialysate is pumped at a rate of 500 to 800 mL/min through the dialyzer countercurrent to the flow of blood. The rate of fluid removal from the patient is controlled by adjusting the pressure in the dialysate compartment.



Hemodiafiltration (HDF), another variant of traditional HD, enhances convective solute and water transport in addition to diffusive clearance to a much greater extent than high-flux HD.[10,12,13] When fluid losses exceed those desired for the patient, an IV infusion referred to as replacement fluid may be administered. HDF may improve outcomes due to its ability to remove middle molecular weight uremic solutes more efficiently than the other HD variants. HDF improves survival compared to conventional HD.[13,14] Preliminary information suggests that HDF enhances clearance of phosphate, beta-2 microglobulin, and pro-inflammatory solutes. This procedure is not used extensively in the United States. Barriers to its use are the high cost and logistic issues associated with providing the fluid replacement needs.

Dialyzers are made up of a polyurethane container containing hollow fibers which are suspended in dialysate. These hollow fibers, or dialysis membranes, are made up of three substances, unmodified cellulose (cuprophan), substituted cellulose (cellulose acetate), and cellulosynthetic materials. The permeability of these membranes varies and the membranes are divided into three general types: low flux, high efficiency, and high flux. Low-flux and high-efficiency membranes have small pores that limit clearance to relatively small molecules (size less than or equal to 500 daltons) such as urea and creatinine and are utilized for less than 20% of chronic HD procedures.[10] High-flux membranes are now used in the vast majority of patients because they are capable of removing high-molecular-weight endogenous substances, such as β2-microglobulin, and medications such as vancomycin.[10] The primary reason for using high-flux membranes is that clearance of water as well as low- and high-molecular-weight substances is much greater, allowing for shorter treatment times. To maximize the clearance capacity of high-flux dialyzers, the blood flow rates should be 400 to 600 mL/min, and dialysate flow rates greater than 500 mL/min, which necessitates strict controls and active monitoring of the rate of fluid removal. Typically, these dialyzers are composed of polysulfone, polymethylmethacrylate, polyamide, cellulose triacetate, and polyacrylonitrile.[10]

HD is usually prescribed as three sessions per week for 3 to 5 hours/session. These sessions are usually performed in “in-center” dialysis units. This is a large time commitment for any patient undergoing HD and results in substantial loss of control over their life. Several alternatives to this type of HD have been explored in an effort to balance dialysis adequacy with patient outcomes and quality of life. These alternatives include procedures that increase dialysis frequency, enhance dialysis duration, or both.[15-18] Examples are as follows: (1) frequent HD (5-7 sessions/week), which can be frequent short (less than 3 hours/session), frequent standard (3-5 hours/session), or frequent long sessions (longer than 5 hours/session); (2) long HD (more than 5 hours/session given 3-7 times/week, which can be long thrice weekly (administered either at night or during the day), long every other night (administered at night), and long frequent (administered at night 5-7 nights/week). Many of these alternatives are suggested to be associated with improved survival.[16-18] For example, in-center, thrice weekly HD was associated with a higher risk of the composite outcome of death, left-ventricular mass, and change in health composite score than in-center six times per week HD.[19] Intensive dialysis has been associated with reductions in left-ventricular mass and improved blood pressure control, both surrogates for improved cardiovascular outcomes, and improved phosphate removal. Lastly, and perhaps most importantly, these procedures are associated with a reduction in dialysis-related symptoms and improved quality of life.[16-18] Despite the perceived advantages and more frequent use in other countries such as New Zealand and Canada, the use of home HD is uncommon, albeit increasing in use in the United States, still less than 2% of dialysis patients receiving HD care at home at the end of 2018.[1] Potential obstacles to home HD include patient factors (eg, lack of self-efficacy, fear of self-cannulation, fear of catastrophic event, and fear of lack of quality care) and a lack of awareness of the availability of this type of dialysis. Finally, there are suggestions that patients receiving intensive dialysis may be at

higher risk of access infections and need for vascular access procedures. Further clinical trials are needed to elucidate the role of these types of dialysis therapy. The 2015 KDOQI guidelines provide suggestions and/or recommendations that all patients be offered short frequent HD as an alternative to standard HD in addition to providing patients with information about the potential risk associated with them.[3]

Adequacy of Hemodialysis

The optimal dose of HD, the patient's dialysis prescription, is that amount of therapy above which there is no cost-effective increment in the patient's quality-adjusted life expectancy. The two primary goals of the dialysis prescription are to achieve the patient's dry weight and the adequate removal of endogenous waste products such as urea. Dry weight is the target post-dialysis weight at which the patient is normotensive and free of edema. Measurement of urea removal, while imperfect, is the typical method used to quantify dialysis adequacy. Urea removal reflects the "delivered dose" of dialysis and is utilized as the surrogate for removal of other toxins.

The delivered or desired dose of dialysis in terms of solute removal can be expressed as the urea reduction ratio (URR) or the *Kt/V* (pronounced "K-T-over-V"). The URR is a simple concept and is easily calculated as follows:

$$\text{URR} = \frac{\text{Predialysis BUN} - \text{Postdialysis BUN}}{\text{Predialysis BUN}} \times 100.$$ URR=Predialysis BUN−Postdialysis BUNPredialysis BUN×100.

The URR is frequently used to measure the delivered dialysis dose; however, it does not account for the contribution of convective removal of urea. The *Kt/V* is a unitless index based on the dialyzer clearance of urea (*K*) in L/h multiplied by the duration of dialysis (*t*) in hours, divided by the urea distribution volume of the patient (*V*) in liters.[10] The *Kt/V* is thus the fraction of the patient's total body water that is cleared of urea during a dialysis session. Urea kinetic modeling, using computer software, is the optimal means to calculate the *Kt/V*.[10] An in-depth discussion of the pros and cons of various methods of calculating and interpreting *Kt/V* is beyond the scope of this chapter. The reader is referred to other sources for more in-depth information.[10]

3 For patients who receive thrice weekly HD, KDOQI recommends that the minimally adequate delivered dose of dialysis is a *Kt/V* of 1.2 (equivalent to an average URR of 65%).[3] To achieve this goal, the recommended target prescribed *Kt/V* is 1.4 (equivalent to an average URR of 70%).[3] For patients who receive HD on a schedule other than thrice weekly, the KDOQI suggests a target standard *Kt/V* of 2.3 volumes/week with a minimum delivered dose of 2.1. Lower doses of dialysis treatment are thought to be associated with increased morbidity and mortality. Many nephrologists believe that even greater doses of dialysis would have positive outcomes in dialysis patients, and so the average dose of dialysis has been increasing in the United States although the evidence for this is not strong. The results of HEMO study, a prospective, randomized trial that assigned patients to either standard (*Kt/V* = 1.25) or high-dose (*Kt/V* = 1.65) dialysis with high-flux or low-flux membranes, revealed that the risk of death was similar in both the standard and high-dose therapy and the low- and high-flux groups. Thus, there is no benefit in increasing the dose of dialysis above the current recommendations. The HEMO study only enrolled patients who were on traditional thrice-weekly dialysis, so the applicability of these findings to patients on more intensive regimens such as daily or nocturnal HD regimens remains to be determined. However, intensive HD regimens may result in better control of blood pressure, anemia, phosphate, and sleep apnea.[15] In those relatively few patients who are below the adequacy goal, the deficiency may be related to patient compliance with the dialysis prescription (ie, ending dialysis early) or low blood flow rates caused by access stenosis or thrombosis, or due to the use of catheters. Adequate dialysis may not be achieved in some patients despite compliance and sufficient blood flow. For these patients, there are two options to increase urea clearance: use a larger membrane or increase the treatment time.

Complications of Hemodialysis

4 HD is a life-extending therapy for patients with kidney failure but HD is associated with short- and long-term complications. Complications associated with HD can decrease the efffectiveness of therapy, quality of life and life expectancy. This chapter discusses complications that occur during an HD session (intradialytic) and complications associated with vascular access.

Hemodialysis Procedure Complications

The most common complications that occur during HD include hypotension, hypertension, cramps, nausea and vomiting, headache, chest pain, back pain, and fever or chills.[20] Table 64-3 lists these complications and their etiology and predisposing factors.

TABLE 64-3

Common Complications During Hemodialysis

	Incidence (%)	Etiology/Predisposing Factors
Hypotension	20-30	Hypovolemia and excessive ultrafiltration
		Antihypertensive medications prior to dialysis
		Target dry weight too low
		Diastolic dysfunction
		Autonomic dysfunction
		Low calcium and sodium in dialysate
		High dialysate temperature
		Meal ingestion prior to or during dialysis
Hypertension	5-15	Plasma sodium concentration
		Intravascular volume
		Dialytic removal of antihypertensive medications
		Activation of the Renin Angiotensin Aldosterone system
Cramps	5-20	Muscle hypoperfusion due to ultrafiltration and hypovolemia
		Hypotension
		Electrolyte imbalance
		Acid–base imbalance
Nausea and vomiting	5-15	Hypotension
		Dialyzer reaction
Headache	5	Disequilibrium syndrome
		Caffeine withdrawal due to dialysis removal
Chest and back pain	2-5	Unknown
Pruritus	5	Inadequate dialysis
		Skin dryness
		Secondary hyperparathyroidism

		Abnormal skin concentrations of electrolytes
		Histamine release
		Mast cell proliferation
Fever and chills	<1	Endotoxin release; infection of dialysis catheter

Data from Reference 10.

Intradialytic hypotension (IDH) as defined by the National Kidney Foundation Kidney Disease Outcomes Quality Initiative (NKF KDOQI) is a decrease in systolic blood pressure by ≥20 mm Hg or a decrease in mean arterial pressure (MAP) by 10 mm Hg. A patient with IDH may experience abdominal discomfort, yawning, sighing, nausea, vomiting, muscle cramps, restlessness, dizziness or fainting, and anxiety. A decrease in BP can increase the risk of vascular access thrombosis, induce a cardiac arrhythmia, or predispose a patient to a coronary or cerebral ischemic event. Hypotension during HD can decrease the effectiveness of a dialysis session resulting in a lower Kt/V_{urea}.[21] A systolic blood pressure <90 mm Hg has been associated with increased mortality.[22]

A primary cause of IDH is related to the rate and amount of fluid removed during[10,23] typical HD treatments, although other causes, as listed in Table 64-4, may also play a role.[10,23] Symptoms such as nausea and cramping are often present during acute hypotensive episodes. The replacement of acetate with bicarbonate as the dialysate buffer, the use of volumetric ultrafiltration controllers, and individualized or modeled dialysate sodium concentrations have helped reduce the incidence of IDH. Sodium modeling uses a higher initial dialysate sodium concentration (145-155 mmol/L [mEq/L]) and tapers sodium concentration down (135-140 mmol/L [mEq/L]) over the dialytic session. Dialytic treatment modifications such as sodium individualization or modeling may decrease post-HD thirst and subsequent intradialytic weight gain. This modification may decrease the need for aggressive dialytic fluid removal and the incidence of IDH.[24-26]

TABLE 64-4

Management of Hypotension

Acute treatment	Place patient in Trendelenburg position
	Decrease ultrafiltration rate
	Give 100-200 mL bolus of normal saline intravenous
	Give 10-20 mL of hypertonic saline (23.4%) intravenous over 3-5 minutes
	Give 12.5 g mannitol
Prevention	
Nonpharmacologic	Accurately set “dry weight”
	Use steady constant ultrafiltration rate
	Keep dialysate sodium >serum sodium
	Lower dialysate temperatures
	Bicarbonate dialysate
	Avoid food before or during hemodialysis
Pharmacologic	Midodrine 2.5-10 mg orally 30 minutes before hemodialysis (start at 2.5 mg and titrate)
	Droxidopa 100-600 mg orally 1 hour before hemodialysis (start at 100 mg and titrate up to 600 mg)
	Other options (limited evidence):
	Levocarnitine 20 mg/kg IV after hemodialysis
	Sertraline 50-100 mg daily
	Fludrocortisone 0.1 mg before hemodialysis
	DDAVP 1-2 intranasal sprays (150 µg/spray)
Counsel patients	Administer antihypertensive medications in the evening or after hemodialysis
	Minimize intradialytic weight gain by decreasing salt content in their diet

Intradialytic or post-HD hypertension can occur in 5% to 15% of patients receiving HD and may increase post-HD fatigue and the risk of cardiovascular and all-cause mortality.[27] Underlying causes include, not achieving post-HD dry weight goal, over-estimation of dry weight, dialytic removal of antihypertensive medications, or the activation of the renin-angiotensin system secondary to abrupt hypovolemia.[28]

Skeletal muscle cramps complicate 5% to 20% of HD treatments. Although the pathogenesis of cramps is multifactorial, plasma volume contraction

and decreased muscle perfusion caused by excessive ultrafiltration are frequently the initiating events.[10] Pruritus may increase in severity during the HD treatment and is a complication of CKD. The management of pruritus is discussed in Chapter 63.

