Section 3

Therapeutic techniques

28

Hemodialysis

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Terminology

Renal replacement therapies include dialysis and transplantation. Dialytic therapies include peritoneal dialysis (Chapter 30), an intracorporeal technique, and extracorporeal renal replacement therapies (ERRT), which include intermittent and continuous hemodialysis (Chapter 29). The principles of intermittent and continuous therapies are the same, but there are practical differences between the techniques, and the reader is referred to the chapter on continuous renal replacement therapy for further information.

The basic premise of ERRT involves withdrawing blood from the patient, circulating it through a dialyzer composed of a semi-permeable membrane to allow removal of uremic toxins, and returning the cleansed blood to the patient. By creating a continuous loop of blood circulation, although only a portion of the blood volume is out of the patient at any given time, the entire blood volume is circulated through the dialyzer many times over during the course of the treatment. At the conclusion of the treatment, the blood in the circuit is generally returned to the patient. Dialysate may be circulated through the dialyzer to allow diffusive clearance (hemodialysis), or fluid may be removed from the patient to allow convective clearance (hemofiltration), or both techniques may be used simultaneously (hemodiafiltration). Intermittent hemodialysis relies on diffusive clearance, but may include hemofiltration. Continuous therapies may be diffusive, convective, or both.

In this chapter, the term dialysis is used to indicate peritoneal dialysis (PD), intermittent hemodialysis (IHD), and continuous renal replacement therapy (CRRT), and the term extracorporeal renal replacement therapy (ERRT) is used to include intermittent and continuous hemodialysis therapies.

Nephrology and Urology of Small Animals. Edited by Joe Bartges and David J. Polzin.

Epidemiology

Who to dialyze and when

In veterinary medicine, dialysis is used most commonly for acute kidney injury (Chapter 49). Dialysis is indicated for patients with anuria or oliguria, life-threatening fluid overload (i.e., pulmonary edema), or hyperkalemia (Chapter 62), if attempts to induce urine production are unsuccessful. In human pediatric patients, fluid overload (>10%) is associated with a worse outcome (Gillespie et al. 2004; Goldstein et al. 2005). Uremic symptoms, progressive azotemia, or azotemia that does not improve with standard medical therapy are indications for dialysis, even if urine output is adequate or increased. In one human study, nonoliguric patients were referred for dialysis later during hospitalization compared to oliguric patients, and they suffered a worse outcome (Liangos et al. 2005). Whether initiating dialysis early in the course of AKI improves outcome compared to later initiation is unresolved. Some studies have shown an advantage to early initiation, although others have not (Gettings et al. 1999; Bouman et al. 2002; Liu et al. 2006). However, these studies are all confounded by differences in defining early versus late, only one was randomized, and cohort size was generally small. In many situations, AKI is reversible, and because there are no studies that clearly predict which patients will need dialysis, it is possible that results of studies on early versus late initiation will be biased toward early initiation because of inclusion of patients in the early group that did not need dialysis (Waikar and Bonventre 2006). Despite the lack of an adequate study to answer this question, waiting until uremic symptoms are severe and patient condition has deteriorated may be disadvantageous, but the risk of early initiation in a patient

that may not need dialysis must be weighed against the potential risks and cost of ERRT.

Dialysis is reserved until standard medical management has been attempted. Standard medical management includes adequate volume expansion. Because dehydration of less than 5% cannot be clinically detected, patients that appear normally hydrated but not overhydrated should receive a dose of IV fluid equal to 5% of body weight. The systemic blood pressure should be adequate to perfuse the kidneys (>80–100 mmHg systolic or >60–80 mmHg mean arterial pressure). The use of diuretics is widespread in both human and veterinary medicine despite lack of conclusive evidence of a positive impact on outcome (Bagshaw et al. 2008). Loop diuretics, specifically furosemide, are most commonly used. If loop diuretics, osmotic diuretics (i.e., mannitol), or other diuretics fail to induce adequate urine production within hours, early referral for dialysis is appropriate.

In people, hemodialysis is used primarily to treat end-stage renal disease (Stage V chronic kidney disease; Chapter 48). People may be maintained on chronic hemodialysis for years while waiting for a renal transplant (Chapter 31) or for decades if transplantation is not possible. Transplantation is generally preferred over chronic hemodialysis, as it more completely replaces renal function, but transplantation is not readily available for dogs. Chronic hemodialysis is an alternative in those cases and in cats in which there are clear contraindications to transplantation. The goal of chronic hemodialysis is to maintain a satisfactory quality of life, which should take precedence over longevity. Chronic hemodialysis should be recommended when the signs of uremia are no longer controlled by medical management (Chapter 41). The serum creatinine concentration is generally over 5 mg/dL. In some patients, the main sign of uremia is anorexia. If few other uremic signs are present or can be controlled, placement of a feeding tube prior to initiating dialysis may be prudent. Although patients may decompensate acutely and unpredictably, the decision to initiate chronic dialysis ideally should be planned in advance, allowing scheduling of surgical placement of a permanent hemodialysis catheter in conjunction with feeding tube placement. Although return of a normal appetite is expected with adequate dialysis, anorexia can be expected during prolonged interdialysis intervals, when catheter function is temporarily inadequate, or when concurrent illness is present, and use of a feeding tube during those times allows better over all patient care.

Outcome

Overall survival of dogs and cats treated with hemodialysis for AKI is 41–52%, but survival is dependent on etiology, with infectious and ischemic causes faring better than toxic causes, in general (Table 28.1) (Langston et al. 1997; Adin and Cowgill 2000; Francey and Cowgill 2002; Fischer et al. 2004b; Pantaleo et al. 2004; Francey 2006a). Of the nonsurviving patients, about half of those die or are euthanatized due to extra-renal conditions (e.g., pancreatitis, respiratory complications). About a third of nonsurvivors are euthanized due to failure of recovery of renal function. On going uremic signs, dialysis complications, and unknown causes account for the remaining patient deaths. Of the surviving patients, approximately half regain normal renal function (defined by normal serum creatinine concentration) and half have persistent chronic kidney disease.

Table 28.1 Survival rates with intermittent hemodialysis for various etiologies of renal failure

Category	Survival rate
Obstructive (cats)	70–75%
Infectious	58–86%
Metabolic/hemodynamic	56–72%
Other	29–56%
Toxic	18–35%

A clinical scoring system for outcome prediction of dogs with AKI receiving hemodialysis has been developed (Chapter 49). The model uses data that is commonly available prior to instituting dialysis, although knowledge of the specific etiology, which is frequently not known initially, improves the accuracy of the outcome prediction. Although this scoring system has not yet been independently validated and should not be used in the decision-making process for an individual patient, use of scoring systems will hopefully help in determining appropriate candidates for dialysis (Segev et al. 2008).

Equipment

Vascular access

Catheter design

An adequately functioning dialysis catheter allows smooth and efficient treatment and patient management; a poorly functioning catheter frustrates the technician, doctor, and patient. In veterinary medicine, catheters are the predominant form of vascular access. Much thought and care should go into choosing the appropriate catheter, placing it, and maintaining it.

A variety of materials can be used to make a catheter that is minimally thrombogenic, flexible, and nonirritating to the vessel wall. Polyurethane, polyethylene,

polytetrafluoroethylene (PTFE), silicone, and carbothane are suitable choices. Polyethylene is stiff and kinks when bent. It can be used for temporary catheters but is not appropriate for long-term use (Ash 2007). Polyurethane has some rigidity at room temperature, which assists in placement, but it becomes softer and more flexible at body temperature. Alcohol containing antibiotic ointments will weaken the material (Ash 2007).

To allow simultaneous removal and return of blood, a dialysis catheter has two lumens. Although catheters are placed in a central vein, the lumen that provides blood egress from the body is generally referred to as the "arterial" port, and the lumen that provides blood return to the body is termed the "venous" port. The arterial lumen is usually shorter than the venous return lumen, to avoid uptake of blood returning from the dialyzer (access recirculation), which would decrease the efficiency of treatment (Figure 28.1). In some situations, two single lumen catheters are placed to provide blood egress and return, either in separate vessels or in the same vessel. In lumens with a single opening (either at the tip or a side port), partial occlusion from thrombosis or a fibrin sheath can decrease catheter function to the point of being unable to provide adequate dialysis. The risk of complete occlusion is lessened by having multiple ports (Figure 28.2). If the ports are positioned circumferentially around the catheter, even if the vessel wall is sucked against the ports on one side of the catheter, blood flow can continue on the opposite side. If the side ports are small, blood will preferentially flow through the tip, making the side ports superfluous. If the side ports are large, they weaken the catheter and increase the amount of heparin that diffuses out of the catheter between dialysis treatments (Depner 2001).

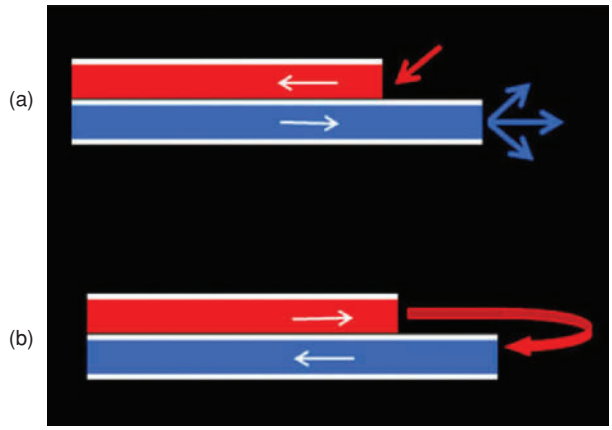

Figure 28.1 Configuration of arterial and venous lumen catheter tips. The tip of the "arterial" port, or intake port, is shorter than the "venous" port, or blood return port (1A). If the connections are reversed (1B), there is a greater percentage of returned blood that is immediately recirculated through the catheter.

Figure 28.2 Common ERRT catheter configurations. (a) and (b) are tunneled cuffed catheters. (c) is a nontunneled noncuffed catheter ("temporary"). (d) shows catheter C rotated 90° to demonstrate placement of multiple openings. (e) is a split tip catheter. Cross-section of lumen configurations on right.

A double D configuration provides the highest lumen volume with lowest surface contacting the blood to diminish shear stress, while maintaining a modest outer circumference (Ash 2007). Other configurations are commonly used, however, including round or C-shaped lumens (Figure 28.2) (Wentling 2004). Temporary catheters are generally designed with a tapering tip to facilitate percutaneous placement. Permanent catheters may have the tips separated, such that the intravenous portion acts like two separate catheters placed in the same vein, whereas the external portions are bound together. By having separated tips, side ports can be placed circumferentially, and the increased flexibility of the tips and their movement with each cardiac cycle may help decrease fibrin sheath formation (Depner 2001). An arteriovenous fistula or graft is the preferred access in people receiving chronic hemodialysis. An artery is surgically anastomosed to a vein with a section of autologous vein or synthetic graft (typically, PFTE). Within approximately a month, endothelial cells line the graft, and the endothelial cells of the autologous vein segment take on characteristics of arterial endothelium instead of venous. The access can be then used by percutaneous puncture of the arterial and venous segments with large gauge needles at each dialysis treatment. Between treatments, no anticoagulant is needed because blood is continually flowing through the graft/fistula. Because it is completely enclosed under the skin, the infection rate is extremely low in comparison to catheters. A model of AV fistula has been developed for canine hemodialysis, and a brachial-cephalic access could be considered for dogs receiving chronic dialysis (Adin et al. 2002).

Catheter placement and care

Temporary, nontunneled catheters can be placed in an operating room, but are frequently placed in a clean

Table 28.2 Common ERRT catheter specifications and approximate blood flow rates[a]

Manufacturer	Type	Lumens	Fr size	Length (cm)	Max blood flow (mL/min)
Quinton PermCath	Cuffed	2	15	45	370
Quinton PermCath	Cuffed	2	15	40	400
Quinton PermCath	Cuffed	2	15	36	410
MedComp Pediatric	Cuffed	2	8	18	120
Hohn	Cuffed	2	7	36	30
MedComp Temporary	Noncuffed	2	11.5	24	360[b]
Arrow[c]	Noncuffed	2	7	20	100
Arrow, 20 ga lumen[c]	Noncuffed	3	5.5	13	40
Arrow, 22 ga lumen[c]	Noncuffed	3	5.5	13	20
Arrow, 20 ga lumen[c]	Noncuffed	3	5.5	8	50
Arrow, 22 ga lumen[c]	Noncuffed	3	5.5	8	30
Intracath through the needle[c]	Noncuffed	1	19 ga	30.5	20

[a]Maximum blood flows determined in vitro using canine packed red blood cell solution (29% packed cell volume). Arterial chamber pressure maintained at −250 mmHg or higher. Maximum blood flow rates in vivo may be lower.
[b]Maximum blood flow determined in vivo.
[c] Not designed for dialysis.

procedure room. Caps, masks, gowns, gloves, and a large sterile drape should be used to maintain sterility during placement. Sedation and/or a local anesthetic may be necessary depending on the patient's clinical status and demeanor. These catheters are usually placed percutaneously (or through a small skin incision) with a guidewire using the Seldinger technique. Temporary hemodialysis catheters are intended for acute dialysis of less than a few weeks duration.

So-called permanent hemodialysis catheters have an external cuff, generally made of Dacron. The catheter is placed with a portion in a subcutaneous pocket, which separates the site where the catheter exits the skin from the site where the catheter enters the vessel by several centimeters. The Dacron cuff is positioned in this subcutaneous pocket and allows fibroblasts to adhere, thus securing the catheter in place and decreasing bacterial migration to the vessel. These catheters are intended for use for up to two years.

Cuffed, tunneled hemodialysis catheters should be placed in an operating room with full sterile technique. Although they can be placed with sedation and a local anesthetic in humans, general anesthesia is generally used when placing permanent catheters in veterinary patients. A skin incision is made over the vessel, and the jugular vein is cleared of all fascia. A separate small incision just large enough to allow placement of the catheter is made through the skin at the exit site. The tip of the catheter is placed through this incision and tunneled under the skin to exit at the skin incision over the vessel. A small venotomy incision is made and the catheter introduced into the vessel and advanced. Alternately, the catheter can be tunneled under the skin and exit a small incision near the vessel. Instead of dissecting to the vessel for a venotomy, a guidewire can be placed into the vessel, followed by placement of a dilator inside a sheath. The dilator is removed and replaced with the catheter, and the sheath peels away, leaving the catheter in place. An esophagostomy or gastrostomy feeding tube is frequently placed at the same time as catheter placement.

The largest catheter that can be placed is preferred. Flow is proportional to the catheter diameter and inversely proportionally to catheter length. Minor changes in catheter diameter have very large changes in flow, based on Poiseuille equation: $Q_b = k \cdot P \cdot D^4/(L \cdot V)$, where Q_b is blood flow, k is a proportionality constant, P is the change in pressure, D is the luminal diameter, L is catheter length, and V is blood viscosity. A 19% increase in diameter doubles the blood flow; a 50% increase in the diameter of the catheter increases the flow five-fold (Depner 2001). Approximate blood flow rates for various catheters are presented in Table 28.2. For intermittent treatment, the catheter should ideally provide over 15 mL/kg/min blood flow. Flow rates of 3–5 mL/kg/min are adequate for CRRT.

With any method of placement, flow through both lumens of the catheter should be brisk when aspirated with a large syringe. Fluoroscopic guidance is helpful to ensure that the tip of the catheter is appropriately placed at the junction of the cranial vena cava and right atrium. If fluoroscopy is not used during placement, a postprocedure radiograph to confirm accurate placement should be performed.

The ERRT catheter should be used only for ERRT procedures and should be handled only by ERRT personnel. At each ERRT treatment, the exit site should be inspected and cleaned with antiseptic solution. When the ERRT catheter is accessed at the beginning and end of each ERRT treatment, or at any other time, the catheter ports should receive an aseptic scrub for 3–5 minutes. The ERRT technician should wear examination gloves and a mask when opening or closing the catheter. When not in use, the catheter is bandaged in place.

Between ERRT treatments, each lumen of the catheter is filled with an anticoagulant solution. Unfractionated heparin is currently used most commonly. A concentration of 500–1,000 unit/mL is generally used for cats, and 1,000–5,000 u/mL for dogs. A portion (15–20%) of the instilled heparin will diffuse out of the tip of the catheter (Sungur et al. 2007). An alternative locking solution is sodium citrate. A 4% trisodium citrate solution has similar rates of catheter thrombosis, dysfunction, and infection compared to 5000 u/mL heparin locking solution, with fewer episodes of major systemic bleeding (Grudzinski et al. 2007; MacRae et al. 2008). Higher citrate concentrations (>30%) are also antimicrobial (Weijmer et al. 2002; Weijmer et al. 2005). Any locking solution should be removed prior to the next use of the catheter, but with catheter malfunction, it is sometimes not possible to aspirate the locking solution. Injection of a highly concentrated (46.7%) citrate solution may cause symptomatic hypocalcemia and sudden death. Aspirin is routinely used in veterinary patients as an antiplatelet agent (0.5–2 mg/kg PO q 24 h in dogs, q 48 h in cats) to decrease catheter-associated thrombosis. Catheter function can decrease over time if thrombosis or stenosis occurs gradually, or it can decline abruptly. A simple way of monitoring function at each dialysis treatment is recording the blood speed when the pressure in the arterial chamber (pre-pump) is −200 mmHg. A gradual decline in the blood speed at a standardized pressure predicts catheter malfunction. The arterial pressure should be maintained above −200 to −250 mmHg, because at more negative values, the pump speed indicated on the machine is likely higher than the actual blood flow (Depner 2001).

Access recirculation decreases the efficiency of treatment by "diluting" the blood being withdrawn with blood that has just returned from the dialyzer and has a low concentration of uremic solutes. With the extracorporeal circuit blood lines attached in the normal configuration, recirculation is usually less than 5%, but reversing the connections such that blood is withdrawn from the distal port ("venous") increases recirculation to 13–24% (Carson et al. 2005). If the blood flow rate that can be achieved in this reversed configuration is much greater than the blood flow rate in the normal configuration, the increase in flow more than offsets the decrease in efficiency (Carson et al. 2005). During initial IHD treatments when efficiency is purposefully limited to decrease complications, the blood lines may be reversed to create recirculation.

Access recirculation can be measured by a variety of techniques, all of which seek to alter the venous line blood in some fashion and then detect the presence of altered blood in the arterial line blood. Some alterations include dilution with saline (detected by ultrasound or light transmission), change in temperature (cooling) or conductivity (added hypertonic saline), and hemoconcentration (via ultrafiltration) (Sherman and Kapoian 2008). The indicator dilution method is the most accurate method of determining access recirculation (Transonic Systems, Inc., Ithaca, NY). Injection of a bolus of saline in the venous line will dilute the blood, which will be detected by an ultrasonic sensor placed on the venous blood line. If there is recirculation, the blood entering the arterial line will also be diluted, to a smaller degree, which is measured by an arterial line ultrasonic sensor. The percent of blood recirculation is then calculated by the machine. Hemoglobin monitors (i.e., Critline III TQA, Hemametrics) can detect access recirculation by injection of saline first in the venous line, followed by saline injection in the arterial line, but are not accurate measures of recirculation compared to ultrasonic dilution technique (Lopot et al. 2003). Some dialysis machines have incorporated technology to automate measurement, utilizing changes in dialysate in lieu of injection of a substance directly into the blood line, and include use of temperature or conductivity changes. These measurements can be made repeatedly throughout the dialysis treatment.

Catheter complications

Despite the use of the least thrombogenic materials possible, hemodialysis catheters have a high rate of thrombosis. Thrombosis may be intraluminal or extraluminal. Both ports of the catheter should be flushed with saline or heparinized saline after every use (approximately 10–12 cc for a large catheter, 3–6 cc for smaller gauge catheters) to prevent intraluminal thrombosis. Each port is then filled with the locking solution (heparin, citrate, or other). Systemic anticoagulation has not been shown to decrease intraluminal thrombosis (Beathard 2001). Treatment of thrombosis should be initiated as soon as detected. Delays in treatment may decrease the adequacy of dialysis and may allow the thrombus to enlarge. Signs of intraluminal thrombosis include inadequate blood flow during dialysis, or an inability to aspirate the catheter. A first step to attempt is forceful flushing of the catheter with saline.

Dislodgement of the thrombus does not appear to cause clinically relevant pulmonary thromboembolic disease (Beathard 2001). If a saline flush does not restore catheter flow, tissue plasminogen activator (tPA) can be instilled in the occluded lumen (Alteplase, CathFlow, Genentech). The lumen is aspirated after a 10 minute dwell time, and if the thrombus is not aspirated, the dwell time is prolonged to 1–2 hours, with intermittent aspiration. If the catheter can be cleared sufficiently to perform a dialysis treatment, but flow remains suboptimal, tPA can be instilled in the catheter lumen for up to 48 hours and removed at the start of the next dialysis treatment (Lok et al. 2006). In our experience, tPA dwell protocols are successful in allowing sufficient blood flow to perform a dialysis treatment, but the effects are short-lived, with re-treatment or catheter replacement being necessary within a week.

Other methods of improving function of an occluded or partially occluded catheter include mechanical disruption. A guidewire can be placed in the catheter to dislodge a thrombus at the tip of the catheter, but is less effective at dislodging thrombi that have formed at side ports.

Extraluminal thrombi include thrombi that form around the tip of the catheter and may be attached to the vessel wall, and thrombi in the right atrium. These thrombi may act as a ball valve, allowing infusion but occluding the catheter and preventing aspiration. Thrombi in the right atrium and in the cranial vena cava near the heart may be imaged with echocardiography (Figure 28.3). Risk factors for thrombosis include venous stasis (from volume depletion, hypotension, immobilization, CHF), enhanced coagulability, and vessel wall trauma (Liangos et al. 2006). In our experience, over 50% of patients with a catheter in place for over 3 weeks have thrombus formation, based on routine surveillance. Thrombi can be detected echocardiographically in about 20% of our patients within 1 week of catheter placement, although catheter flow problems become apparent around 2 weeks after catheter placement.