Vascular Access Complications

The most common vascular access complications in patients receiving HD are thrombosis and infection. The highest occurrence of complications is found in patients with a central venous catheter (CVC) compared with those with an AV graft or AV fistula.[10,29] A majority of patients initiate HD with a CVC (80.8%), and of those patients 65.2% did so without a maturing AV fistula or graft. In prevalent patients receiving HD, 82.4% had either an AV fistula or graft.[1] The maintenance of vascular access patency is critical for patients receiving HD. Predisposing factors are often described using Virchow's triad of blood flow stasis, hypercoagulability, and endothelial injury. An aneurysm or stenosis of an AV fistula, graft or surrounding vasculature generally require a surgical intervention. Several pharmacologic therapies have been evaluated to maintain vascular access patency but results are conflicting.[30] Vascular access stenosis can contribute to decreases in blood flow (blood flow <300 mL/min) and increase the risk of thrombus formation within the access. A decrease in blood flow through the access can occur abruptly, or over days to weeks or intermittently and may require ultrasound, venography, or computed tomography scans for a definitive diagnosis.[29,30] Catheter-related thrombosis can form either inside (intrinsic) or outside (extrinsic) the catheter. An occlusion can form within the lumen, at the tip or develop a fibrin sleeve around the catheter where this fibrin sleeve can serve as a nidus for infection and ultimately require catheter removal.[31,32]

Infection is a leading cause of mortality in HD patients.[1] The risk of sepsis-related death is 100 times greater in patients receiving HD than the general population, and those with an indwelling catheter have the highest risk.[32] A comparison of patients receiving HD with a catheter compared to those without a catheter found a higher rate of bloodstream infections in patients with a catheter.[33] An examination of the United States Renal Data System identified patients initiating HD with a central venous catheter (CVC), AV fistula or graft from 2006 through 2014 who developed sepsis. The highest rate of sepsis was found in patients with a CVC (31.2%) followed by an AV graft (30.6%) and an AV fistula (22.9%, $P < 0.001$).[34]

The National Healthcare Safety Network (NHSN) dialysis event surveillance report found that 69.8% of access-related blood stream infections (ARBSIs) were in patients with an indwelling CVC.[35] The most prevalent pathogens for blood stream infections (BSIs) were gram-positive (64%) followed by gram-negative (35%) and Candida species (0.2%). The most frequently isolated micro-organisms in ARBSIs were as follows: *S. aureus* (31.8%), *S. epidermidis* (15.6%), coagulase-negative staphylococcus (9.7%), *E. faecalis* (4.9%), and *E. coli* (2.9%). The incidence with methicillin-resistant *S. aureus* (39.5%) and cephalosporin-resistant *E. coli* (17.8%) organisms were highest in patients with a CVC.[35]

Catheter-related infections can develop at the insertion site, hub, or both. The infection source for long-term catheters such as a tunneled cuffed catheter is usually the hub where bacteria can enter the blood leading to a BSI.[29,32] Overall, HD access with a catheter is associated with higher rates of bacteremia, osteomyelitis, septic arthritis, endocarditis, thrombus, and death, as well as increased treatment costs compared with an AV fistula or AV graft.[36]

Complications of CKD

Patients receiving HD are likely to have at least one additional comorbid disease such as diabetes, hypertension, cardiovascular disease, or obesity (BMI greater than or equal to 30 kg/m^2) and older age (greater than or equal to 60). The pharmacotherapy management of most CKD complications and comorbid diseases that persist in patients receiving HD are discussed in Chapter 63. The daily medication burden for HD patients is one of the highest for any chronic disease state. The pill burden in HD patients was reported as an average of 15.1 ± 7.6 pills/day of which phosphate binder medications accounted for 6.44 ± 4.78 pills/day.[37] Adherence to phosphate binder regimens is reported to be 43% in US patients receiving dialysis. Patients taking more than the average pills/day of phosphorus binders were more likely to miss a dose than patients taking less than the average pills/day. The increased pill burden is associated with a lower quality of life in patients receiving dialysis.[38]

Management of Hemodialysis Complications

The management of HD complications is discussed in this section. The most common causes of HD complications and appropriate management are reviewed.

Hypotension

Acute management of intradialytic hypotension (IDH) includes decreasing the ultrafiltration rate or stopping ultrafiltration, placing the patient in the Trendelenburg position, lowering the dialysate temperature, modifying dialysate electrolyte concentrations, and/or administering normal or hypertonic saline.[23,39,40] IDH may not occur during each HD session and a patient's response to therapeutic modifications can be variable, which could necessitate modification of their HD prescription. Patients with IDH will need a careful review of all medications including antihypertensive medications. Evaluation should consider the timing of antihypertensive medication administration and may require adjustments to medications administered the day prior to and the day of HD therapy.[23] Patients with IDH should be counseled to take their blood pressure medications after HD and avoid the consumption of food during HD.

IDH is often due to an insufficient cardiac response to reduced circulating blood volume, which may occur when aggressive ultrafiltration is required to restore dry weight. Most treatments for IDH are directed toward restoring or maintaining adequate blood vessel perfusion in these patients. One approach is to limit interdialytic weight gain (IDWG) that may decrease the rate and volume of fluid removal during HD. Patients are counseled to limit dietary salt intake especially hidden sodium in processed foods. A reduction in dietary sodium could decrease a patient's thirst and subsequent fluid intake.[10] Another approach, decreasing the dialysate temperature to 36.5°C (97.7°F), may help reduce core body temperature, which can decrease vasodilation.[30,41] If nonpharmacologic interventions are not adequate to prevent or reduce the incidence of symptomatic IDH, then pharmacologic interventions should be considered (see Table 64-4).

Oral midodrine (5-10 mg) given two to three times daily can increase blood pressure in patients receiving HD with chronic hypotension. Midodrine, an alpha-1 adrenergic agonist, can also be administered 30 minutes prior to initiating HD to increase intradialytic blood pressure. It is rapidly absorbed in the gastrointestinal tract and will begin to increase blood pressure within 60 minutes. Midodrine's half-life during HD can be less than 2 hours but on nondialysis days it is approximately 10 hours. HD will remove the prodrug and metabolite of midodrine which contributes to the drug's decreased half-life during HD. It is important to note that the effects of midodrine are probably best in patients with hypotension related to autonomic dysfunction. Patients with peripheral vascular disease should be monitored for digital or lower limb ischemia.[42]

Droxidopa is an oral synthetic amino acid analog metabolized by the catecholamine pathway to norepinephrine, resulting in vasoconstriction of peripheral veins and arteries. Droxidopa is FDA-approved for neurogenic orthostatic hypotension. Droxidopa was studied in patients with a history of IDH that were randomized to receive droxidopa 400 mg, 600 mg, or placebo 1 hour prior to HD. The patients receiving droxidopa when compared to placebo had a lower rate of early HD termination due to IDH. Gastrointestinal disorders were the most frequent adverse effect reported in the treatment groups.[43]

Fludrocortisone is a potential agent for symptomatic IDH, including patients with an inadequate response to midodrine. It increases blood pressure through several mechanisms including enhancing blood vessel sensitivity to circulating catecholamines. Fludrocortisone dosing for orthostatic hypotension generally ranges from 0.1 mg to 1.0 mg/day but IDH dosing has not been determined. A case report described a patient receiving HD with IDH and a decreased response to midodrine that resulted in early termination of HD sessions. Fludrocortisone 0.2 mg was administered with 10 mg of midodrine 30 minutes prior to the start of HD. Prior to initiating fludrocortisone, 6 out of 45 HD sessions were terminated early but after fludrocortisone initiation, no HD sessions were terminated early in the subsequent 45 HD sessions.[44] The use of fludrocortisone may be beneficial in select patients with IDH but adverse effects such as sodium and water retention could increase edema in patients with congestive heart failure.

The treatment of IDH with levocarnitine, sertraline, and intranasal desmopressin acetate (DDAVP) have been reported to improve IDH. Administration of levocarnitine (20 mg/kg IV at the end of each HD session) may reduce hypotensive episodes, particularly in patients with carnitine deficiency.[45] High cost and limited efficacy precludes a strong recommendation for routine levocarnitine use. The administration of sertraline 50 mg daily titrated to 100 mg daily after 1 week improved systolic and diastolic blood pressure in a small trial.[46] Sertraline 50 mg was administered daily to patients receiving HD, but sertraline did not increase in post-HD blood pressure.[47] The mixed results do not support routine sertraline administration for hypotension. Overall, the use of DDAVP increased post-HD blood pressure and decreased the incidence of IDH.[48] These medications have limited clinical evidence and should be used with caution in patients receiving HD with IDH. Overall, the best evidence for an oral pharmacological treatment of IDH is with midodrine. Alternative agents have been studied but the evidence is limited for each of these agents as many of the studies had a small sample size and did not have a placebo control.

Hypertension

An elevated blood pressure in a patient prior to receiving HD is often attributed to volume expansion. A decline in blood pressure is expected during and after HD and improves survival, but a dramatic increase or decrease in blood pressure during or after HD decreases overall survival.[49] An increase in blood pressure of >10 mm Hg either during or post-HD may require a change in the delivery of an HD session, antihypertensive medications or adjustments to the timing of medication administration.[28] Although the underlying mechanism may be multifactorial, antihypertensive medication dialyzability could play a role in HD-related increases in blood pressure.[50] HD enhances the clearance of metoprolol, atenolol, and angiotensin-converting enzyme inhibitors (ACE-Is). An angiotensin receptor blocker (ARB), carvedilol or amlodipine is minimally removed during HD and may be an option in patients experiencing a rise in blood pressure during or post-HD. Antihypertensive medication regimes need to be individualized based on a patient's comorbid conditions and risk of HD-related blood pressure changes. A retrospective cohort examined patients with heart failure receiving HD and either taking a daily beta-blocker (carvedilol, bisoprolol, or metoprolol CR/XL) or those patients not taking a daily beta-blocker. Patients receiving either carvedilol, bisoprolol, or metoprolol had lower all-cause mortality at 5 years.[51] However, in patients at risk of IDH, a large retrospective study found an increased rate of IDH and risk of all-cause mortality in patients taking carvedilol compared to metoprolol.[52] Initiation of any antihypertensive medication in patients at high-risk should be followed with close monitoring pre- and post-HD in addition to during HD. One small study found an improvement in patients with intradialytic hypertension when low-dose carvedilol (6.25 mg twice daily) was initiated and titrated as tolerated.