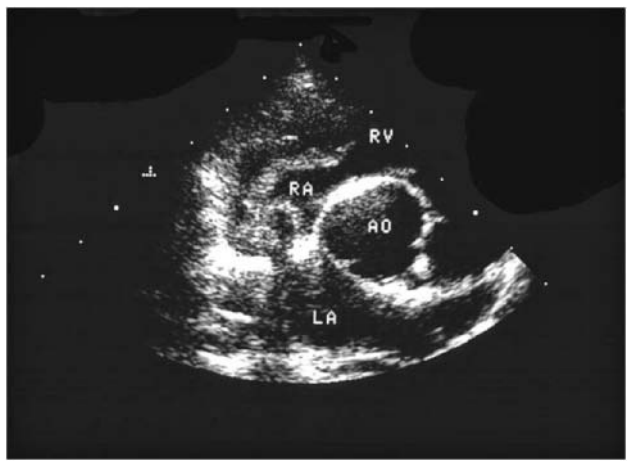

Figure 28.3 Echocardiogram of thrombus on tip of dialysis catheter. Thrombus is visible in the right atrium (RA), trailing into the right ventricle (RV). AO, aorta; LV, left ventricle.

Prophylactic administration of aspirin or warfarin decreases catheter thrombosis when compared with no treatment. Bleeding complications were more common with warfarin, and its routine use is not recommended for thrombus prevention (Willms and Vercaigne 2008).

If a small mural or right atrial thrombus is detected, the recommendation for people is 6 months of systemic anticoagulation. If the thrombus is large, the catheter should be removed and systemic anticoagulation started with unfractionated or low-molecular weight heparin for 5–7 days and warfarin for at least 1 month. If the thrombus is large and infected, surgical thrombectomy is recommended (Liangos et al. 2006). In veterinary patients, a long-standing thrombus may become covered with endothelium or fibrous tissue. Surgical removal has not been attempted in veterinary patients.

A sheath of fibrin may form around the catheter within 24 hours of placement, and this form of obstruction accounts for 38–50% of catheter malfunctions in people (Figure 28.4) (Liangos et al. 2006). In people, tPA infusion should likely be specified here. Infusion through the dialysis catheter over 2–3 hours during or after a dialysis treatment may be effective in disrupting a fibrin sheath (Lok et al. 2006).

Thrombolytic infusion to dissolve extraluminal thrombi or a fibrin sheath has been used with variable results in veterinary patients. A technique of fibrin sheath stripping involves placement of a femoral catheter advanced to cranial vena cava. A snare is used to encircle the fibrin sheath around the dialysis catheter and gently remove the sheath. This technique has not been attempted in veterinary medicine.

Replacement of the catheter over a guidewire is a simple and effective method of treating intraluminal thrombosis or fibrin sheath formation. A guidewire is placed in the dysfunctional catheter. If angiography is desired, the catheter is partially removed, leaving the tip within the vessel, and contrast agent is injected through the catheter. If a fibrin sheath is detected, the old catheter is removed and a balloon catheter inserted over the guidewire. The balloon is inflated to disrupt the fibrin sheath. A new catheter is placed over the guidewire, through the same exit site and subcutaneous tunnel (if present). Disrupting the fibrin sheath with catheter replacement has better results than catheter replacement alone in people (Oliver et al. 2007).

Careful attention to asepsis is necessary during the entire procedure. If angiography is not performed,

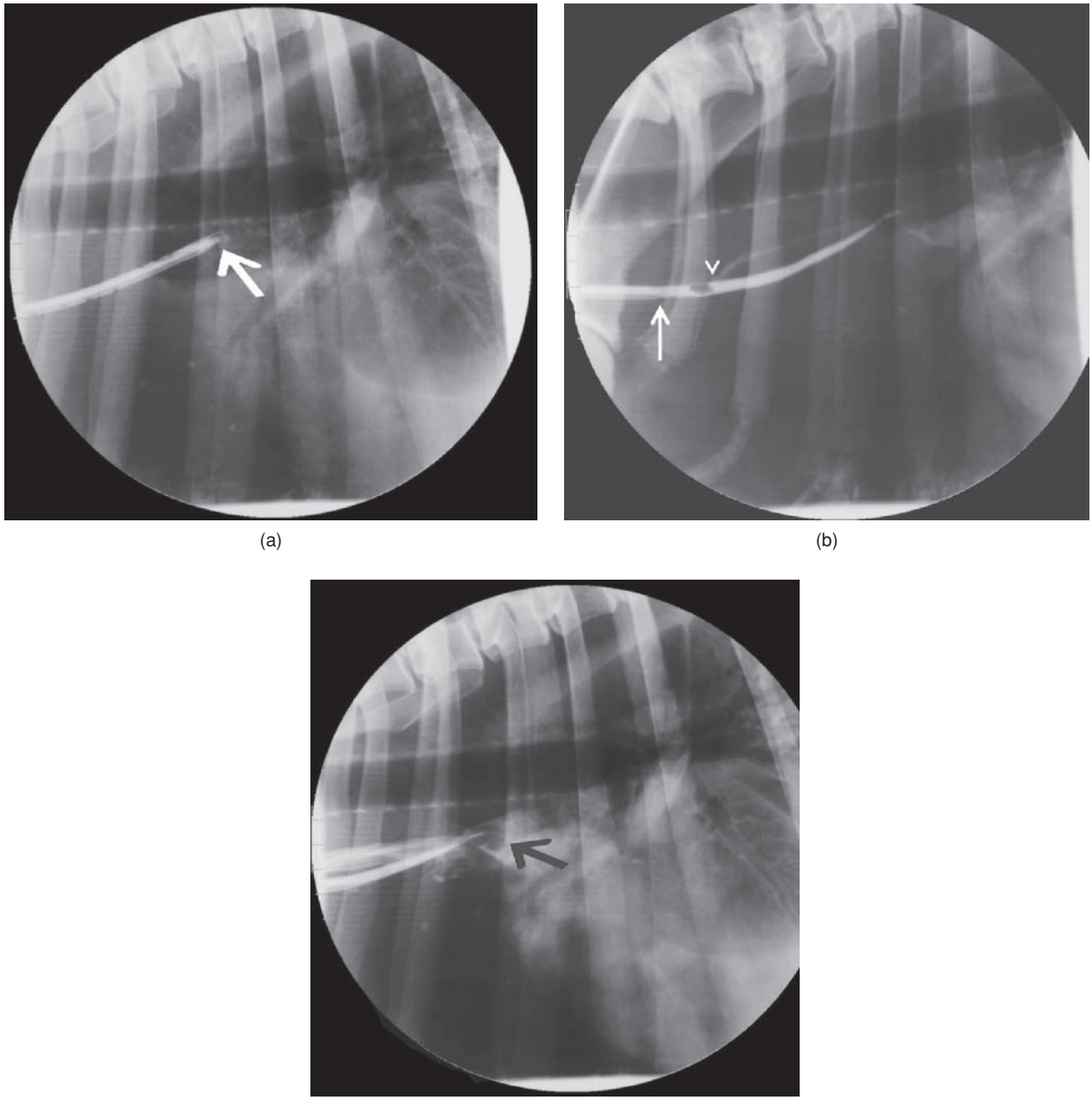

Figure 28.4 Nonselective angiogram of fibrin sheath. (a) Dialysis catheter is visible in cranial vena cava. The distal tip of the catheter is indicated by white arrow. (b) Catheter was partially retracted (distal tip indicated by white arrow) and contrast was injected through the catheter. A very narrow stream of contrast is visible within the fibrin sheath, with a breach in the fibrin sheath (arrowhead) allowing contrast to stream out of the sheath and into the surrounding cranial vena cava. (c) Contrast in and around the fibrin sheath demonstrates partial filling of the cranial vena cava. A filling defect (black arrow) indicates a thrombus that was at the tip of the dialysis catheter.

catheter replacement over a guidewire can be performed in the dialysis unit if needed.

Central venous stenosis occurs in 27–38% of human patients but is frequently asymptomatic (Liangos et al. 2006). The incidence and significance of this condition in veterinary patients is unknown, but facial edema, which can be a sign of cranial vena caval stenosis or obstruction, is a common finding in dogs receiving hemodialysis and stenosis may cause a marked decrease in dialysis treatment efficiency.

Infections are the most frequent serious complication of catheter use in people and are discussed more thoroughly in "Patient Management" section later (Himmelfarb et al. 2005). Inadvertent catheter dislodgement is an

infrequent complication. During each dialysis treatment, the extracorporeal tubing is securely taped to a harness placed on dogs or directly to the forelimb in cats so that exuberant motion of the patient does not unduly stress the sutures anchoring the catheter in place.

Dialyzer

Almost all dialyzers used today are configured with the semi-permeable membrane arranged in hollow fibers. Blood flows through the center of the fibers, and the fibers are bathed in dialysate. This configuration provides a large surface area for diffusive clearance while minimizing the volume of blood used to fill the dialyzer. The fibers are held in place by potting material (termed header or footer, depending on position), and careful design helps allow blood to completely fill every fiber equally. Blood enters at the top of the dialyzer and exits at the bottom. Dialysate generally enters at the bottom and exits at the top, in order to maintain a countercurrent flow pattern that maximizes the concentration gradient across the length of the dialyzer.

The most common methods of dialyzer sterilization are ethylene oxide gas, heat, or gamma-irradiation, although some membranes cannot withstand heat sterilization (Hoenich and Ronco 2008a). All dialyzers need to be rinsed prior to use to remove any sterilant byproducts and microorganisms killed by the sterilization process (Hoenich and Ronco 2008a). In veterinary medicine, dialyzers are used for one dialysis treatment and then discarded. For people receiving chronic hemodialysis, a dialyzer may be rinsed, disinfected, and reused for up to 30 treatments in the same individual. Advantages of dialyzer reuse include cost savings (although the cost of disinfecting offsets replacement cost) and decrease in bioincompatibility reactions (see below). Disadvantages include increased time and equipment for the disinfection process, risk of infection, and risk of exposure of the patient to the disinfectant.

Semi-permeable membranes can be categorized as cellulosic, modified cellulosic, or synthetic. Cuprophane is an example of a cellulosic membrane. Modified cellulosic membranes, such as hemophan, have substituted hydroxyl groups with a substance less likely to activate the patient's complement system (Hoenich and Ronco 2008a). Although hemophan was the most commonly used dialyzer membrane in early years in veterinary dialysis, synthetic membranes are used almost exclusively now. Synthetic membranes have larger pores and allow better middle molecule clearance. They are also less reactive, thus decreasing bioincompatibility reactions. Examples of synthetic membranes include polysulfone, polymethylmethacrylate (PMMA), polycarbonate, polyamide, polyacrylonitrile and methallyl sulfonate (AN-69), and polyacrylonitrile polyacrylonitrile (PAN).

The ideal pore size in a dialyzer would allow easy passage of small- to middle-sized uremic toxins while restricting loss of albumin. Cellulosic and modified cellulosic membranes have smaller pores than synthetic membranes, which limits clearance of middle molecules. Synthetic membranes are thicker than cellulose-based membranes (20–55 μm versus 5–11 μm). The synthetic membranes have an asymmetric structure, with a dense blood contact surface and more open supporting structure (Hoenich and Ronco 2008a). Most dialyzer membranes have limited adsorptive capacity.

During the course of dialysis, blood is exposed to the dialysis catheter, blood lines, potting material of the dialyzer, the dialyzer membrane, and any contaminants in the water or dialysate. Any of these could potentially cause an adverse reaction. However, the dialysis membrane has the largest surface area and is the most likely component to induce the strongest biologic reaction. Cellulosic materials generally induce the strongest reaction, although clinically significant reactions may occur with the more biocompatible synthetic membranes.

Exposure of blood to the dialysis membrane activates the complement cascade, which activates the coagulation cascade. In addition to causing inflammation and thrombosis, contact proteins activated by exposure to the dialysis membrane convert high molecular weight kininogen to kinin. The kinins, including bradykinin, increase vascular permeability, diminish arterial resistance, and mediate inflammatory responses.

Within 15 minutes of starting dialysis, neutrophil and platelet counts decrease as these cells become sequestered in the pulmonary capillaries. The effect of a bioincompatibility reaction on lymphocytes is fairly minimal. Macrophages/monocytes play a more prominent role in this phenomenon. Monocytes become activated and increase production of cytokines such as interleukin-1β, tumor necrosis factor α, and interleukin-6. Within 3 to 4 hours, neutrophil and platelet counts return to pretreatment values. Neutrophil and platelet aggregation in the pulmonary capillaries impairs oxygen transport. Additionally, complement components induce airway and vessel constriction and increase edema in the lungs due to an increase in permeability, further decreasing oxygen transport. Other clinical signs of a dialyzer reaction include hypertension, hypotension, dyspnea, cough, sneezing, wheezing, choking, rhinorrhea, conjunctival injection, headache, muscle cramps, back pain, abdominal pain, chest pain, nausea, vomiting, fever, chills, flushing, urticaria, pruritis, and death (Jaber and Pereira 2005; Hoenich and Ronco 2008b).

Complement activation can be decreased by cooling the blood, which can be achieved by setting the dialysate temperature slightly lower than body temperature. Adhesion of proteins such as albumin to the dialyzer membrane decreases the bioincompability reaction, and subsequent reuse of dialyzers reduces the reaction. Since synthetic membranes are much less likely to induce significant first use reactions, reuse is becoming less common in human hemodialysis.

Clearance of a dialyzer is the volume of blood completely cleared of a certain solute during a single pass through the device and is identical to the concept of clearance in the kidney. Dialyzer clearance is calculated by measuring the concentration of the substance at the inlet and outflow of the dialyzer, at standardized blood flow (usually 200, 300, and 400 mL/min), dialysate flow (500 mL/min), and ultrafiltration (0) rates. Clearance of urea, creatinine, phosphorus, vitamin B12, and inulin are commonly reported, as substances of interest, or markers of other solute clearance (i.e., vitamin B12 (MW 1355 Da) and inulin (MW 5200 Da) as markers of middle molecule clearance). Clearance is reported in mL/min and abbreviated $K_{d[solute]}$. Dialyzer specification data is derived from in vitro measurements, and actual performance is generally slightly lower.

The coefficient of ultrafiltration (K_{UF}) is a measure of the hydraulic permeability of the membrane, or the water flux. It is the number of milliliters of water that can be removed per hour for each 1 mmHg transmembrane pressure (the difference in hydraulic pressure between the blood compartment and the dialysate compartment). Dialyzers with a higher K_{UF} can remove larger volumes of fluid from the patient in a given time with a lower transmembrane pressure. In the average veterinary dialysis patient, even dialyzers with a low K_{UF} can remove adequate volumes of fluid to normalize patient hydration. Because of the decrease in hydrostatic pressure from the top to the bottom of the blood fibers, and because of the increase in oncotic pressure at the bottom of the dialyzer due to ultrafiltration and the resultant hemoconcentration, it is possible to get back-filtration at the bottom of the dialyzer. Back-filtration allows endotoxins or other contaminants from the dialysate to enter the blood compartment. Back-filtration is more likely to occur when a dialyzer with a high K_{UF} is used without ultrafiltration. In order to prevent this from occurring when a dialyzer with a high K_{UF} is being used, a nominal rate of ultrafiltration should always be applied, with intravenous fluid replacement if the patient does not need fluid removal.

High-flux dialyzers are characterized by a membrane with larger pore size, which possess high ultrafiltration coefficients and permits clearance of middle molecules (Jaber and Pereira 2005; Yeun and Depner 2005). High-efficiency dialyzers have high urea clearance by virtue of the large surface area, but they also have a larger priming volume (Table 28.3).

Extracorporeal circuit

Extracorporeal circuit is the tubing that carries the blood from the catheter to the machine and dialyzer and returns it to the patient. It should be made from a nonthrombogenic material. The pressure in the extracorporeal circuit before and after the dialyzer is routinely monitored by the dialysis machine, to detect any unsafe conditions, such as a line disconnection or occlusion. Any air–blood interface creates a potential site for thrombosis. The dialysis machine detects any air bubbles in the venous return segment, which triggers automatic clamping of the blood line until the situation is corrected. The volume of blood contained in the extracorporeal circuit depends on the specific tubing used and should be selected based on the patient's size.

Dialysate

Dialysate is the solution that bathes the blood-filled hollow fibers in the dialyzer. It is physiologically similar to the aqueous portion of plasma. A typical IHD treatment uses 150 L of water for dialysate. Contaminants in the water can diffuse into the bloodstream, and as discussed above, some small volume of dialysate may enter the blood compartment via back-filtration. Multiple steps are involved in purifying water used for dialysate.

Water quality

The appropriate design of a water treatment system depends on the quality of source water and may include all or most of the following components. A filter, such as a mixed bed multimedia filter, removes particulate matter in the water. An ion exchanger absorbs cations and anions and releases sodium and chloride in exchange. The predominant ions removed in this fashion are calcium and magnesium. Carbon filtration adsorbs organic toxins, including chlorine and chloramines. A small filter is placed after the carbon tanks to catch small particles of carbon that became dislodged. Reverse osmosis is usually the final step in water purification. Pressure applied to the water forces it through a semi-permeable membrane that excludes contaminants. Deionization can be used instead of reverse osmosis. With deionization, cations are bound to the resin, releasing H^+, and anions are bound, releasing OH^-. All of the pipes and materials the water contacts should be PVC, stainless steel, or glass to avoid leeching of potentially toxic components (such as copper or zinc). There should be no dead-end loops in the system because

Table 28.3 Common dialyzers used in veterinary ERRT

Manufacturer/ machine	Dialyzer	Membrane	Surface area (m^2)	Priming volume — dialyzer (mL)	Priming volume — dialyzer and tubing (mL)	Kd_{urea} (mL/min)	Kd_{creat} (mL/min)	Kd_{phos} (mL/min)	Kd_{B12} (mL/min)	K_{UF} (mL/h/mmHg)
Conventional										
Gambro	100HG[bcd]	Hemophan	0.22	18		102	82	69	25	2.0
Fresenius	F3	Polysulfone	0.4	28		125	95	50	20	1.7
Fresenius	F4	Polysulfone	0.7	42		155	128	78	32	2.8
Fresenius	F5	Polysulfone	1.0	63		170	149	103	45	4.0
High-efficiency										
Gambro	500HG[c]	Hemophan	1.1	58		184	171	144	66	7.6
Fresenius	F8	Polysulfone	1.8	110		186	172	138	76	7.5
Medium-flux										
Fresenius	F40	Polysulfone	0.7	42		165	140	138	75	20
Fresenius	F80 M	Polysulfone	1.8	110		190	177	170	110	27
High-flux										
Fresenius	F160 NR	Polysulfone	1.5	84		194	181	178	128	45
Fresenius	F200 NR	Polysulfone	2	112		195	191	183	148	56
Gambro	Polyflux 140 H	Polyamix™	1.4	94		193	181	174	128	60
Gambro	Polyflux 170 H	Polyamix™	1.7	115		196	186	180	137	70
Prisma CRRT sets										
Gambro Prisma	M10[g]	AN-69	0.042	3.5	45	9.7	8.1		3.6	
Gambro Prisma	M60[a,e]	AN-69	0.6	48	90	37	30	29	25	15
Gambro Prisma	M100[b,e,f]	AN-69	0.9	65	107	43	33	32	35	22

Measurements performed in vitro at Qb = 200 mL/min, Qd = 500 mL/min, UF = 0, except where otherwise noted.
[a]Q_b = 100 mL/min, UF = 5 mL/min
[b]Q_b = 150 mL/min
[c]UF = 13 mL/min
[d]Discontinued
[e]Q_d = 2 L/h (33 mL/min)
[f]UF = 10 mL/min
[g]Q_b = 20 ml/min, Q_d = 1 L/h, UF = 1 ml/min
Polyamix™ = Polyarylethersulfone, polyvinylpyrrolidone, and polyamide
With some dialysis machines, various tubing configurations are available, allowing flexibility with tubing volume. The Gambro CentrySystem 3 and Phoenix machines have specific tubing sets. The tubing volume for the neonatal set is 40 mL, and the volume for the pediatric set is 75 mL. The volume of the dialyzer is added to this volume to determine the total extracorporeal circuit volume. With the Gambro Prisma, the tubing and dialyzer are one integrated set.

they increase the risk of bacterial growth. Hot and cold water entering the system are usually blended to enhance function because excessively hot or cold water decreases the efficiency of the reverse osmosis machine. Routine maintenance of the system is performed to maintain adequate function and to disinfect the system. In most new models of dialysis machines, an additional filtration step is provided by the dialysis machine, using a device similar to a dialyzer. Using the same principles of ultrafiltration, dialysate entering the device is ultrafiltered, and the ultrafiltrate is passed to the patient dialyzer, leaving behind any bacterial contaminants or endotoxins, producing what is termed ultrapure dialysate.

Water treatment systems can be sized to produce adequate water for one or many dialysis machines. Self-contained water treatment systems with the capacity to produce only enough water for one dialysis machine are available and are designed to attach to the back of the dialysis machine.

Water and dialysate should routinely be tested for chemical and bacterial contamination. Culture media should be restricted in nutrients (i.e., tryptic soy agar)

and a pour plate method is preferable to a calibrated loop method. The Association for the Advancement of Medical Instrumentation (AAMI) has established standards for dialysis water quality. Standard dialysis water should have a bacterial count of less than 200 CFU/mL, and prepared dialysate should have a count less than 2,000 CFU/mL. Endotoxin levels are commonly measured using the limulus ameobocyte lysate assay and should be less than 0.25 endotoxin units/mL. Ultrapure dialysate should have fewer than 0.1 CFU/mL bacterial count and <0.03 endotoxin units/mL. Continuous renal replacement therapies generally use prepackaged sterile dialysate, thus avoiding the necessity for a water treatment system and associated monitoring. In addition to bacterial contaminants, AAMI has established guidelines for acceptable levels of chemical components of water (Table 28.4).

Production of cytokines in dialysis patients is related to the endotoxin load in the dialysate and the permeability of the dialysis membrane to endotoxin. Whether use of ultrapure dialysate will decrease chronic inflammatory conditions associated with dialysis has not clearly been established yet (Bommer and Jaber 2006).