Muscle Cramps

The cause of muscle cramps in patient receiving HD may be multi-factorial and include aggressive removal of fluid and electrolyte imbalances. Nonpharmacologic interventions related to dialytic therapy may help alleviate muscle cramps. These measures include adjusting the ultrafiltration rate to avoid hypotension, volume contraction, or hypoosmolality. Other methods to reduce muscle cramps, including compression devices, moist heat, massage, exercise, stretching, or muscle flexing, should be considered first to minimize adverse consequences (Table 64-5).[10,23]

TABLE 64-5

Management of Cramps

Acute treatment	Give 100-200 mL bolus of intravenous normal saline
	Give 10-20 mL of intravenous hypertonic saline (23.4%) over 3-5 minutes
	Give 50 mL of 50% intravenous glucose (nondiabetic patients)
Prevention	
Nonpharmacologic	Accurately set "dry weight"
	Keep dialysate sodium >serum sodium
	Stretching exercises, massage, flexing, or compression devices
Pharmacologic	Vitamin E 400 international units at bedtime
	Quinine sulfate 324 mg daily (second-line therapy)

Pharmacologic interventions include increasing the magnesium concentration in dialysate, supplementation with oral magnesium, vitamin E, or vitamin C or a trial of gabapentin or quinine. Vitamin E and quinine can reduce the incidence of muscle cramps.[53,54] Quinine is associated with temporary sight and hearing disturbances, thrombocytopenia, or gastrointestinal distress. Quinine is FDA-approved for malaria only and the FDA has warned against the off-label use of quinine for muscle cramps.[55]

In a small prospective study of patients receiving HD with at least six episodes of intradialytic muscle cramps in the 30 days prior to enrollment, patients received either placebo or gabapentin 300 mg three times a week administered 5 minutes prior to HD. After 1 month, patients experienced less episodes of muscle cramps in the treatment arm.[56] Both vitamin E (400 mg) and vitamin C (250 mg) reduced the frequency of cramps in patients receiving dialysis.[57] The combination of these two drugs had an additive effect. Although these data further strengthen the case for vitamin E and vitamin C, long-term therapy must be used with caution. Doses of vitamin E greater than 400 U/day have been reported to increase mortality and high doses of vitamin C increase the risk of oxalate accumulation and developing oxalosis. Pharmacologic interventions to diminish muscle cramps are limited and vitamin E has the strongest evidence-based efficacy and safety profile.

Vascular Access Thrombosis

Vascular access patency is key to maintaining effective dialytic therapy for patients receiving HD. Multiple pharmacologic agents have been studied including oral and intravenous anticoagulant and antiplatelet agents and intravenous thrombolytic agents to assess their clinical value.

The efficacy of oral antiplatelet therapy for the prevention of vascular access thrombosis has not been well established. Studies in patient receiving HD have shown an increased risk of bleeding with minimal benefit in maintaining vascular access patency. Therapy with antiplatelet agents should be individualized based on the patient's risk factors and comorbidities.[30] A meta-analysis of randomized controlled trials for the prevention of vascular access failure identified nine trials assessing antiplatelet therapy and dialysis access patency in AV fistula ($n = 6$) and graft ($n = 3$).[58] This analysis found a lower rate of thrombosis or patency failure in patients with an AV fistula taking either aspirin, ticlopidine, or clopidogrel for up to 6 months (RR, 0.49; 95% CI, 0.30-0.81). In patients with an AV graft, there was no benefit with any of these antiplatelet therapies (RR, 0.94; 95% CI, 0.80-1.10). A post-hoc analysis identified that patients receiving aspirin prior to AV graft placement had improved graft patency but not graft survival.[59] An observational study in patients undergoing surgery for the creation of an HD-related vascular access examined primary patency at 12 months and compared antiplatelet therapy (aspirin or a platelet adenosine diphosphate receptor [$P2Y_{12}$] inhibitor) versus no antiplatelet therapy. There was no difference in primary patency between antiplatelet versus no antiplatelet therapy in patients receiving an AV fistula. There was a significant increase in primary patency in patients receiving an AV graft and antiplatelet therapy ($P = 0.04$). In hospital bleeding was assessed but long-term bleeding and bleeding risk were not reported and these results need to be interpreted with caution as previous studies have found an increased risk of bleeding with $P2Y_{12}$ inhibitors.[60] Overall, the studies have reported conflicting results, and patients with an AV graft taking antiplatelet therapy prior to a procedure may have some benefit but initiating aspirin post-surgery may increase the risk of thrombosis.

The use of anticoagulation to maintain vascular access patency remains controversial with some trials suggesting an increase in morbidity and mortality.[61,62] Patients receiving HD generally require a lower dose of anticoagulation and are at a much higher risk of a major hemorrhagic event.[61,62] An examination of patients receiving a new AV fistula or graft from 2011 to 2019 were identified in the Vascular Quality Initiative database. Patients received either no anticoagulation or anticoagulation (warfarin, dabigatran, or rivaroxaban) post-procedure. At 6 months post procedure patients who received anticoagulation had a higher rate of wound infections (3.8% vs 2.3%) and a lower rate of access patency (84.3% vs 85.7%) compared to patients receiving no anticoagulation.[63] The decision to initiate anticoagulation in patients receiving HD should be individualized for a patient's comorbid diseases and bleeding risk.

The effect of fish oil supplementation, a combination of eicosapentaenoic acid (EPA) 400 mg and docosahexaenoic acid (DHA) 200 mg, on AV graft patency for 12 months after graft placement revealed that the loss of patency was lower in the fish oil (48%) than the placebo (62%). Fish oil thus may benefit some patients with an AV graft since time to thrombus was longer and thrombus rates were about half that of placebo.[64] Based on this evidence, the KDOQI guidelines are suggesting the use of fish oil supplements in patients with a newly created AV graft to reduce morbidity and the frequency of thrombosis. The guidelines state there is inadequate evidence to recommend fish oil supplementation in patients with an AV graft to prolong graft patency.

Fish oil supplements were also studied in patients scheduled to receive surgery for an AV fistula. Patients were randomized to receive either placebo (olive oil) or fish oil 4 g/day (EPA 46% and DHA 38%) starting the day prior to surgery for 12 weeks. The patients receiving aspirin 100 mg/day were similar in each study arm. The AV fistula failure rate during the first 12 months post-surgery was 47% in both groups with similar rates of thrombus formation in patients receiving fish oil versus placebo (22% vs 23%) including those receiving aspirin or placebo (20% vs 18%).[65] The KDOQI guidelines do not recommend the use of fish oil supplementation to prevent flow dysfunction in an AV fistula.[30]

Catheter-locking solutions have been associated with a reduction in catheter thrombosis. The instillation of unfractionated heparin (UFH), recombinant tissue plasminogen activator (rt-PA), or sodium citrate in each HD catheter lumen between HD sessions have demonstrated efficacy in reducing catheter thrombosis. Sodium citrate 4% is as effective as UFH but may offer a better safety profile at a reduced cost.[66] A systematic review and meta-analysis of randomized controlled trials of HD locking solutions containing UFH and citrate found significantly fewer bleeding episodes in the patients receiving citrate. The analysis found no difference between citrate and UFH for catheter patency.[67] Unfractionated heparin 5,000 units/mL twice weekly and recombinant tissue plasminogen activator (rt-PA) 1 mg/catheter lumen once weekly were instilled in patients receiving HD with a CVC. Alternating the catheter-locking solution regimen with rt-PA significantly decreased catheter malfunction compared to the patients receiving UFH only for catheter patency. The cost of catheter replacement and hospitalization may offset the cost of once weekly administration of rt-PA.

Based on their medical history, patients at high risk for catheter malfunction or bacteremia ($n = 373$) received post-HD catheter-locking solutions of rt-PA (1 mg/lumen) once weekly plus routine care with either sodium citrate 4% or UFH on the remaining post-HD sessions. Catheter malfunction significantly declined with weekly rt-PA treatment from 18.4 to 10.1 days/1,000 catheter days and the episodes of bacteremia declined from 0.28 to 0.25/1,000 catheter days. Most patients (96%) received routine care with sodium citrate 4%, which may account for the small decline in bacteremia episodes. Overall, the increased cost of weekly rt-PA was not offset by the decline in catheter malfunction or bacteremia.[68] Taurolidine-based catheter solutions were examined in patients with a tunneled catheter ($n = 177$). Patients were randomized to receive either taurolidine citrate with urokinase (Tauro/U) once weekly plus taurolidine citrate with heparin (Tauro/Hep) twice a week ($n = 84$) or Tauro/Hep ($n = 93$) three times a week. During the 6-month study, no patients in the Tauro/U group required catheter replacement compared with three patients in the Tauro/Hep group. The use of rt-PA to restore catheter patency occurred at a lower rate with Tauro/U ($n = 5$) compared to Taurolock/Hep ($n = 12$). This was a short-term study; therefore, it is difficult to extrapolate long-term benefits until further studies are completed.[69] A catheter locking solution of taurolidine (1.35%), citrate (3.5%), and heparin (1,000 units) is seeking FDA approval for the prevention of CRBSI in patients receiving HD.

A prospective cohort study in patients ($n = 451$) receiving HD with a tunneled or non-tunneled catheter and either sodium bicarbonate 7.5% or 8.4%, or 0.9% normal saline as a catheter locking solution. Patients receiving the sodium bicarbonate locking solution had a significantly lower rate of thrombosis and blood stream infections compared the 0.9% NaCl group ($P < 0.0001$).[70] UFH and citrate (concentrations less than 5%) are listed by KDOQI as catheter locking solution options. The KDOQI guidelines consider citrate and UFH to have similar efficacy for survival and maintaining patency. Catheter locking solutions to prevent infections with taurolidine, tinzaparin, or gentamicin are not recommended by KDOQI based on the current evidence. In patients with an indwelling catheter at high risk for a catheter-related blood stream infection (CRBSI) defined as patients with multiple prior CRBSIs and/or an *S. aureus* nasal carriers may benefit from prophylactic instillation of rt-PA once weekly.[30]

The therapeutic alternatives for the management of venous catheter thrombosis are listed in Table 64-6. If a catheter-related thrombus is suspected, a forced saline flush should be used to clear the catheter, followed by installation of a thrombolytic. A number of studies have been published using alteplase and reteplase and initial reperfusion rates for both were approximately 90%, respectively.[71] The efficacy, safety, and cost of alteplase, reteplase, and tenecteplase were compared, and venous catheter clearance rates were similar with reteplase (88% ± 4%) and alteplase (81% ± 37%), but markedly lower with tenecteplase (41% ± 5%).[71] The cost analysis favored the use of reteplase, however, to attain these savings, reteplase must be batch-prepared. Reteplase is not FDA-approved for this indication which may limit it use.[71] The instillation of a tissue plasminogen activator once weekly in a catheter may reduce catheter dysfunction and could be considered in select patients at a high risk of thrombosis.[30]

TABLE 64-6

Management of Hemodialysis Catheter Thrombosis

Nonpharmacologic therapy
Forced saline flush
Referral to vascular surgeon
Pharmacologic therapy
Alteplase: instill 2 mg/2 mL/catheter lumen port; attempt to aspirate after 30 minutes; may repeat dose if catheter function is not restored in 120 minutes; longer durations of instillation have been used.
Reteplase: instill 0.4 U/0.4 mL in each lumen, attempt to aspirate after 20-30 minutes, may repeat if necessary.