Table 28.4 AAMI guidelines for dialysate water

Contaminant	Allowable range (mg/L = ppm)
Sodium	0–70
Potassium	0–8
Alminum	0–0.01
Calcium	0–2
Copper	0–0.1
Magnesium	0–4
Selenium	0–0.09
Zinc	0–0.1
Chromium	0–0.014
Lead	0–0.005
Arsenic	0–0.005
Mercury	0–0.0002
Cadmium	0–0.001
Beryllium	0–0.0004
Antimony	0–0.006
Thallium	0–0.002
Silver	0–0.005
Barium	0–0.1
Fluoride	0–0.2
Nitrate	0–2
Sulfate	0–100

Bacteriological:
- Maximum 200 CFU (colony forming unit) for RO water
- Maximum 2,000 CFU for dialysate

Endotoxin: 2 EU (endotoxin units)

Clinical toxicity may occur with inadequately treated water. Municipal water treatment facilities add aluminum sulfate or alum to water to clear flocculent debris, and this aluminum must be completely removed before use in dialysate. Signs of aluminum toxicity in people include neurologic signs, including personality change, decreased short-term memory, speech disturbance, myoclonic muscle spasm, hallucinations, seizures, and dementia; bone disease (such as osteomalacia, osteodystrophy); and microcytic hypochromic anemia. Chloramines are added to water as bactericidal agents. Toxic effects of chloramines are primarily hematologic, including hemolysis, heinz body anemia, and methemoglobinemia. Fluoride is added to prevent dental disease, but overexposure to fluoride can cause osteomalacia and osteoporosis. Copper can leech from copper pipes in the water system. Signs of copper toxicosis include chills, nausea, headaches, liver damage, and hemolysis. Zinc can also leech from pipes or galvanized containers and causes nausea, vomiting, fever, and anemia. Nitrates are not added to water via the treatment process, but may appear due to bacterial contamination or run-off from fertilizers used in the area of the source water. Nitrates cause methemoglobinemia, cyanosis, hypotension, nausea, and potentially hemolysis. Sulphates may cause nausea, vomiting, or metabolic acidosis. Although calcium and magnesium are normally found in the body, extremely high levels, as may occur with malfunction of the water-softening process, can cause nausea, vomiting, muscular weakness, skin flushing, hypertension, or hypotension. An extremely high sodium level could occur if the ion exchanger goes through a regeneration cycle during the dialysis treatment (D'Haese and De Broe 1996; Langston 2004).

Dialysate production

Purified water is combined with the electrolyte and buffer solutions to create the final dialysate. With IHD, the dialysis delivery machine performs this procedure, creating dialysate at a rate of 300–800 mL/min. A highly concentrated salt solution, containing sodium, chloride, glucose, and other components as desired (potassium, calcium, magnesium) is diluted with the purified water to the desired sodium concentration, based on measurement of conductivity. The concentration of other components will be proportional to the sodium concentration and cannot be individually adjusted by the dialysis machine. However, different salt solutions can be used, such as potassium-free or calcium-free solutions. Bicarbonate is provided individually, and the concentration can be adjusted independent of the sodium concentration. An alternate method of producing dialysate involves mixing

the salt and buffer solutions with water in a large bulk tank, where it is stored until being piped to the individual dialysis machines in the unit. Every patient in the unit would use the same dialysate composition. With continuous therapies (CRRT), dialysate is prepackaged in sterile bags, similar to intravenous fluids. This has the advantage of sterility and ease of use, but the disadvantages of large storage requirements and higher cost. Dialysate flow rates are much lower in CRRT (0–2.5 L/hour) compared to IHD (≈30 L/hour).

Dialysis machine

There are several basic types of dialysis machines, also called the dialysis delivery system. In general, machines are designed to be used either for intermittent or for continuous therapy. IHD machines can be used to provide sustained low-efficiency dialysis (SLED) treatments in addition to highly efficient intermittent treatments. CRRT machines are usually smaller and more mobile because they do not need to produce dialysate. In the past several years, "hybrid" machines have become available, which are intended to perform both intermittent and continuous therapies. Some machines (e.g., Fresenius 2008 K) are adaptations of intermittent machines. The NxStage machine is intended to be a portable home hemodialysis machine for intermittent treatment, using prepackaged dialysate in bags. Many machines approved for use in Europe have the capability of on-line hemodialfiltration, which means they can provide large volumes of solutions to infuse into the patient as replacement fluid, in addition to producing large volumes of dialysate.

In the United States most veterinary units performing IHD use either Gambro (Centrysystem 3 or Phoenix models) or Fresenius machines. The Gambro machines have a cartridge system for the extracorporeal circuit that includes all the necessary tubing in one piece. The dialyzer is separate. The snap-in cartridge simplifies machine set-up, but limits tubing choices. In the Fresenius machine, several tubing components are incorporated separately during machine set-up. This provides more flexibility with tubing sizing and volumes, as well as multiple choices for independent manufacturers, but lacks the simplicity of the Gambro machines. Most US units performing CRRT use the Gambro Prisma (now discontinued) machine. The Prisma utilizes a combined dialyzer and extracorporeal circuit. This allows almost automated machine set-up, but limits selection to three available options (plus a plasmapheresis cartridge option).

The ERRT machine has many built-in sensors and alarms to ensure patient safety. In addition to pressure sensors and air bubble detectors mentioned above, the dialysis machine monitors the waste dialysate for evidence of blood leak. Dialysate composition and temperature are constantly monitored. If any unsafe or potentially unsafe conditions are detected in the dialysate, dialysate flow is diverted from the dialyzer. If blood path conditions are potentially compromised, the blood pump stops and the blood lines are automatically clamped. On-screen instructions notify the operator of the specific alarm, which must be remedied in order to restart the treatment. Despite the myriad, and in many cases, duplicate, monitors installed in the machine, operator error can still occur. Only personnel specifically trained to use and troubleshoot the specific machine should be performing ERRT treatments.

Prescription

Methods of clearance

Diffusion is defined as the movement of particles from an area of higher concentration to an area of lower concentration. Particles in solution have kinetic energy causing movement, and smaller particles tend to have more movement than larger particles. If two identical solutions are separated by a membrane that is permeable to a substance, individual particles may cross the membrane in either direction, and although the individual particle on either side of the membrane may change, there is no net change in the concentration of particles. If, however, the concentration on one side is lower, there will be net diffusion from the higher concentration to the lower concentration. Over time, the two solutions will equilibrate to the same concentration on both sides. The higher the concentration gradient between the two sides, the faster the rate of diffusion. With dialytic therapies (including extracorporeal and peritoneal), the solution on one side of the membrane is the blood, and dialysate is the solution on the other side of the membrane. By constant replenishment of the dialysate, a large concentration gradient is maintained and equilibrium is never reached, so diffusive clearance continues. Extracorporeal therapies have a constant dialysate flow, although the rate of dialysate flow generally varies dramatically between intermittent and continuous therapies. Extremely fast dialysate flow rates maximize diffusive clearance, and flow rates of 300–800 mL/min are typical with IHD (usually 500 mL/min). Continuous therapies in a diffusive clearance mode typically use lower dialysate flow rates (up to 40 mL/min). PD involves instillation of a discrete volume of dialysate that is periodically removed and replaced with fresh dialysate. During the dwell time, diffusion occurs.

Although we are composed of approximately 60% water and could not live without it, water can be considered a "uremic toxin" that needs to be removed in the oliguric renal failure patient. Diuretics may be ineffective in this patient population, leaving ultrafiltration (UF) as

the only effective means of removing fluid. As opposed to diffusion, in which a concentration gradient causes solute movement, UF involves a hydrostatic pressure gradient to cause water movement. By creating negative pressure on the side opposite the blood compartment, water is "pulled" out of the blood. The water removed in this fashion is termed ultrafiltrate. With machines used today, the transmembrane pressure is automatically controlled by the dialysis machine to achieve the desired fluid removal in the time specified.

Convective clearance removes solutes by removing the water in which they are dissolved, a process that is also called solute drag. Middle molecules (compounds with a molecular weight of 500 to 5,000 Da) are more efficiently cleared with convection compared to diffusion, whereas diffusion is a very efficient method of removing small molecules (e.g., urea, creatinine, sodium). The term hemofiltration indicates using convective clearance for uremic toxin removal. When UF is used for net fluid removal, convective clearance will occur. If a larger degree of convective clearance is desired, the UF rate can be increased dramatically (up to 35 mL/kg/h or higher), with administration of intravenous fluids to avoid volume depletion.

Certain substances, like cytokines, will bind to the dialyzer membrane and thus can be removed from the circulation. The adsorptive capacity of the dialysis membrane is limited, and some studies show saturation after about 30 minutes, making this an ineffective method of removal (Lonneman et al. 2001). Charcoal and other hemoperfusion techniques are better suited for significant adsorption.

Prescription components

Although the overall goal of hemodialysis is to control uremic symptoms, the specific goals of an individual treatment vary based on the situation. The components of a dialysis prescription include modality (i.e., intermittent versus continuous), schedule (i.e., daily versus alternate day), intensity (i.e., amount of blood processed, convective clearance rate, and diaysate flow rate), dialyzer type and size, dialysate composition, and UF rate.

Prescribing the dialysis dose requires an ability to predict the adequacy of treatment. The most commonly used measure of clearance in veterinary hemodialysis is the urea reduction ratio (URR), which can be calculated by the formula: (pre-treatment BUN—post-treatment BUN)/pre-treatment BUN. The most commonly used measure of dialysis dose in humans is Kt/V, a dimensionless unit of measurement that incorporates the dialyzer clearance, time on dialysis, and volume of distribution. The adequacy of dialysis is discussed more fully below.

Mode and schedule

The mode and schedule recommended differs for acute and chronic disease. With acute kidney injury, the two major initial considerations are the rate of clearance and the intensity of treatment. When azotemia is severe, rapid clearance may induce dialysis disequilibrium syndrome. One method of limiting clearance during the initial few dialysis treatments is a short dialysis treatment time, coupled with a moderately slow blood flow rate. The target URR of 0.25–0.5 can be reached in 1.5 hours at a blood flow rate of 3–5 mL/kg/min. Despite the low overall clearance, this rate can induce complications, particularly in severely uremic patients (BUN > 200 mg/dL) or small patients. An alternative approach would be sustained low efficiency dialysis (SLED) or CRRT. SLED is performed with an IHD machine and involves a very slow blood flow rate (1–3 mL/kg/min) for 6–24 hours. CRRT also uses a similar slow blood flow rate, markedly slower dialysate flow rate (0–40 mL/min for CRRT versus 300–500 mL/min for IHD), and frequently relies on more convective clearance than most IHD prescriptions. Despite these differences, SLED and CRRT appear to have similar outcomes (Berbece and Richardson 2006; Ghahramani et al. 2008).

The hemodynamic stability of the patient is another factor that is generally included in the decision of dialysis modality. CRRT and SLED are generally preferred in the hemodynamically unstable patient. Rapid fluid removal in IHD treatments can cause hypotension, which is thought to induce on going renal damage (Conger 1990). Slow or continuous fluid removal in SLED or CRRT intuitively is less likely to cause intermittent hypotension. Although clinical impressions support this, there is no evidence of superior hemodynamic stability in SLED or CRRT compared to IHD in randomized trials (John et al. 2001; Gasparovic et al. 2003; Uchino 2008).

Treatment intensity for acute kidney injury is an area of on going research. Although CRRT does not improve survival rates compared to IHD, early studies suggested that renal recovery was more complete with CRRT, with more patients becoming dialysis independent (Mehta et al. 2001; Bell et al. 2007; Uchino et al. 2007). In a recently published meta-analysis, modality did not affect survival or renal recovery outcomes, although a subsequent study did find a lower rate of dialysis dependence with CRRT compared to IHD (Bell et al. 2007; Ghahramani et al. 2008). However, intermittent IHD is less resource-intensive. Daily 6–8 hour treatments (6–7 days a week) can be performed by day staff. Although some studies have shown a survival advantage with a higher dialysis dose, results have been inconsistent, and a recently published randomized trial showed no advantage to intensive therapy (daily IHD/daily SLED with a

Kt/V of 1.2 per treatment or CRRT with a total effluent of 35 mL/kg/h) compared to less intensive therapy (alternate day IHD/SLED with a Kt/V of 1.2 per treatment or CRRT with a total effluent of 20 mL/kg/h) (Ronco et al. 2000; Bouman et al. 2002; Schiffl et al. 2002; Saudan et al. 2006; Network 2008; Tolwani et al. 2008). During the recovery phase of acute kidney injury, a less intensive schedule (4–5 hour treatments three times a week, decreasing to twice weekly as function improves) may be adequate.

The typical human patient on hemodialysis for chronic kidney disease has traditionally been treated 3–4 hours three days a week. In veterinary medicine, treatment times have been longer (4 hours for cats, 5 hours for dogs) to provide better clearance. Occasionally, patients with significant residual renal clearance may be maintained on twice weekly treatments, although this likely represents the minimal recommendation that will be beneficial to the patient (Cowgill 2008).

Alternative schedules for chronic hemodialysis are being used more frequently for human patients. Daily dialysis with 1.5–2.5 hour treatments 6–7 days a week provides more complete control of uremia (Kjellstrand et al. 2008). Nocturnal dialysis involves 7–10 hour treatments while the patient sleeps and allows people on chronic dialysis to maintain a more normal daytime schedule, but this schedule is not advantageous in veterinary dialysis. Home hemodialysis for chronic kidney disease is possible for people, with remote monitoring and ready access to support staff via telephone (for both daytime and nocturnal dialysis treatments), but is unlikely to be feasible in veterinary dialysis because most patients currently have acute rather than chronic disease, and the support network is not established.

Guidelines for treatment intensity for veterinary patients have been established through clinical experience (Table 28.5). After determining the desired URR, the number of liters of blood to be processed to achieve the goal are based on weight of the patient and can be estimated from Figures 28.5 and 28.6. In early treatments, a slow rate of reduction decreases complications, so a longer treatment duration is selected, whereas in later treatments, a rapid blood flow rate can achieve the treatment goals faster (or achieve greater clearance in a set time interval). Once the desired amount of blood to be processed and the duration of treatment are selected, the average blood flow rate to achieve these goals can easily be calculated.

Limiting factors for blood flow rate are the catheter and the patient. Larger diameter catheters can provide much faster blood flow rates than smaller catheters (Table 28.2). Minor hemolysis may occur if the pressure in the "arterial" limb of the extracorporeal circuit before the

Table 28.5 Treatment intensity prescription guidelines (adapted from Cowgill 2008)

1st treatment	
BUN <200 mg/dL	URR < 0.5 @ no greater than 0.1 URR per hour
200–300 mg/dL	URR 0.3–0.5 @ no greater than 0.1 URR per hour
>300 mg/dL	URR ≤ 0.3 @ no greater than 0.05–0.07 URR per hour
2nd treatment	
BUN < 200 mg/dL	URR 0.6–0.7 @ 0.01–0.15 URR per hour
200–300 mg/dL	URR 0.4–0.6 @ 0.10–0.12 URR per hour
>300 mg/dL	URR ≤ 0.4 URR @ no greater than 0.05–0.1 URR per hour
3rd and subsequent treatments	
BUN < 150 mg/dL	URR > 0.8 @ > 0.15 URR per hour
150–300 mg/dL	URR 0.5–0.6 @ 0.10–0.15 URR per hour
>300 mg/dL	URR 0.5–0.6 @ < 0.1 URR per hour

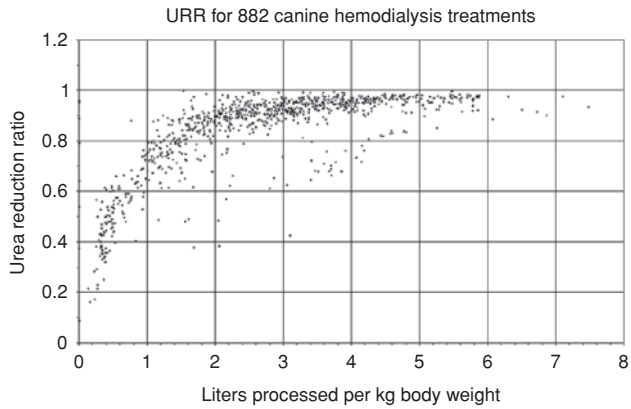

Figure 28.5 Treatment intensity (urea reduction ratio) as a function of amount of blood processed in dogs. Treatments with over 8 L/kg of processed blood were excluded.

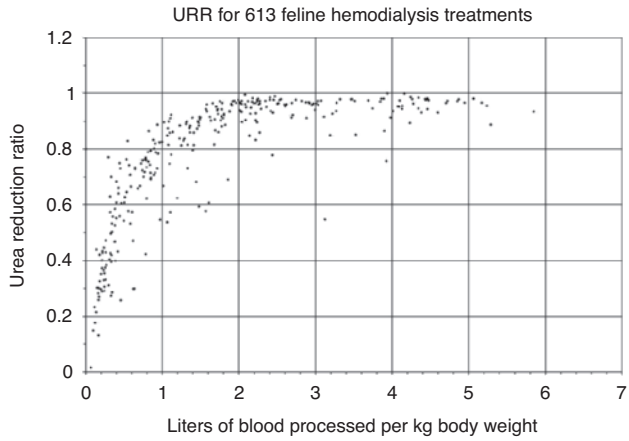

Figure 28.6 Treatment intensity (urea reduction ratio) as a function of amount of blood processed in cats.

Table 28.6 Recommended extracorporeal volumes for ERRT in dogs and cats (adapted from Cowgill 2008)

Species	Body weight	Dialyzer volume	Total extracorporeal volume (mL)	% Blood volume
Cats, dogs	<6 kg	<20 mL	<60 mL	13–40%
Cats	>6 kg	<30 mL	<70 mL	<23%
Dogs	6–12 kg	<45 mL	<90 mL	9–19%
Dogs	12–20 kg	<80 mL	100–160 mL	6–17%
Dogs	20–30 kg	<120 mL	150–200 mL	6–13%
Dogs	≥30 kg	>80 mL	150–250 mL	6–10%

blood pump is more negative than −350 mmHg (Twardowski 2000). Of more clinical significance, prepump pressures more negative than −200 mmHg will cause the pump to deliver less blood flow than is indicated, causing an overestimation of the amount of dialysis delivered (Daugirdas 1994). If the blood flow rate is less than desired due to catheter flow problems, the treatment time may need to be prolonged to achieve the desired clearance.

Dialyzer and extracorporeal circuit selection

Various dialyzers are available. Differences in the membrane type were discussed above. The choice of dialyzer size depends on desired clearance and patient size. Although pediatric hemodialysis recommendations include limiting the total volume of the extracorporeal circuit and dialyzer to less than 10% of the infant's blood volume, this guideline may be impractical in veterinary dialysis (Table 28.6) (Ellis 2008). In a standard treatment, the largest feasible dialyzer is generally preferred, but for the first 1–3 treatments, when slower clearance is desired, a slightly smaller dialyzer is generally recommended.

When preparing for the dialysis treatment, the dialyzer is flushed with saline to remove any particulate matter or residual disinfectant or materials from production. This solution is discarded and refreshed with saline that will be infused into the patient as the blood is being withdrawn, and this volume of saline helps maintain the patient's blood pressure. In small animals, if the total extracorporeal circuit volume represents >20% blood volume, a colloid solution is used instead of saline. Dextran 70 6% can be diluted with an equal volume of saline, to provide colloid support without risking excessive volume overload, or other colloid solutions such as Hetastarch can be used. In rare situations, diluted oxyglobin can be used as a priming solution. Priming with banked blood is commonly performed with human pediatric patients. At the end of the treatment, the patient's blood is not returned, to avoid volume overload. A blood prime is not commonly used in veterinary medicine for IHD for various practical reasons, including limited availability of blood for daily treatments and concern about transfusion reaction due to the rapid infusion rate. With CRRT, theoretically the same circuit can be used for 3 days, potentially reducing some of the mentioned concerns.

Dialysate composition

The composition of dialysate is similar to the composition of plasma water. The sodium concentration can be readily adjusted to avoid large or rapid changes in the patient. Sodium profiling is a feature of most machines that allows the dialysate sodium concentration to automatically adjust throughout the treatment to a match a preset pattern. The dialysate sodium may be set slightly higher than the patient's at the start of the treatment and gradually decreased to normal over the course of the treatment. This profile enhances diffusion of sodium into the patient early in the course of treatment when urea removal is most rapid, and helps maintain a stable patient osmolality, thus decreasing the risk of dialysis disequilibrium syndrome. The sodium concentration is lowered by the end of the treatment to avoid loading the patient with sodium, which can enhance thirst and water retention in the interdialysis interval (Stiller et al. 2001). Sodium profiling is not possible with CRRT because dialysate is supplied in premixed sterile bags, but sodium profiling is not necessary given the slow and continual nature of CRRT.

Because the dialysis machine proportions the dialysate concentrate based on the sodium concentration, individual adjustments of other dialysate components are not possible, but can be made by using different concentrates. Dialysate typically contains approximately 3 mEq/L of potassium, but potassium-free dialysate is used for hyperkalemic patients. Several concentrations of dialysate calcium are available, including calcium-free dialysate, used with some citrate anticoagulation protocols (see below). Various magnesium concentrations are also available. Bicarbonate is incorporated separately and can be adjusted independently from sodium

concentration. To combat metabolic acidosis that is commonly present, the dialysate bicarbonate concentration is usually higher than the patient's, allowing diffusion of bicarbonate from the dialysate into the patient. The typical dialysate bicarbonate concentration used in people (35 mEq/L) leads to panting in dogs; a slightly lower concentration (30 mEq/L) is typically used in veterinary hemodialysis. If acidosis is severe, a high dialysate bicarbonate concentration may cause paradoxic CNS acidosis and dialysis disequilibrium syndrome.