Alteplase is available commercially and is the only agent that is FDA-approved, for venous catheter clearance, and is administered as a short dwell for 30 to 60 minutes, as a long dwell, or left in the catheter between treatments. No difference in patency rates between the short or long dwells has been demonstrated. Alteplase has also been given as a short infusion of 2 mg/h over 4 hours for a blocked catheter and 1 mg/h over 4 hours for sluggish blood flow. Infusions may theoretically be more efficacious than the dwell technique because the thrombus is only exposed to the thrombolytic at the tip of the catheter. Another consideration is dwell versus push techniques for thrombolytic therapy, with recent data indicating that a push protocol with alteplase is as effective and safe for managing HD catheter dysfunction and might be more practical than a dwell technique.[72]

A retrospective single-center study evaluated the dose of alteplase in patients receiving HD with a catheter requiring a thrombolytic for catheter dysfunction. Patients during the first 3 years of the study received alteplase 2 mg/lumen and during the last 3 years received alteplase 1 mg/lumen. Dwell time was 30 minutes and independent of dose. Patients receiving alteplase 2 mg dose had a lower rate of catheter removal due to dysfunction (10.2% vs 19.4%). Overall, the instillation of alteplase 2 mg compared to 1 mg resulted in a 89.2% success rate at resolving catheter occlusions versus 80.6% ($P = 0.036$).[73]

Infection

Patients who develop a fever during dialysis should immediately be evaluated for infection; blood cultures should be collected prior to the administration of any antibiotics. When an AV fistula infection is suspected, empiric broad-spectrum antimicrobial therapy must be initiated usually with vancomycin plus an aminoglycoside or extended spectrum beta-lactamase inhibitor. Antimicrobial therapy, if the infection is confirmed, should continue for a total of 6 weeks and should be tailored to culture sensitivities. Unfortunately, a suspected infection in an AV graft may require a surgical procedure to remove the infected graft material in addition to antimicrobial therapy. A suspected infection in a temporary catheter may warrant catheter removal and a culture of the catheter tip should be obtained.[31,74] Catheter-related infections are more common than infections of an AV fistula or graft; therefore, preventative care approaches are paramount. Preventative care includes minimizing the use and duration of catheters, proper disinfection and sterile technique, and the use of an antimicrobial ointment at the exit site (mupirocin 2%, povidone-iodine).[75] Dialysis unit protocols that employ universal precautions, limit the manipulation of the catheter, and utilize an antiseptic wash (tincture of iodine, chlorhexidine, etc.) for skin preparation, and the use of facemasks by the patient and caregiver can significantly reduce the incidence of catheter-related bacteremia.[31,74,76] Topical application of 2% mupirocin ointment to a tunneled HD catheter exit site after each HD session can increase infection-free days. Current recommendations are to apply either povidone-iodine antiseptic ointment or polysporin triple ointment (bacitracin/gramicidin/polymyxin B) to the exit site after each HD session. Long-term monitoring of infection rates of patients receiving HD with a catheter did not reveal an increase in antibiotic resistance with a once-a-week application of a topical polysporin triple ointment to catheter exit sites.[77]

The Infectious Disease Society of America (IDSA) and KDOQI guidelines address catheter care and the diagnosis and management of catheter-related infections.[30,76] Peripheral blood draws, although recommended by IDSA, are often avoided in patients receiving HD to protect potential or future HD vascular access sites. Blood cultures are generally obtained from the blood tubing connecting the catheter to the HD machine. A prospective study examined blood cultures (n = 178) obtained from patients receiving HD suspected of a CRBSI. The blood cultures obtained from the HD circuit and venous catheter hub were the most sensitive, specific, and accurate for diagnosing CRBSI compared to blood cultures taken from a peripheral vein and either catheter hub or HD circuit.[78] A full-course of antimicrobial treatment is warranted if blood cultures are positive.[31,76] Empiric therapy with coverage for both gram-positive and gram-negative bacteria should be initiated after the blood cultures are obtained. The incidence of MRSA bacteremia warrants initial treatment for gram-positive coverage with vancomycin or daptomycin. If gram-negative antimicrobial coverage is warranted, an aminoglycoside or third-generation cephalosporin should be initiated depending on a center's protocols and antimicrobial susceptibilities.[31,76] Antimicrobial therapy de-escalation should occur once blood cultures identify an organism and antimicrobial susceptibility. For example, if the isolated organism is methicillin-sensitive *S. aureus*, administer IV cefazolin (20 mg/kg, rounded to the nearest 500 mg) after each dialysis session. Antibiotic selection should be based on bacterial coverage and the ability to optimize pharmacokinetics by administering a dose either during the last 30 to 60 minutes of HD treatment or during the rinse bath. This method minimizes additional dosages between HD sessions. Examples of antimicrobial agents that meet these objectives are vancomycin, cefazolin, ceftazidime, daptomycin, and aminoglycosides.[76,79]

The IDSA guidelines recommend removal of an infected catheter if *S. aureus*, *Pseudomonas* species, or *Candida* species are the infectious cause. Although removal of the catheter is warranted, this is not always possible in patients receiving HD because of limited vascular access options. Retaining an infected catheter significantly increases a patient's risk of bacteremia recurrence after completing a course of antibiotics; therefore, other options need to be considered. Options such as replacing the catheter over a guidewire or using a catheter-lock solution in conjunction with IV antibiotics are alternatives.[31,76]

The catheter salvage success rate when a catheter-lock solution is used in addition to systemic antibiotics is highly variable and pathogen dependent.[31,76] The IDSA guidelines recommend the use of catheter-lock solutions as adjunctive therapy after each dialysis session for 10 to 14 days in a patient whose catheter was not removed and bacteremia symptoms resolved in 2 to 3 days. The IDSA recommendations for antibiotic therapy are listed in Table 64-7.[76]

TABLE 64-7

Management of Hemodialysis Access Infection

1. Primary arteriovenous fistula
   A. Treat as subacute bacterial endocarditis for 6 weeks.
   B. Initial antibiotic choice should always cover gram-positive organisms (eg, vancomycin 20 mg/kg IV with serum concentration monitoring or cefazolin 20 mg/kg IV three times/week or after each dialysis session).
   C. Gram-negative coverage is indicated for patients with diabetes, human immunodeficiency virus infection, prosthetic valves, or those receiving immunosuppressive agents, gentamicin 2 mg/kg IV with serum concentration monitoring.
2. Synthetic arteriovenous grafts
   A. Local infection—empiric antibiotic coverage for gram-positive, gram-negative, and *Enterococcus* (eg, gentamicin plus vancomycin then individualized after culture results available). Continue for 2-4 weeks.
   B. Extensive infection—antibiotics as above plus total resection.
   C. If access is less than 1-month-old, antibiotics as above plus remove the graft.
3. Tunneled cuffed catheters (internal jugular, subclavian)
   A. Infection localized to catheter exit site.
      i. No drainage—topical antibiotics (eg, mupirocin ointment).
      ii. Drainage present—gram-positive antibiotic coverage, vancomycin 20 mg/kg IV with serum concentration monitoring or cefazolin 20 mg/kg IV three times/week.
   B. Bacteremia with or without systemic signs or symptoms.
      i. Gram-positive antibiotic coverage as above.
      ii. If symptomatic at 36 hours, remove the catheter.
      iii. If stable and asymptomatic, change catheter and provide culture-specific antibiotic coverage for a minimum of 3 weeks.

Data from References 76 and 80.

Microbial colonization of a catheter could affect patency and a patient's access to dialytic treatment. An examination of the catheter-lock solutions, UFH 5,000 U/mL and tetra-sodium EDTA, found an increased rate of microbial colonization with UFH but the tetra-sodium EDTA solution had an increased rate of thrombosis.[81] Alternative solutions to UFH and tetra-sodium EDTA including catheter-lock solutions containing ethanol 30% combined with sodium citrate 4% or ethanol 70% with UFH 2,000 U/mL have been effective at decreasing CRBSI and improving catheter survival.[82]

Catheter-locking solutions have been utilized to prevent infection and thrombosis in HD catheters. A meta-analysis of randomized control trials of catheter-related bacteremia and antimicrobial lock solutions identified eight studies with 829 patients and more than 90,100 catheter days. Overall analysis found that the use of an antimicrobial locking solution significantly reduced the risk of a catheter-related infection (relative risk [RR] 0.32; 95% confidence interval [CI] 0.10-0.42).[83] A comparison of UFH 1,000 U/mL to the combination solution of 4% sodium citrate with gentamicin 320 µg/mL as a catheter-lock solution significantly reduced the incidence of catheter-related bloodstream infections.[84] The value of catheter-locking solutions for treatment and prevention of catheter-related infections is increasingly becoming evident, but the possibility of antibiotic resistance with the wide use of antibiotics in catheter locks remains a concern. Gentamicin resistance to coagulase-negative *Staphylococcus* was reported in a retrospective study using routine post-HD administration of gentamicin (4 mg/mL) combined with UFH (5,000 U/mL) as a catheter-lock solution. Over the 4-year study, there were 80 CRBSIs with 21 episodes (26%) of gentamicin resistance identified. The increase in gentamicin resistance led to a discontinuation of the gentamicin-heparin catheter-lock solutions.[85]

PERITONEAL DIALYSIS

Although the concept of peritoneal lavage has been described as far back as the 1700s, it wasn't until the 1920s that PD was first employed as an acute treatment for uremia. It was used infrequently during subsequent years until the concept of PD as a chronic therapy for ESRD was proposed in the 1960s. Over the ensuing years, the number of patients receiving PD increased slowly until the early 1980s. At that time, several innovations in PD

delivery systems were introduced, such as improved catheters and dialysate bags. These innovations led to improved outcomes, decreased morbidity, mortality, and a corresponding increase in the use of PD as a viable alternative to HD for the treatment of ESRD. However, the worldwide use of PD has declined over the past decade. Some patients, such as those with more hemodynamic instability (eg, hypotension) or significant residual renal function (RRF), and perhaps patients who desire to maintain a significant degree of self-care may be better suited to PD than to HD. Table 64-2 shows the advantages and disadvantages of PD.

Principles of Peritoneal Dialysis

5 The three basic components of HD—namely, a blood-filled compartment separated from a dialysate-filled compartment by a semipermeable membrane—are also present in PD.[4] In PD, the dialysate-filled compartment is the peritoneal cavity, into which dialysate is instilled via a peritoneal catheter that traverses the abdominal wall. The contiguous peritoneal membrane surrounds the peritoneal cavity. The cavity, which normally contains about 100 mL of lipid-rich lubricating fluid, can expand to a capacity of several liters. The peritoneal membrane that lines the cavity functions as the semipermeable membrane, across which diffusion and ultrafiltration occur. The peritoneal dialyzing membrane is comprised of a monocellular layer of peritoneal mesothelial cells, the basement membrane, and underlying connective and interstitial tissue. The peritoneal membrane has a total area that approximates body surface area (approximately 1-2 m^2). Blood vessels supplying and draining the abdominal viscera, musculature, and mesentery constitute the blood-filled compartment.

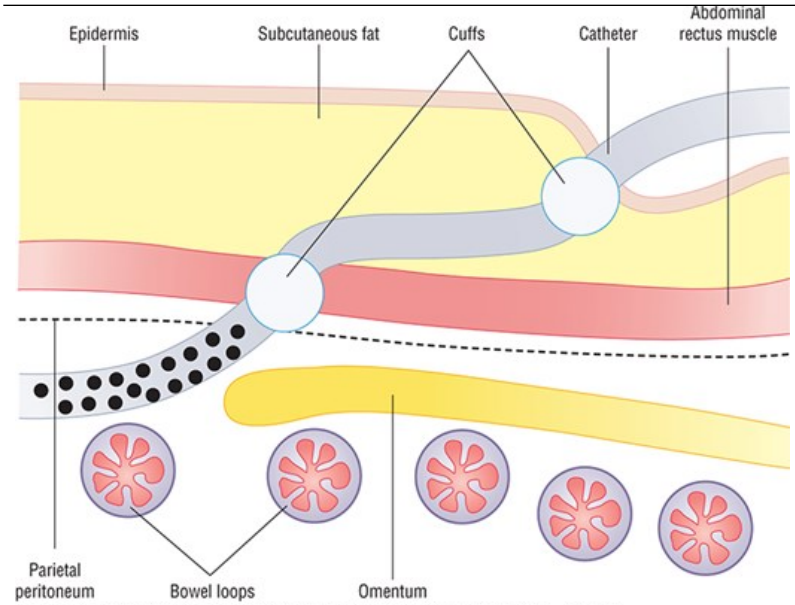
Unlike HD, the crucial components of PD cannot be manipulated to maximize solute and fluid removal. Because the blood is not in intimate contact with the dialysis membrane as it is in HD, metabolic waste products must travel a considerable distance to the dialysate-filled compartment. In addition, unlike HD, there is no easy method to regulate blood flow to the surface of the peritoneal membrane, nor is there a countercurrent flow of blood and dialysate to increase diffusion and ultrafiltration via changes in hydrostatic pressure. Similarly, there is no easy means available to manipulate the peritoneal membrane. Thus, to enhance PD clearance involve alterations in dialysate volume, dwell time, and the number of exchanges per day. For these reasons, PD is a less efficient process per unit time compared with HD, and must, therefore, be a virtually continuous procedure to achieve acceptable goals for clearance of metabolic waste products.

Peritoneal Dialysis Access

Access to the peritoneal cavity is via the placement of an indwelling catheter. Many types are available, and Fig. 64-3 shows an example.[4] Most catheters are manufactured from silicone rubber, which is soft, flexible, and biocompatible. A typical adult catheter is 40 to 45 cm long, 20 to 22 cm of which is inside the peritoneal cavity. Placement of the catheter is such that the distal end lies low in a pelvic gutter. The center section of the catheter has one or two cuffs made of a porous material that is tunneled inside the anterior abdominal wall so that the cuffs provide mechanical support and stability to the catheter, serve as a mechanical barrier to skin organisms, and prevent their migration along the catheter into the peritoneal cavity. The cuffs are placed at different sites surrounding the abdominal rectus muscle. The remainder of the central section of the catheter is tunneled subcutaneously before exiting the abdominal surface, usually a few centimeters below and to one side of the umbilicus.