Although most intermittent dialysis treatments use a dialysate flow rate of 500 mL/min, the dialysate flow rate is adjustable. With IHD, clearance depends more on blood flow rate than on dialysate flow rate. At a slow blood flow rate and rapid dialysate flow rate, blood leaving the dialyzer may be completely cleared of a solute. With a fast blood flow rate and the same dialysate flow rate, the blood spends less time in the dialyzer and a lower percentage of the solute is extracted. For example, at a blood flow rate of 20 mL/min, blood entering the dialyzer with a urea concentration of 100 mg/dL may have a 0 mg/dL concentration when leaving the dialyzer. At a blood flow rate of 200 mL/min, blood entering the dialyzer with a urea concentration of 100 mg/dL may have a 30 mg/dL concentration when leaving. In the first example, 20 mL/min of blood are completely cleared of urea, whereas in the second example, 140 mL/min of blood are completely cleared. Thus, despite the decrease in efficiency from 100% to 70% clearance in one pass, there is an overall greater clearance with a higher blood flow rate. Increasing the dialysate flow rate from 500 mL/min to 800 mL/min will increase the clearance by 5–10%, if the blood flow rate is already at very high rate (>350 mL/min). A lower dialysate flow rate (i.e., 300 mL/min) will modestly decrease clearance. Dialysate flow rates in CRRT are generally between 0 and 40 mL/min. With CRRT, dialysate is saturated with one pass through the dialyzer, and faster dialysate flow rates have a substantial effect on clearance (Clark and Ronco 2001).

In most treatments, dialysate flows from the bottom of the dialyzer to the top, while blood flows in the opposite direction, to maximize the concentration gradient across the length of the dialyzer. By reversing the dialysate connectors, dialysate can flow in a concurrent direction instead of countercurrent, thus decreasing efficiency by about 10%, which may be indicated in the first 1–3 treatments (Yeun and Depner 2005).

Blood leaving the dialyzer is in thermic equilibrium with the dialysate. Higher patient temperatures promote vasodilation of the skin and periphery, which may cause cardiovascular instability and intradialytic hypotension. A dialysate temperature slightly (2°C) below body temperature promotes mild patient cooling and vasoconstriction to the periphery and decreases the risk of intradialytic hypotension (Selby and McIntyre 2006). Because basal temperatures of dogs and cats are higher than that for humans, dialysate temperature settings available with currently used machines are typically slightly below normal for veterinary patients.

When dialysis is used for nonrenal indications, such as removal of a toxin, hypophosphatemia can develop as a result of rapid clearance of phosphorus. Although phosphorous concentration may rebound shortly after the dialysis treatment, there is a risk of hemolysis with severe hypophosphatemia (serum phosphorus <1.0 mg/dL). Addition of phosphate to the dialysate may prevent this from occurring. Addition of 16 mL of a neutral sodium phosphate (Fleet Enema, Fleet Brand Pharmaceuticals, C.B. Fleet Company, Inc., Lynchbrg, VA) per liter of dialysate concentrate produces a dialysate concentration of approximately 2 mg/dL (Cowgill 2008).

Ethylene glycol intoxication is efficiently treated with hemodialysis. Fomepizole (Antizole-Vet, Jazz Pharmaceuticals, Palo Alto, CA) or ethanol should be administered intravenously as soon as possible to delay metabolism of ethylene glycol while the patient is being prepared for dialysis. Because ethanol is also readily dialyzable, addition of ethanol to the dialysate can maintain a steady state in the patient. Enough ethanol is added to create a 0.1% ethanol concentration in the dialysate (Cowgill 2008).

Ultrafiltration

The desired volume of UF depends on the patient's hydration status. Some patients may be 10–25% overhydrated, in the most severe cases. In severe cases, the excess fluid cannot generally be removed in a single short dialysis treatment because the rate of fluid removal should not exceed 20 mL/kg/h, to avoid intradialytic hypotension. Some newer machines can be set to remove fluid at variable rates during the dialysis treatment. An effective profile involves a faster rate of fluid removal at the beginning of the treatment, when the extra fluid is readily accessible in the bloodstream, and a slower rate toward the end, to account for a slower transfer from the interstitium to bloodstream and thus to dialyzer as the patient nears the optimal fluid status (Stiller et al. 2001). In IHD, with its high dialysate flow rate, the addition of UF for convective clearance contributes relatively little to the overall solute clearance (Yeun and Depner 2005).

Single needle dialysis

If only one vascular access lumen is available, either because a single lumen catheter was placed or because one lumen of a double lumen catheter is nonfunctional,

dialysis can be performed in what is termed single-needle mode. A Y-connector is attached to the single lumen so that both the "arterial" and "venous" extracorporeal tubing segments can be attached. The venous side is automatically clamped while the blood pump draws blood from the arterial side into the dialyzer. Blood already in the dialyzer is displaced into a reservoir placed in the extracorporeal circuit on the venous return side (after the dialyzer but before the clamp). The arterial side is then clamped and the venous side is unclamped, allowing the dialyzed blood to be returned to the patient, and the cycle is repeated. Single-needle dialysis is far less efficient than double needle, as less than half of the dialysis time is spent withdrawing blood. There is also a decrease in efficiency due to recirculation of the returned blood in the catheter that is withdrawn on the next cycle. By maintaining a fast blood flow rate and a higher stroke volume (amount of blood removed in each cycle), the effect of recirculation is decreased, but in many situations, a fast blood flow rate is limited by the type and condition of the functional lumen of the catheter.

Anticoagulation

Exposure of blood to the extracorporeal circuit and dialyzer membrane induces coagulation, and some method of eliminating or decreasing this effect is necessary. The most common method of anticoagulation of the extracorporeal circuit in IHD is unfractionated heparin. An intravenous bolus of heparin (20–50 units/kg) is given at the start of the dialysis treatment, followed by a constant infusion during the treatment. The infusion rate is adjusted during treatment to maintain the clotting time at about 1.6–2 times normal. Most dialysis machines can be programmed to discontinue the heparin infusion prior to the end of treatment (generally 30–60 minutes), allowing the clotting times to start decreasing toward normal. The half-life of heparin is 40–120 minutes (Ward 2005).

The coagulation cascade is heavily dependent on calcium as a cofactor at several steps. Because citrate binds calcium, it is an effective anticoagulant. Regional citrate anticoagulation involves infusing citrate into the extracorporeal circuit as the blood is being withdrawn from the patient, anticoagulating only the blood in the extracorporeal circuit. In order to avoid hypocalcemia in the patient, calcium is infused into the patient, preferably through a catheter separate from the extracorporeal circuit and dialysis access. If no other venous access is available, calcium can be infused into the extracorporeal circuit at the point where the blood is returned to the patient. This increases the risk of thrombosis in the catheter, however. Regional citrate anticoagulation has the advantage of not causing systemic anticoagulation, which is desirable, especially in patients at high risk for bleeding (i.e., patients with GI ulceration or bleeding diathesis or after surgery). Disadvantages include an increase in complexity of treatment, because the citrate infusion rate is adjusted based on both the blood flow rate and the ionized calcium concentration of the extracorporeal circuit, and the calcium infusion rate is adjusted based on the citrate infusion rate and the patient's ionized calcium concentration. The dialysate should not contain calcium. Although protocols have been investigated using calcium-containing dialysate to avoid the need for intravenous calcium administration, thrombosis in the circuit occurs more frequently (Buturovic-Ponikvar et al. 2008). Because citrate is metabolized by the liver, regional citrate anticoagulation is contraindicated in patients with hepatic dysfunction. Metabolic alkalosis may occur since citrate is metabolized to bicarbonate; use of a lower dialysate bicarbonate concentration may be advisable.

In high-risk patients, dialysis can sometimes be performed without anticoagulation. The extracorporeal circuit is flushed with saline (50–150 mL) every 15–30 minutes to flush any fibrin strands that are starting to form. The extra volume infused is removed by UF to avoid volume overload in the patient. Rapid blood flow rates are necessary to decrease clotting. An increase in transmembrane pressure may predict clotting; careful attention to this parameter and narrow alarm settings are recommended if performing dialysis without anticoagulation. It has been the author's clinical experience that even with aggressive saline flushing, dialyzer and circuit clotting limit treatment to less than 1.5 hours without anticoagulation in many patients.

Protamine counteracts the effects of heparin and can be administered to the patient as a constant IV infusion to reverse the heparin anticoagulation in the patient while heparin maintains anticoagulation in the extracorporeal circuit. This technique of regional heparinization is rarely used. Low-molecular weight heparin can be used instead of unfractionated heparin in patients at high risk of bleeding, but is not commonly used in routine patients, due to the additional expense and inability to monitor in real time. Other anticoagulants have been investigated, including prostacyclin, recombinant hirudin (lepirudin), danaparoid (a heparinoid), and argatroban (direct thrombin inhibitor) (Pun and Kovalik 2008).

Complications of anticoagulation include excessive bleeding or thrombosis in the patient (discussed below) or thrombosis in the catheter or extracorporeal circuit. Thrombosis is most likely to occur in the dialyzer, which decreases the surface area available for diffusive clearance and decreases the efficiency of treatment. Thrombosis may also occur at the air–blood interface in the arterial

or venous drip chamber. Catastrophic coagulation of the entire extracorporeal circuit can occur, necessitating discontinuation of the treatment and preventing return of the blood to the patient, but this complication is uncommon if rapid blood flow is maintained without excessive periods of stopped flow due to catheter malfunction.

Intradialysis patient monitoring

Blood pressure disorders are common in the dialysis patient population during and between dialysis treatments. Numerous factors contribute to hypotension during dialysis. The volume of blood in the extracorporeal circuit compared to the blood volume is a major contributor in smaller patients. The smallest extracorporeal circuit currently available for IHD is about 70 mL (including the dialyzer volume). Removal of this volume of blood, which may be 15–40% of the total blood volume of a cat or small dog, consistently causes a decrease in blood pressure. In stable patients, the magnitude of decrease may only be 20–30 mmHg, and most patients have compensatory mechanisms that increase the blood pressure within 30 minutes of starting the treatment. Some patients seem to be unable to autoregulate, however. UF removes fluid from the intravascular compartment, which is then refilled from the interstitial and intracellular compartments. Rapid UF can induce hypotension that generally responds rapidly to a temporary discontinuation of UF or small boluses of crystalloid fluid. Exposure of the blood to the dialysis membrane can activate the complement cascade, leading to hypotension. The AN69 membrane is particularly capable of activating bradykinin, especially in an acidic environment. Blood pressure should be monitored carefully throughout the entire dialysis treatment. In stable patients, monitoring every 30 minutes is generally adequate.

The intravascular blood volume can be monitored during dialysis using a continuous hemoglobin monitor (Figure 28.7). The hemoglobin content can be measured optically with a sensor placed on the blood tubing. Presuming the patient is neither gaining hemoglobin (transfusion) nor losing hemoglobin (bleeding), changes in the hemoglobin concentration reflect changes in plasma volume from UF or fluid infusion. Monitoring the rate of decline in the intravascular volume can allow prediction of hypotension from rapid UF before it occurs. A general guideline is that if the blood volume decreases by more than 10% per hour, the rate of UF should be decreased.