FIGURE 64-3

Diagram of the peritoneal dialysis catheter placement through the abdominal wall into the peritoneal cavity. *(Reprinted, with permission, from Sherman R, Daugirdas J, Ing T. Complications during hemodialysis. In: Daugirdas J, Blake P, Ing T, eds. Handbook of Dialysis. 5th ed. Philadelphia: Wolters Kluwer; 2014.)*



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The placement of the catheter exit site is one of the factors related to the development or prevention of exit-site infections and peritonitis. The external section of most peritoneal catheters ends with a Luer-Lok connector, which can be connected to a variety of administration sets. These catheters can be used immediately, if necessary, provided small initial volumes are instilled; however, a maturation period of 2 to 6 weeks is preferred.

Peritoneal Dialysis Procedures

6 Several variants of PD are clinically utilized in the United States. All variants of PD require the placement of a dialysis solution to dwell in the peritoneal cavity for some period, removing the spent dialysate, and then repeating the process. PD prescriptions can be delivered as continuous or intermittent and use manual or automated exchanges. Continuous PD involves intraperitoneal dialysate 24 hours/day, 7 days/week. A continuous ambulatory PD procedure uses manual exchanges, versus a continuous cycling PD procedure uses a cycler to perform the exchanges. Whereas an intermittent procedure involves the use of cycler to deliver PD for a portion of the day.[4] The prescribed dose of PD may be altered by changing the number of exchanges per day, by altering the volume of each exchange, or by altering the strength of dextrose or other osmotic agent in the dialysate for some or all exchanges. Increasing any one of these variables increases the effective osmotic gradient across the peritoneum, leading to increased ultrafiltration and diffusion (solute removal). If the dwell time is extended, equilibrium may be reached, after which time there will be no further water or solute removal. In fact, after a critical period, reverse water movement may occur.[4] In a basic CAPD system, the patient or caregiver is manually responsible for performing the prescribed number of dialysate exchanges. The patient is connected to a bag of prewarmed peritoneal dialysate via the PD catheter, by a length of tubing called a transfer set. The most common transfer set used is the Y transfer set which consists of a Y-shaped piece of tubing that is attached at its stem to the patient's catheter, leaving the remaining two limbs of the Y attached to dialysate bags, one filled with fresh dialysate and the other empty. The spent dialysate from the previous dwell is drained into the empty bag, and the peritoneum is subsequently refilled from the bag containing fresh dialysate. The Y set is then disconnected and the bag containing the spent fluid and the empty bag that had contained fresh dialysate are detached and discarded. Typically, a patient instills 2 to 3 L of dialysate three times during the day with each exchange lasting 4 to 6 hours, and then a single dialysate exchange overnight lasting 8 to 12 hours. At the end of the prescribed dwell period, a new Y set is attached and the process is repeated. The process of outflow, aseptic manipulation of the administration set and catheter, and inflow requires a total time of approximately 30 minutes.

As described earlier, CAPD involves performing the dialysate exchanges manually, whereas automated systems collectively termed automated peritoneal dialysis (APD) performs the exchanges with a cycler. APD systems are designed for patients who are unable or unwilling to perform the necessary aseptic manipulations and for those who require more dialysis. The device is set up in the evening, and the patient attaches the peritoneal catheter to it at bedtime. The machine performs several short-dwell exchanges (usually 1-2 hours) during the night. This permits a long cycle-free daytime dwell of up to 12 to 14 hours. Typical APD regimens involve total 24-hour exchanges of approximately 12 L, which include one or more daytime instillations and dwell periods.[86] This type of regimen is referred to as APD with a "wet" day. The APD variant, nightly intermittent PD, has a similar

theme, except that the peritoneal cavity tends to be dialysate-free during the day. This type of regimen is frequently referred to as APD with a “dry” day. A number of variants exist and depend largely on equipment availability, patient and prescriber preference, and whether the patient retains any RRF, which influences the quantity of dialysis prescribed.

The APD systems include continuous cycling PD (CCPD), tidal PD, and nocturnal intermittent PD. The prototypic form of APD is usually a hybrid between CAPD and continuous cycling PD, in which some of the daily exchanges (usually the overnight exchanges) are completed using an automated device. Other advances in PD procedures involve using continuous flow PD. This technique maintains a fixed intraperitoneal volume and rapid, continuous movement of dialysate into and out of the peritoneal cavity. To accomplish this, two PD catheters (an inlet and outlet catheter) and a means of generating a large volume of sterile dialysate are required. Dialysate is generated via conventional HD equipment or sorbent technology. In continuous flow PD, clearance of small solutes is three to eight times greater than with APD and approximates daily HD. Potential applications of continuous flow PD include daily home dialysis, treatment of acute kidney injury in the intensive care unit, and ultrafiltration of ascites.

Peritoneal Dialysis Solutions

All forms of PD use dialysate solutions, which are commercially available in volumes of 1 to 3 L in flexible polyvinyl chloride plastic bags. The most commonly used solutions that are commercially available contain an osmotic agent, electrolytes, and buffer. The solutions contain electrolytes, such as sodium (132-134 mEq/L [mmol/L]), chloride (96 mEq/L [mmol/L]), calcium (2.5-3.5 mEq/L [1.25-1.75 mmol/L]), and magnesium (0.5 mEq/L [0.25 mmol/L]). These solutions may contain dextrose (1.5%, 2.5%, 3.86%, or 4.25%) or icodextrin (a glucose polymer) at a concentration of 7.5%. The dextrose solutions are hyperosmolar (osmolarity range, 345-484 mOsm/L) and induce ultrafiltration (removal of free water) by crystalline osmosis. Dextrose is not the ideal osmotic agent for peritoneal dialysate because these solutions are not biocompatible with peritoneal mesothelial cells or with peritoneal leukocytes. The cytotoxic effects on these cells are mediated by the osmolar load and the low pH of the solutions, as well as the presence of glucose degradation products formed during heat sterilization of these products. Icodextrin PD solution contains icodextrin, a starch-derived glucose polymer. It has an osmolality of 282 to 286 mOsm/kg (mmol/kg), which is isoosmolar with serum. Icodextrin produces prolonged ultrafiltration by a mechanism resembling colloid osmosis resulting in ultrafiltration volumes similar to those with 4.25% dextrose. Icodextrin may have fewer of the metabolic effects associated with dextrose, such as hyperglycemia and weight gain. It is indicated for use during the long (8-16 hours) dwell of a single daily exchange in CAPD and APD patients. Lower glucose degradation product dialysate solutions are also available with similar solute concentrations, but with pH of 7.3.[4] These newer, biocompatible dialysate solutions are described as less harmful to the peritoneal membrane and preserve RRF to a greater extent than the available standard solutions.[4] Preservation of RRF in PD and HD patients is important as it decreases mortality and increases the time to the first episode of peritonitis. However, the putative benefits of the biocompatible dialysate solutions have not been completely borne out: their use has not consistently slowed the rate of decline in glomerular filtration rate as compared to standard solutions, although the incidence of peritonitis has been lower. Finally, the solutions contain buffers, lactate (0-40 mmol/L), and/or bicarbonate (0-34 mmol/L).

Adequacy of Peritoneal Dialysis

The most recent International Society of Peritoneal Dialysis practice guidelines argue that the assessment and prescription of PD should be a shared decision-making process between the patient and the care giving team. Ideally assessments should focus on (1) patient reported outcome measures (well-being, quality of life, symptomatology, etc.), (2) fluid status, (3) nutrition status, and (4) toxin removal (ie, solute clearance determination).[87] As in HD, toxin removal can be quantified by the clearance of urea, by calculating *Kt/V*. The calculations determine a daily *Kt/V*, which is then converted into a weekly value that is relevant to PD patients.

PD adequacy is a major issue that has received considerable attention. The most recent KDOQI guidelines recommend that patients on PD have a total *Kt/V* of at least 1.7/week, including both PD *Kt/V* and residual kidney *Kt/V*.[86] It is important to note that RRF may provide a significant component of the total *Kt/V*. Patients may commence PD with a residual CLcr of approximately 9 to 12 mL/min (0.15-0.20 mL/s), which contributes a renal *Kt/V* of 0.2 to 0.4. Over a period of 1 to 2 years, if RRF progressively deteriorates, the total *Kt/V* will progressively diminish unless PD *Kt/V* is increased (by increasing the prescribed dose of PD) to compensate for the reduced renal *Kt/V*.

For patients producing less than 100 mL urine/day, the weekly *Kt/V* dose of 1.7 must be provided entirely by peritoneal clearance. For patients producing greater than 100 mL urine/day, combined renal and peritoneal urea clearances must exceed the weekly *Kt/V* dose of 1.7.[86] The weekly *Kt/V* dose should be measured within the first month of PD initiation and at least once every 4 months thereafter. It is imperative to detect subtle decreases in RRF along with poor adherence to make necessary alterations to the prescribed PD dose to attain adequate clearance of waste products.

The KDOQI guidelines also stress the importance of preserving RRF in PD patients because it is associated with decreased mortality. Typical measures to preserve RRF include preferential use of ACE-Is or ARBs, regardless of blood pressure, and avoidance of medications or procedures that are associated with insults to the kidney (eg, nonsteroidal anti-inflammatory drugs, cyclooxygenase-2 inhibitors, aminoglycosides, intravenous iodinated radiocontrast dyes, withdrawal of immunosuppressant therapies from a transplanted kidney, hypovolemia, urinary tract obstruction, and hypercalcemia).[86]

Complications of Peritoneal Dialysis

Mechanical, medical, and infectious problems complicate PD therapy. Mechanical complications include kinking of the catheter and inflow and outflow obstruction; excessive catheter motion at the exit site, leading to induration and possible infection and aggravation of tissues; pain from impingement of the catheter tip on the viscera; or inflow pain resulting from a jet effect of too rapid dialysate inflow.

Table 64-8 lists the numerous medical complications of PD. An average PD patient absorbs up to 60% of the dextrose in each exchange. This continuous supply of calories leads to increased adipose tissue deposition, decreased appetite, malnutrition, and altered requirements for insulin in diabetic patients. Fibrin formation in dialysate is common and can lead to obstruction of catheter outflow. Infectious complications of PD are a major cause of morbidity and mortality and the transfer of patients from PD to HD therapies. A leading cause of infections is related to technique failure during PD exchanges. The two predominant infectious complications are peritonitis and catheter-related infections, which include both exit-site and tunnel infections.

TABLE 64-8

Medical Complications of Peritoneal Dialysis

Cause	Complication	Treatment
Glucose load	Exacerbation of diabetes mellitus	IP insulin
Fluid overload	Exacerbation of heart failure Edema Pulmonary congestion	Increase ultrafiltration Diuretics, if the patient has residual renal function
Electrolyte abnormalities	Hypercalcemia/Hypocalcemia	Alter dialysate calcium content
PD additives	Chemical peritonitis	Discontinue PD additives
Malnutrition	Albumin loss Loss of amino acids Muscle wasting Increased adipose tissue	Dietary changes Parenteral nutrition Discontinue PD
Unknown	Fibrin formation in dialysate	IP heparin

IP, intraperitoneal; PD, peritoneal dialysis.

Peritonitis

The incidence of peritonitis is influenced by connector technology, by the composition of patient populations, and by the use of APD versus CAPD. The Peritoneal Dialysis Outcomes and Practice Patterns Study (PDOPPS) is an international cohort study reporting on PD-related peritonitis and potential contributing factors such as exit-site prophylaxis. The rate of peritonitis was 0.26 (95% CI, 0.24-0.27) per patient-year in the United States with the causative organisms as gram-positive (37%), gram-negative (13%), culture-negative (16%), polymicrobial (5%), and yeast (1%). The most common exit-site prophylaxis was topical aminoglycoside (72%) and topical mupirocin (13%).[88]

Peritonitis is a major cause of catheter loss in PD patients. The clinical presentation and diagnosis are listed in Table 64-9. A retrospective cohort study found a mortality rate of 0.07 per patient-year (95% CI, 0.06-0.08). The cause of mortality was identified as cardiovascular (56.3%) and infectious disease (17.6%). Patients who died from an infectious cause, 41.3% were related to peritonitis.[89] A statistically significant correlation between infectious complications and death rates has been reported: patients who had more than 1 peritonitis episode/year, 0.5 to 1 episode/year, or less than 0.5 episode/year, 50% died after 3, 4, and 5 years of therapy, respectively. It is important to note that these relationships are not necessarily cause and effect, as many of these patients succumb to cardiovascular events.[90]

TABLE 64-9

Clinical Presentation and Diagnosis of Peritoneal Dialysis-Related Peritonitis

General • Patients generally present with abdominal pain and cloudy effluent
Symptoms • The patient may complain of abdominal tenderness, abdominal pain, fever, nausea and vomiting, and chills
Signs • Cloudy dialysate effluent may be observed • Temperature may or may not be elevated
Laboratory Tests • Dialysate white blood cell count >100/mm^3 (0.1×10^9/L), of which at least 50% are polymorphonuclear neutrophils • Gram stain of a centrifuged dialysate specimen
Other Diagnostic Tests • Culture and sensitivity of dialysate should be obtained

Peritonitis has several imprecise definitions, but guidelines suggest that an elevated dialysate white blood cell count of greater than 100/μL (0.1×10^9/L) with at least 50% polymorphonuclear neutrophils indicates the presence of inflammation, of which peritonitis is the most likely cause.[91] A patient who presents with abdominal pain and a cloudy effluent is usually given a provisional diagnosis of peritonitis. Inherent in this definition is a number of false-positive and false-negative diagnoses, because a small percentage of patients with culture-proven peritonitis will have clear dialysate, and some patients, such as menstruating females, may have cloudy PD effluent without clinical infection. Sterile culture peritonitis remains problematic; it is defined as an episode in which there is clinical suspicion of peritonitis, but for which the culture of the dialysate reveals no organism. There are several postulates for the high incidence (up to 20% of episodes) of culture-negative peritonitis. Many peritonitis-producing organisms are slime producers and may adhere to the peritoneal membrane or to the catheter surface and may be protected from exogenous antibiotics. Sufficient numbers of these bacteria may proliferate to cause peritoneal membrane inflammation and clinical peritonitis, but an inadequate number may seed into the peritoneal cavity to be recovered by conventional microbiologic techniques. In addition, free-floating planktonic bacteria may be rapidly phagocytosed by peritoneal white blood cells, thereby rendering them unavailable for culture.[92]

Contemporary methods have increased the recovery rate of organisms and decreased the culture-negative rate. Centrifugation is recommended as the optimum culture method. Centrifugation of a large volume of dialysate (50 mL), resuspension of the sediment in 3 to 5 mL of sterile saline, and subsequent inoculation in culture media produce a culture-negative rate less than 5%. If centrifuge equipment is not available, blood culture bottles can be directly injected with 5 to 10 mL of dialysate effluent. However, this method results in a culture-negative rate of up to 20%.[91]

The majority of infections are caused by gram-positive bacteria, of which *Staphylococcus epidermidis* is the predominant organism. There is no single predominant gram-negative organism. Together, gram-positive and gram-negative organisms account for 80% to 90% of all episodes of peritonitis and constitute the spectrum against which initial empiric therapy is directed.[93]

Catheter-Related Infections

A catheter-related infection in patients receiving PD includes both exit-site infection (ESI) and tunneled infection. Patients with previous infections tend to have a higher subsequent incidence. A case-controlled study found that 69.8% of patients receiving PD had at least one ESI over a 3-year period and are more likely to develop peritonitis (64%) compared to patients without an ESI.[94] The majority of ESIs are caused by *S. aureus*. In contrast to peritonitis, *S. epidermidis* accounts for less than 20% of ESIs. Although gram-negative organisms, such as *Pseudomonas*, are less common, they can result in significant morbidity. The diagnostic characteristics of these infections are somewhat vague but generally include the presence of purulent drainage, with or without erythema at the catheter exit-site. The risk of ESIs is increased several-fold in patients who are nasal carriers of *S. aureus*.[94]

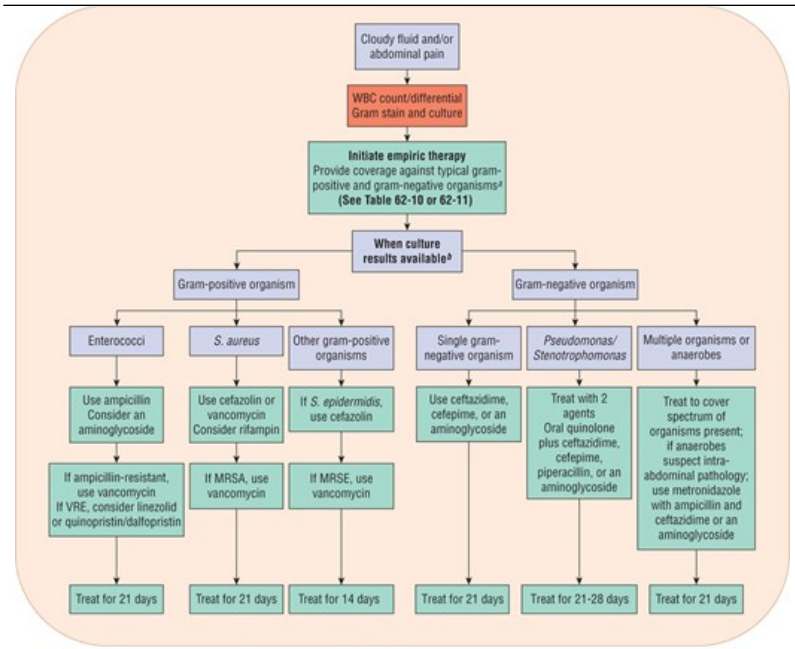
Management

Peritonitis

The International Society of Peritoneal Dialysis (ISPD) updated the Peritoneal Dialysis-Related Infections recommendations in 2016, which provide guidelines for treatments for peritonitis and tunneled and exit-site infections.[91] These PD-related infections are associated with dialysis modality treatment failures and substantial morbidity and mortality; therefore, appropriate pharmacotherapy treatment is essential. The ISPD guidelines specifically address the importance of peritonitis prevention, dialysis center antibiotic selection, and intraperitoneal (IP) antibiotic dosing and treatment duration for peritonitis.[91] In 2017, ISPD published catheter-related infection recommendations to prevent ESIs and described routine catheter care for PD patients.[93] Both guidelines provide a summary of best practices based on available evidence or consensus in areas where evidence exists. Figure 64-4 shows the pharmacotherapy recommendations for the treatment of bacterial peritonitis.

FIGURE 64-4

Pharmacotherapy recommendations for the treatment of bacterial peritonitis in peritoneal dialysis patients. [a]Choice of empiric treatment should be made based on the dialysis center's and the patient's history of infecting organisms and their sensitivities. [b]Final choice of therapy is guided by culture and sensitivity results. (MRSA, methicillin-resistant *Staphylococcus aureus;* MRSE, methicillin-resistant *Staphylococcus epidermidis; S. aureus, Staphylococcus aureus; S. epidermidis, Staphylococcus epidermidis;* VRE, vancomycin-resistant enterococci; WBC, white blood cell.)



Source: Joseph T. DiPiro, Gary C. Yee, Stuart T. Haines, Thomas D. Nolin, Vicki L. Ellingrod, L. Michael Posey: *DiPiro's Pharmacotherapy: A Pathophysiologic Approach, 12e*

The preferred delivery route for antibiotics is IP over IV therapy for the treatment of peritonitis. Antimicrobial dosing recommendations provided in the ISPD guidelines for CAPD dosing distinguish between intermittent (one exchange per day) and continuous therapy (all exchanges). The 2016 guidelines no longer provide APD IP drug dosing recommendations due to a "substantial knowledge gap" within this treatment area. The ISPD guidelines include oral and IV dosing recommendations that can be dosed either independent of or in conjunction with IP dosing.[91,93]

Following a single IP antibiotic dose, the drug concentrations achieved in dialysate and serum differ between intermittent and continuous methods. Intermittent IP therapy necessitates that a sufficient amount of drug transfers from the peritoneal cavity to the systemic circulation, thus allowing drug to diffuse back into the peritoneum during drug-free dialysate dwell time(s). Therefore, once daily dosing requires drug(s) be added to the exchange with the longest dwell time (at least 6 hours) to ensure maximum systemic exposure.

Continuous dosing recommendations may require a loading dose with the first IP dose and a maintenance dose for each subsequent exchange. Vancomycin, aminoglycosides, and cephalosporins generally are administered by either dosing method. It is recommended that a continuous dosing method be used for penicillins and fluoroquinolones. No matter which CAPD drug dosing method is used, the goal is to deliver and maintain adequate peritoneum drug concentrations. Intermittent or continuous dosing is effective for CAPD patients but IP dosing for APD patients may require a different dosing schedule. The rapid overnight dialysate exchanges with APD will increase solute clearance over a short time period. This is particularly important for first-generation cephalosporin agents. The ISPD guidelines recommend continuous dosing of a first-generation cephalosporin because of concerns over inadequate IP drug concentration during the shorter APD dialysate dwells. To maintain adequate peritoneum drug concentrations, patients may be advised to temporarily switch to CAPD delivery or manually instill dialysate with an antimicrobial agent during the day or the longest dwell. If a patient is not a good candidate for CAPD, the cycler can be reset to provide a longer dwell period or slower exchange rate to allow for drug transfer during APD.[91] Intermittent dosing of first-generation cephalosporin for APD does not sustain adequate drug concentrations for most organisms; therefore, continuous dosing may be more effective in providing better drug coverage. Oral ciprofloxacin attains adequate IP drug concentrations in patients receiving APD and is a therapeutic option if the pathogen is susceptible. Regarding RRF, in patients with substantial residual renal function, previous ISPD guidelines recommended dose adjustments for antibiotics with renal elimination. Recent studies suggest these dosing adjustments are not necessary to maintain adequate drug concentrations, resulting in ISPD removing the recommendation for dose adjustments from the 2016 guidelines. The ISPD dosing recommendations for IP antibiotics in CAPD and systemic therapy are shown in Tables 64-10 and 64-11, respectively.[91]

TABLE 64-10

Intraperitoneal Antibiotic Dosing Recommendations for Continuous Ambulatory Peritoneal Dialysis Patients

Drug	Intermittent (one exchange daily)	Continuous (all exchanges)
Aminoglycosides		
Amikacin	2 mg/kg	LD 25 mg/L; MD 12 mg/L
Gentamicin	0.6 mg/kg	LD 8 mg/L; MD 4 mg/L
Netilmicin	0.6 mg/kg	MD 10 mg/L
Tobramycin	0.6 mg/kg	LD 3 mg/kg; MD 0.3 mg/kg
Cephalosporins		
Cefazolin	15-20 mg/kg	LD 500 mg/L; MD 125 mg/L
Cefepime	1,000 mg	LD 250-500 mg/L; MD 100-125 mg/L
Cefoperazone	ND	LD 500 mg/L; MD 62.5-125 mg/L
Cefotaxime	500–1,000 mg	ND
Ceftazidime	1,000–1,500 mg	LD 500 mg/L; MD 125 mg/L
Ceftriaxone	1,000 mg	ND
Penicillins		
Amoxicillin	ND	MD 150 mg/L
Ampicillin	ND	MD 125 mg/L
Penicillin G	ND	LD 50,000 units/L; MD 25,000 units/L
Quinolones		
Ciprofloxacin	ND	MD 50 mg/L
Others		
Vancomycin	15-30 mg/kg Q5-7d[a]	LD 30 mg/kg; MD 1.5 mg/kg/bag
Daptomycin	ND	LD 100 mg/L; MD 20 mg/L
Aztreonam	2 g	LD 1,000 mg/L; MD 250 mg/L
Teicoplanin	15 mg/kg q 5 days	LD 400 mg/bag; MD 20 mg/bag
Linezolid	ND	Oral 200-300 mg daily
Clindamycin	ND	600 mg/bag

Polymixin B	ND	MD 300,000 Unit (30 mg)/bag
Meropenem	1 g	ND
Antifungals		
Fluconazole	200 mg IP every 24-48 hours	ND
Voriconzaole	2.5 mg/kg IP	ND
Combinations		
Ampicillin/sulbactam	2 g/1 g q 12 h	LD 750 mg/L/100 mg/L; MD 100 mg/L
Pipercillin/tazobactam	ND	LD 4 g/0.5 g; MD 1 g/0.125 g
Imipenem/cilastatin	500 mg in alternate exchanges	LD 250 mg/L; MD 50 mg/L
Quinupristin/dalfopristin[b]	25 mg/L in alternate exchanges[a]	ND

[a]Supplemental doses may be required for APD patients.

[b]Given in conjunction with 500 mg intravenous twice daily.

LD, loading dose in milligram; MD, maintenance dose in milligram; NA, not applicable; ND, no data.

Adapted from Li PK, Szeto CC, Piraino B, et al. ISPD peritonitis recommendations: 2016 update on prevention and treatment. Perit Dial Int. 2016;36:481–508.

TABLE 64-11

Systemic Antibiotic Dosing Recommendations for Treatment of Peritonitis

Drug	Dosing
Ciprofloxacin	Oral 250 mg twice daily
Levofloxacin	Oral 250 mg daily
Moxifloxacin	Oral 400 mg daily
Ertapenem	IV 500 mg daily
Linezolid	IV or oral 600 mg twice daily
Rifampicin	450 mg daily for body weight ≤50 kg, 600 mg daily for body weight ≥50 kg
Trimethoprim/Sulfamethoxazole	Oral 160 mg/800 mg twice daily
Amphotericin	IV test dose 1 mg; starting dose 0.1 mg/kg/day over 6 hours increase to target dose 0.75-1.0 mg/kg/day
Caspofungin	IV 70 mg load, then 50 mg daily
Fluconazole	Oral 200 mg loading, then 50 mg daily
Flucytosine	Oral 1 g daily
Posaconazole	IV 400 mg every 12 hours
Voriconazole	Oral 200 mg every 12 hours

Adapted from Li PK, Szeto CC, Piraino B, et al. ISPD peritonitis recommendations: 2016 update on prevention and treatment. Perit Dial Int. 2016;36:481–508.

Initial empiric therapy for peritonitis, regardless of whether a Gram stain was performed, or organisms were identified, should include agents effective against both gram-positive and gram-negative organisms. Antibiotic selection should be based on a dialysis center's antibiogram or resistance patterns, a history of the patient's infections, and the organism's antibiotic sensitivity profile. In many cases, a first-generation cephalosporin such as cefazolin in combination with a second drug that provides broader gram-negative coverage, such as ceftazidime, cefepime, or an aminoglycoside, will prove suitable. Patients with documented allergy to cephalosporin antibiotics can be treated with vancomycin and an aminoglycoside. High rates of methicillin resistance have been reported by many dialysis centers, and vancomycin should be used as first-line therapy against gram-positive organisms for patients treated at these centers. Monotherapy with agents providing both gram-positive and gram-negative coverage is an alternative option. Both imipenem-cilastin and cefepime are effective in treating CAPD-related peritonitis.[95]

After culture and sensitivity results are obtained, antibiotic therapy should be adjusted appropriately (see Fig. 64-4). Tables 64-10 and 64-11 list doses for antibiotics. Treatment should be continued for 14 to 21 days. If the patient does not show signs of clinical improvement within 72 hours after antibiotic treatment is initiated, the culture should be repeated, and the patient reevaluated. If the peritoneal dialysate white blood cell count remains high after 4 days of appropriate antibiotic therapy, clinicians should consider removing the peritoneal catheter, starting IV antibiotics, and initiating HD for dialytic maintenance therapy.

Fungal peritonitis is associated with a poor prognosis and high morbidity and mortality. One problem with prospective assessment of antifungal regimens is the infrequency with which these infections occur. This makes it difficult to design and implement comparative studies. Most literature

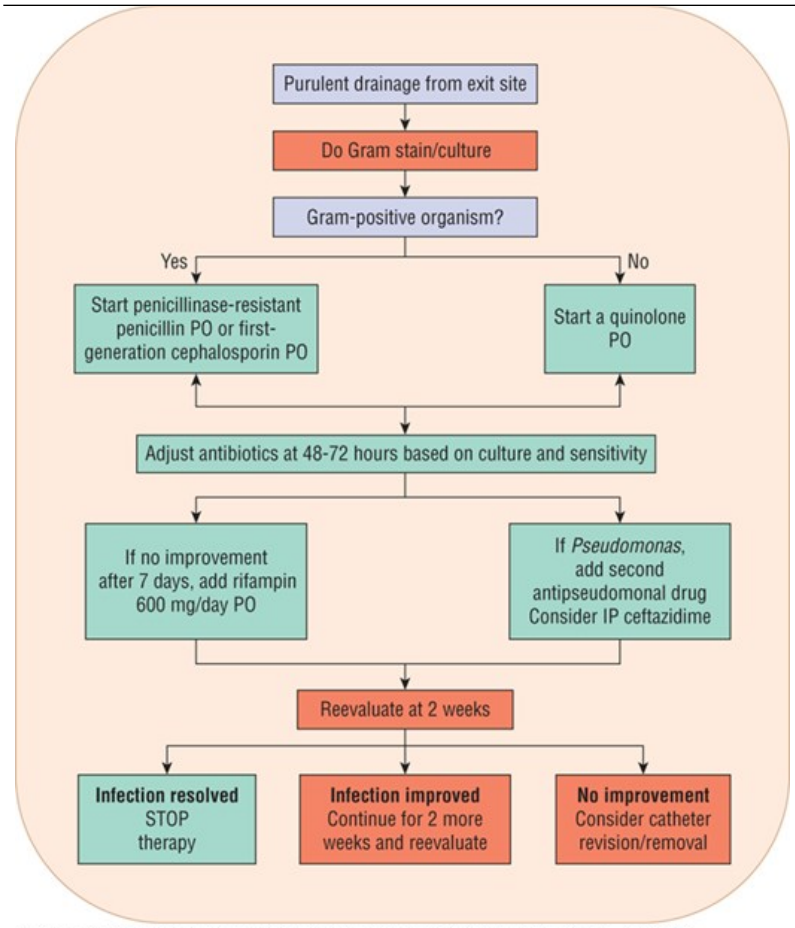
about antifungal treatment is therefore retrospective or limited to reports of local experience. As a result, the ISPD recommendations for treatment of fungal peritonitis are somewhat vague and treatment should be based on culture and sensitivity results. However, one area that has been clarified is the question as to whether the PD catheter should be removed. The ISPD recommendations are to remove the catheter immediately after identifying fungi. If the Gram stain indicates the presence of yeast, treatment may be initiated with IV amphotericin B and oral flucytosine. Once culture and sensitivity results are available, fluconazole, caspofungin, or voriconazole may replace amphotericin B. Guidelines recommend amphotericin B be administered IV and not IP as this agent can cause chemical peritonitis and pain and has poor peritoneal bioavailability. Treatment with an oral agent continues for an additional 10 days after catheter removal. It remains unclear whether there is any benefit from fungal prophylaxis. Recommendations are also provided for the treatment of mycobacterial, or tuberculous peritonitis. Although these infections are rare complications, they can be difficult to diagnose and treatment requires multiple drugs.[91]

Catheter-Site Infections

Topical antibiotics and disinfectants are effective agents for the prevention of ESIs. Gram-positive organisms should be treated with oral penicillinase-resistant penicillin or a first-generation cephalosporin such as cephalexin (Fig. 64-5). Rifampin may be added, if necessary, in slowly resolving or particularly severe *S. aureus* infections. Vancomycin should be avoided in routine or empiric treatment of gram-positive catheter-related infections but will be necessary for methicillin-resistant *S. aureus.* Treatment for gram-negative organisms consists of oral quinolones if the organism is susceptible. The effectiveness of oral quinolones may be diminished owing to chelation interactions with drugs containing divalent and trivalent ions, which are commonly taken by patients receiving dialysis. Administration of quinolones should occur at least 2 hours prior to these drugs. In cases where *Pseudomonas aeruginosa* is the pathogen, a quinolone should not be used as monotherapy. Options for a second anti-pseudomonal drug include the IP administration of an aminoglycoside, ceftazidime, cefepime, piperacillin, imipenem-cilastatin, or meropenem. In all cases, antibiotics should be continued until the exit site is normal; 2 to 3 weeks of therapy may be necessary. A patient with a catheter-related infection that progresses to peritonitis will usually require catheter removal.[91,93]

FIGURE 64-5

Management strategy of exit-site infections for peritoneal dialysis patients. (IP, intraperitoneal; PO, orally.) (*Data from Reference 93.*)



Source: Joseph T. DiPiro, Gary C. Yee, Stuart T. Haines, Thomas D. Nolin, Vicki L. Ellingrod, L. Michael Posey: *DiPiro's Pharmacotherapy: A Pathophysiologic Approach, 12e*

Prevention of Peritonitis and Catheter Exit-Site Infections

Attempts to prevent peritonitis and catheter-related infections have included refinement of connector system technology (Luer-Lok connectors), enhanced patient training techniques, and the use of prophylactic antibiotic regimens and vaccines. Several antimicrobial agents have been examined as prophylaxis against peritonitis and tunnel-related infections. Rifampin 300 mg orally taken twice a day for 5 days, then repeated every 3 months, decreased the number of catheter-related infections, but not the incidence of peritonitis. The efficacy of other antibiotic prophylaxis for peritonitis and catheter-related infections is limited but long-term, extended-duration prophylaxis with penicillins or cephalosporins is not effective.[91,93]

Nasal carriage of *S. aureus* is associated with an increased risk of catheter-related infections and peritonitis.[91,93] In addition, diabetic patients and those on immunosuppressive therapy are at increased risk for *S. aureus* catheter infections. Prophylaxis with intranasal mupirocin (twice daily for 5-7 days every month), mupirocin (daily) at the exit site, or oral rifampin can effectively reduce *S. aureus* ESIs. Because of the minimal toxicity of mupirocin and the risk of rifampin resistance, mupirocin regimens are preferred.[91,93] However, it is important to note that *S. aureus* isolates with a high degree of resistance to mupirocin have been isolated from PD patients using prophylactic mupirocin at the peritoneal catheter exit site. A recent study did not observe resistance patterns with the use of mupirocin. Patients in this study applied mupirocin to the exit site either once or thrice weekly. After 3 years, patients in the once-weekly group had an ESI (0.26 episodes/patient/year) and peritonitis (0.36 episodes/patient/year) but patients in the thrice-weekly group had an ESI (0.11 episodes/patient/year) and peritonitis (0.24 episodes/patient/year). The thrice weekly group had a significant reduction in ESIs ($P = 0.030$) and peritonitis ($P = 0.04$).[96] In addition, gentamicin cream applied daily to the exit site has been found to effectively reduce both *S. aureus* and *P. aeruginosa* ESI.[91,93] However, a comparison of mupirocin 2% and gentamicin 0.1% creams for exit-site prophylaxis noted a decrease in gentamicin susceptibility patterns for *Enterobacteriaceae* (12%) and *Pseudomonas* (14%).[97]

A retrospective study of topical chlorhexidine and mupirocin for the prevention of exit-site infections (ESIs) in patients receiving PD. Patients received

routine exit-site cleaning with 10% povidone-iodine followed by topical application to the exit site with mupirocin ($n = 162$) or chlorhexidine ($n = 175$). Patients receiving chlorhexidine had a higher rate of ESIs compared to mupirocin (0.22 vs 0.12 episodes/year) ($P = 0.048$). This study found no significant difference in time to first ESI ($P = 0.10$), rate of peritonitis ($P = 0.95$), or hospitalizations ($P = 0.21$).[98] A double-blinded, randomized controlled trial compared the use of the topical ointments mupirocin to polysporin triple (P^3; bacitracin, gramicidin, and polymixin B) in PD patients ($n = 201$) for the prevention of PD-related infections. Patients applied the ointment to the exit site with each dressing change and were followed for up to 18 months. No significant difference was found between groups for time to first PD-related infections ($P = 0.41$) for either agent but a significant increase in fungal infections was observed in the P^3 versus mupirocin group (7 vs 0; $P = 0.01$). The authors concluded that the use of P^3 for PD-related infection prophylaxis was not superior to mupirocin and may increase the risk of fungal infections.[99]

The use of polyhexanide was compared to povidone–iodine to prevent ESIs in PD patients in a single-center prospective open label study ($n = 46$). After 12 months, there was a lower rate of overall infections ($P = 0.037$) and exit-site infections ($P = 0.032$) with use of polyhexanide compared to povidone-iodine. The infection source in the polyhexanide group was identified as *P. aeruginosa* ($n = 3$), but in the povidone–iodine group ($n = 9$) three sources were identified: *S. aureus* ($n = 6$), *Corynebacterium jeikeium* ($n = 2$), and *P. aeruginosa* ($n = 1$). During the study, no infected catheters required removal.[100]

CONCLUSION

Because of the limitation of available kidneys for transplantation, HD and PD remain the most widely available and commonly used ESRD treatments. Despite continual advances in dialysis and transplantation, kidney disease is associated with significant morbidity and mortality. Given the lack of a true cure for kidney disease, emphasis has been placed on the prevention and early detection of kidney disease. Goals set by the KDOQI, the Healthy People 2020 initiative, and the Centers for Medicare and Medicaid Services' CPM Project provide guidance and direction for all healthcare practitioners. In fact, there have been significant reductions in the incidence rate of ESRD, enhanced timing and selection of the preferred access placement, and mortality and morbidity.[101,102] For patients with ESRD, a focus on quality of life and rehabilitation is now a valuable and viable goal toward which the nephrology community should direct its research resources. Several links to patient-related videos that discuss CKD patient experiences are presented in Table 64-12. Although prevention of ESRD is the primary goal for clinicians and adequate access to renal transplantation is secondary, dialysis will likely be a part of the treatment paradigm for ESRD for many years to come.

TABLE 64-12

Patient-Related Videos Relative to Renal Disease, Dialysis Procedures, and Therapies

Source	Website
Davita Inc.	www.davita.com/education/videos
NxStage Medical, Inc.	www.nxstage.com/
Fresenius Medical Care	www.freseniuskidneycare.com/tools-and-resources
National Kidney Foundation	www.youtube.com/watch?v=NHS0oyHR4vI

ABBREVIATIONS

APD	automated peritoneal dialysis
AV	arteriovenous
CAPD	continuous ambulatory peritoneal dialysis
CLcr	creatinine clearance
CPM	clinical performance measures
DHA	docosahexaenoic acid
eGFR	estimated glomerular filtration rate
EPA	eicosapentaenoic acid
ESRD	end-stage renal disease
GFR	glomerular filtration rate
HD	hemodialysis
HDF	hemodiafiltration
IDH	intradialytic hypotension
IDSA	Infectious Disease Society of America
IP	intraperitoneal
ISPD	The International Society of Peritoneal Dialysis
KDIGO	Kidney Diseases: Improving Global Outcomes
NKF-KDOQI	National Kidney Foundation's Kidney Disease/Dialysis Outcome Quality Initiative
PD	peritoneal dialysis
RRF	residual renal function
UFH	unfractionated heparin
URR	urea reduction ratio
USRDS	United States Renal Data System

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SELF-ASSESSMENT QUESTIONS

1. The most commonly used treatment for end-stage renal disease is:
   A. Home hemodialysis
   B. Continuous ambulatory peritoneal dialysis
   C. In-center hemodialysis
   D. Renal transplantation
2. In comparison to hemodialysis, peritoneal dialysis is associated with:
   A. Higher clearances of both solutes and water
   B. The need for patients to come to the dialysis clinic three times/week
   C. A lower technique failure rate
   D. The potential for better preservation of residual renal function
3. Which of the following is the most important indication for initiation of chronic dialysis therapy?

A. Elevated blood urea nitrogen concentrations (greater than 60 mg/dL [21.4 mmol/L]).

B. Estimated glomerular filtration rate less than 25 mL/min/1.73 m^2.

C. Persistent symptoms associated with worsening renal function.

D. Hyperphosphatemia.

4. Which one of the following HD vascular access methods is considered to be the most desirable to use clinically and why?

A. Arteriovenous graft, because of the desire for long lasting placement

B. Arteriovenous fistula, because of lower rates of infection and thrombosis

C. Central venous catheter, because of easy placement

D. Venous catheter, because of the desire for long lasting placement

5. Which one of the following dialysis membranes is most likely to remove larger molecular weight drugs, such as vancomycin, during hemodialysis?

A. Conventional hemodialysis

B. High-efficiency hemodialysis

C. High-flux hemodialysis

D. Peritoneal membrane

6. Which one of the following statements is true regarding peritoneal dialysis?

A. In comparison to hemodialysis, peritoneal dialysis is more efficient at removing solutes and water.

B. During peritoneal dialysis, there is countercurrent flow of blood and dialysate, which increases diffusion and convection.

C. Blood flow to the peritoneal membrane can be regulated but to a greater degree than blood flow through a vascular access in hemodialysis.

D. The peritoneal membrane functions as the semipermeable membrane.

7. To provide adequate peritoneal dialysis:

A. Weekly Kt/V should exceed 1.7 for CAPD patients.

B. Daily Kt/V should exceed 1.7 for CAPD patients.

C. Residual renal function is not considered an important factor in the Kt/V.

D. Kt/V should be at least 2.0 for patients without residual renal function.

8. RC is a 63-year-old patient with ESRD receiving outpatient hemodialysis thrice weekly and has experienced several episodes of intradialytic hypotension. Which of the following should be considered to minimize RC's intradialytic hypotension?

A. Stretching exercises

B. Anti-hypertensive medications should be taken 2 to 3 hours prior to hemodialysis

C. Discourage food and beverage intake during dialysis

D. Increase the dialysate temperature

9. The preferred route for antibiotics to treat a patient with PD related peritonitis is:

   A. Intravenous administration with dosing based on an estimated GFR of less than 15 mL/min/1.73 m^2.

   B. Intravenous administration with the dose increased by 25% for patients with urine output greater than 100 mL/day.

   C. Intraperitoneal administration of an antibiotic in one PD exchange per day in patients receiving CAPD.

   D. Intraperitoneal administration of an antibiotic with the same dose for patient receiving either CAPD or APD.

10. Which of the following is true regarding PD catheter–related infections?

   A. Topical antibiotics and disinfectants are ineffective in preventing PD catheter-related infections.

   B. Vancomycin is the antibiotic of choice for gram-positive PD catheter-related infections.

   C. PD catheter-related infections that progress to peritonitis seldom need to have the catheter removed.

   D. Gram-positive organisms should be treated with an oral penicillinase-resistant penicillin or a first-generation cephalosporin such as cephalexin.

11. A 64-year-old male who receives regular hemodialysis for the past 3 years with an AV graft has diminished blood flow through his AV graft. Which one of the following would be best to restore AV graft blood flow for this patient?

   A. Alteplase

   B. Tenecteplase

   C. Heparin

   D. 4% sodium citrate

12. AV graft blood flow for this patient has been restored and the nephrologist is discussing adding an oral agent to prevent AV graft thrombosis in this patient. Which one of the following would be best to recommend for this patient now?

   A. Warfarin

   B. Aspirin

   C. Fish oil supplement

   D. No therapy

13. A 67-year-old female hemodialysis patient receiving regular hemodialysis for the past year has had several episodes of symptomatic intradialytic hypotension that was being treated with midodrine. The patient complained of tingling in her hands and feet and subsequently stopped taking midodrine. Which one of the following would be best to recommend for this patient now?

   A. Advise the patient to take midodrine as needed.

   B. Initiate paroxetine 10 mg once daily on non-hemodialysis days.

   C. Initiate intranasal desmopressin acetate one spray three times a week.

   D. Review vital readings and current medications for this patient.

14. A 71-year-old female peritoneal dialysis patient has been diagnosed with a catheter exit-site infection and empiric antibiotic therapy needs to be initiated. Which one of the following would be best to recommend for this patient now?

A. Vancomycin

B. Rifampin

C. Cephalexin

D. Ciprofloxacin

15. The prevention of hemodialysis catheter exit-site infections requires a multistep approach that includes a topical antibiotic applied to the exit-site and/or catheter tip. Which of the following agents may increase the risk of resistant *Enterobacteriaceae* infections in patients receiving peritoneal dialysis?

A. Mupirocin ointment

B. Gentamicin cream

C. Povidone-iodine solution

D. Polysporin triple ointment

SELF-ASSESSMENT QUESTION-ANSWERS

1. **C.** In-center hemodialysis is the most common treatment for ESRD in the United States

2. **D.** Peritoneal dialysis is associated with greater potential for preservation of residual renal function than the other modalities listed

3. **C.** The decision to initate renal replacement therapy, should not only be based upon a decline in renal function below a cutoff, but based upon the development of symptoms associated with that decline in renal function and complications that arise because of it.

4. **B.** The native AV fistula has many advantages including providing the longest survival time of all blood-access devices and the lowest rate of complications such as infection and thrombosis.

5. **C.** High-flux membranes are now used in the vast majority of patients because they are capable of removing high-molecular-weight endogenous substances, such as β2-microglobulin, and medications such as vancomycin.

6. **D.** The peritoneal membrane lines the highly vascularized abdominal viscera and acts as the semipermeable membrane.

7. **A.** The most recent KDOQI guidelines recommend that patients on PD have a total *Kt/V* of at least 1.7/week, including both PD *Kt/V and* residual kidney *Kt/V*.

8. **C.** Prevention of intradialytic hypotension (IDH) should be tried with nonpharmacologic approaches before pharmacologic agents are prescribed. The ingestion of food and beverage during a hemodialysis session could increase splanchnic blood flow and a redistribution of blood volume. This change in blood flow could decrease blood pressure and result in IDH.

9. **C.** Intraperitoneal administration is the preferred route for antibiotics to treat a patient with PD related peritonitis. The drug therapy is administered directly to the infected area dwells in the peritoneum for at least 6 hours to enhance its effectiveness.

10. **D.** Treatment of PD catheter-related infections require systemic antimicrobial therapy. The ISPD guidelines recommend initial treatment with an oral penicillinase–resistant penicillin or a first-generation cephalosporin such as cephalexin for infections caused by Gram-positive bacteria.

11. **A.** To restore blood flow for an AV graft, a thrombolytic would be the best choice. Alteplase is FDA approved for the treatment of clotted or sluggish hemodialysis vascular access. Heparin and sodium citrate are used to prevent thrombus formation.

12. **D.** The KDOQI 2019 guidelines for vascular access do not recommend oral antiplatelet or anticoagulant agents to diminish the occurrence of flow dysfunction in patients with an existing AV graft. The use of antiplatelet or anticoagulant agents to maintain vascular access patency showed little to

no benefit in several studies but there was an increased risk of bleeding.

13. **D.** Patients with intradialytic hypotension should have their vitals reviewed to determine when blood pressure changes occur during a HD session. A decrease in blood pressure could be due to aggressive fluid removal or dialysate that is too warm causing vasodilation. A patient's medications should be reviewed to determine if drug therapy is contributing to hypotension. A patient taking anti-hypertensive agents may need to adjust the timing of medications to after their HD session or avoid taking on HD days.

14. **C.** Treatment of PD catheter-related infections require systemic antimicrobial therapy. The ISPD guidelines recommend initial treatment with an oral penicillinase-resistant penicillin or a first-generation cephalosporin such as cephalexin for infections caused by gram-positive bacteria.

15. **B.** Gentamicin 0.1% creams is as effective for exit-site prophylaxis but there is concern that gentamicin susceptibility may be decreased. One study found a 12% decrease in gentamicin susceptibility for *Enterobacteriaceae* when gentamicin 0.1% cream was applied topically to a PD catheter.