Some method of monitoring anticoagulation is necessary during hemodialysis. Activated clotting time (ACT) is the most commonly used method. ACT evaluates the intrinsic and common pathways of coagulation, and reliable automated measurement is available at the bedside.

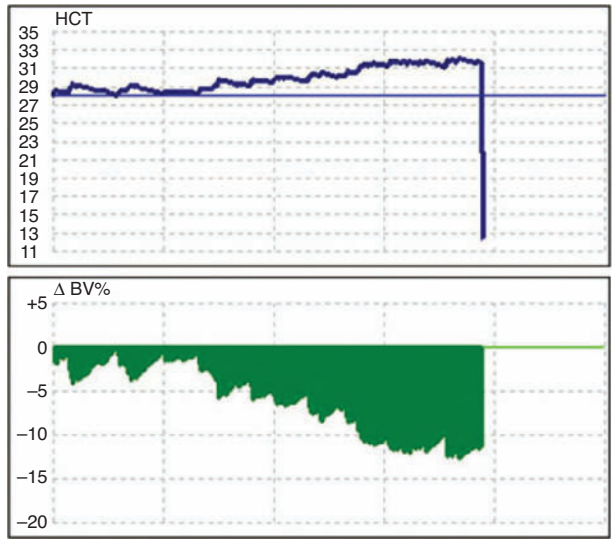

Figure 28.7 Change in blood volume as predicted by CritLine Monitor. Two liters were removed via ultrafiltration during a 3.5 hour dialysis treatment.

Heparin affects the intrinsic pathway, and the effects of heparin can be monitored by ACT or by partial thromboplastin time (PTT). ACT is generally measured before treatment, 30 minutes after starting or any dose adjustment, and then hourly once a stable dose has been reached.

Extracorporeal circuit ionized calcium can be measured in lieu of ACT in patients receiving citrate anticoagulation. An ionized calcium concentration of less than 0.25–0.40 mmol/L will provide sufficient anticoagulation.

Dialysis adequacy

There are many ways to gauge the adequacy of dialysis treatment. The patient's quality of life is a crude (but important) measure, but there are many other factors that impact on quality of life beyond the dialysis treatment, including the nature of the kidney injury, amount of residual renal function and comorbid conditions.

Uremia (Chapter 41) involves a number of metabolic disturbances resulting from the accumulation of a variety of substances, in addition to hormonal imbalances and inflammation. Commonly measured markers of renal function include urea, creatinine, phosphorus, and potassium, but these represent only a small subset of the uremic toxins. In fact, urea is not highly toxic unless present at extremely high concentrations. Despite that, urea concentrations are correlated to outcome, because urea is a suitable marker for other small molecular weight molecules (<500 Da) that diffuse readily. Urea clearance

is not a suitable marker for middle molecular weight uremic toxins (500–15,000 Da) or high molecular weight (>15,000 Da) toxins.

Routine measurement of solutes (urea, creatinine, phosphorus, electrolytes) prior to and immediately following a dialysis treatment provides a simple measure of dialysis adequacy. However, these values are affected by factors beyond the adequacy of dialysis treatment. For example, the predialysis urea concentration may be low due to adequate dialysis or protein malnutrition. Conversely, a high predialysis urea concentration may reflect inadequate dialysis, high protein intake, dehydration, or increased catabolism. Because of vacillations in the predialysis BUN over the week, the time-averaged urea concentration (TAC) has been used to provide a measure of the average urea exposure over the week. It is calculated as the area under the urea measurement curve divided by time of the measurement interval (Leypoldt 2005; Francey 2006b).

Accurate and consistent timing of the postdialysis blood sampling is necessary to avoid introducing error, due to the potential for significant postdialysis rebound of urea. With rapid blood and dialysate flow rates in a short dialysis treatment, the blood compartment is readily cleared of urea, but the intracellular compartment lags behind in clearance. After the end of the dialysis treatment, the intracellular and blood compartments equilibrate, and the blood concentration rapidly (30–60 minutes) increases compared to the immediately postdialysis measurement.

The URR is another simple marker of ERRT adequacy. It is calculated from blood urea measurements taken before and immediately after dialysis. It is calculated from the formula: $URR = (BUN_{pre} - BUN_{post})/BUN_{pre}$. In IHD, URR can be predicted by the volume of blood processed through the dialyzer, presuming standard dialysate flow and no convective clearance. If the actual URR is lower than predicted, there may be substantial clotting of fibers of the dialyzer or substantial catheter recirculation.

The most common measure of dialysis dose in human ERRT is Kt/V, in which K is the clearance of the dialyzer, t is time on dialysis, and V is volume of distribution. Various equations are based on different presumptions about the urea pool and the kinetics of urea movement. The simplest is single pool, in which urea is presumed to diffuse freely and rapidly throughout the entire volume of distribution. The double pool kinetic model presumes differential rates of urea clearance from certain regions (i.e., intracellular space).

The dialyzer clearance can be measured or estimated. Urea is measured in blood entering and leaving the dialyzer, and the clearance is calculated from the formula: $K_d = Q_b \times ((BUN_{in} - BUN_{out})/BUN_{in})$. Note that the blood flow rate readings from the dialysis machine may vary from the actual blood flow rate. Some newer dialysis machines incorporate ionic dialysance measurement. Dialysance is a measure of solute mass transfer from blood to dialysate when the solute is present in both the blood and dialysate. The collective dialysance of small molecular weight ions (such as sodium) is considered equivalent to the dialysance of urea. For conventional single pass hemodialysis circuits, urea dialysance becomes equal to urea clearance. By programmed alterations in dialysate conductivity (by changes in sodium concentration) and measurement of conductivity at the dialysate inlet and outlet, the dialysis machine can calculate the dialyzer ionic dialysance and thus the dialyzer urea clearance. Repeated measurements are made throughout the treatment, allowing calculation of Kt for each dialysis treatment.

The urea volume of distribution is considered to be the same as the total body water and is generally estimated as 58% of body weight. Alterations in water balance and in lean body mass are common in patients with renal failure. Measurement of body water can be performed with dilution techniques or bioimpedance.

More thorough discussions of dialysis adequacy have previously been published for human and veterinary ERRT (Leypoldt 2005; Yeun and Depner 2005; Francey 2006b).

Patient management

Patients with AKI or CKD severe enough to require ERRT are prone to a variety of concurrent conditions induced by the inciting cause of the renal failure, derangement due to the renal failure itself or its treatment, or preexisting comorbid conditions in some. ERRT is able to maintain patients with more severe renal failure for longer periods of time than medical management, which allows development of some late-stage complications that are not commonly encountered in the nondialysis renal failure population. The following discussion will focus on complications unique to the ERRT population or uncommon manifestations that are more likely to be encountered in the ERRT population. The reader is referred to chapters on AKI (Chapter 49) and CKD (Chapter 48) for a general discussion of common manifestations of uremia and appropriate treatment.

Neurologic system

There are a number of potential disturbances of the neurologic system in the dialysis patients. Correctly differentiating the cause of the signs may allow more targeted therapy.

Dialysis Disequilibrium Syndrome (DDS) is characterized by a variety of neurologic signs, including restlessness, nausea, vomiting, muscle twitching, disorientation, tremor, hypertension, obtundation, seizure, coma, and death (Liangos et al. 2005). DDS is more likely to occur in the first few dialysis treatments in patients that are severely azotemic. Risk factors seem to include severe azotemia, small patient size, preexisting neurologic disease, rapid dialysis, and low dialysate sodium relative to the patient. The exact cause of DDS is not clearly defined, but interstitial cerebral edema is a feature (Chen et al. 2007). One theory holds that slower diffusion of urea from cells of the CNS in relationship to removal of urea from the blood compartment during dialysis leads to a relative intracellular hyperosmolality. A decrease in urea transporters and an increase in aquaporins in the brain of uremic rats support this theory (Trinh-Trang-Tan et al. 2005). However, the urea gradient between brain and blood is quantitatively insufficient to cause cerebral edema (Patel et al. 2008). An alternative theory involves paradoxic CNS acidosis from rapid correction of systemic metabolic acidosis during dialysis. The presence of idiogenic osmoles in the brain has been postulated as a contributor to DDS, but concentrations of specific brain organic osmolytes (glutamine, glutamate, taurine, and myoinositol) do not increase with rapid dialysis (Patel et al. 2008). Gradual correction of uremia, as with CRRT or SLED, decreases the risk of DDS. A higher dialysate sodium concentration during periods of rapid urea removal may help decrease the incidence of DDS. In high-risk patients, prophylactic administration of mannitol (0.5 g/kg) about 30–60 minutes after the start of dialysis is recommended. Signs may occur during dialysis or up to 48 hours afterwards and can be treated with mannitol and supportive care. Some patients will recover completely, but this complication can be fatal.

Hypertension can cause neurologic signs that include lethargy, ataxia, blindness, stupor, and seizures (Brown et al. 2005). This condition is called posterior reversible encephalopathy syndrome in people and is characterized by MRI findings suggestive of cerebral edema (Servillo et al. 2007). Hypertensive encephalopathy is not caused by dialysis, but many patients requiring dialysis are hypertensive.

Uremic encephalopathy in people is characterized by diminished concentration, slowed and inefficient cognitive functioning, restlessness, and lowered arousal level or drowsiness (Brown 2008). There are only a few reports of uremic encephalopathy in the veterinary literature. The author has seen a small number of patients that exhibited behavior changes (predominantly agitation and aggression) that resolve immediately after dialysis and return prior to the next dialysis treatment.

Aluminum toxicity can occur acutely from contaminated dialysate source water or chronically from oral aluminum-containing phosphate binders. In addition to hematologic toxicity, aluminum toxicity can cause encephalopathy and neuromuscular disorders (Segev et al. 2008).

Human hemodialysis patients are more likely to suffer from subdural hematoma than the general population, but this complication has not been noted in veterinary dialysis patients (Sood et al. 2007). Other causes of acute localizing neurologic symptoms include intracerebral hemorrhage or ischemic stroke (Murakami et al. 2004).

Uremic polyneuropathy is a common complication of chronic kidney disease in people. Sensory symptoms such as paresthesia, pain, and a burning sensation usually precede motor symptoms, which include muscle weakness and atrophy, myoclonus, and areflexia (Avram and Mittman 2008). Adequate dialysis will usually stabilize the signs, but improvement is rare.

Blood pressure

Hypertension commonly occurs with acute or chronic kidney disease (Chapter 68). Correction of overhydration over the first several days of treatment may decrease the blood pressure, although many patients will need antihypertensive medications. Patients receiving long-term dialysis who are prone to intradialytic hypotension should not receive the antihypertensive medications on the morning of dialysis treatment. Intradialytic hypotension has many potential causes (see Intradialytic Patient Monitoring). Interdialytic hypotension may occur due to sepsis, systemic inflammatory response syndrome, electrolyte and acid–base disturbances, and hypoxia (Waddell 2005).

Hemostasis

Anticoagulation during dialysis (or between treatments) and uremic bleeding tendencies contribute to the risk of hemorrhage in the dialysis patient. Clinical signs may include obvious bleeding, such as bleeding from the catheter exit site or melena, or may be more insidious. A decreasing hemoglobin concentration may not be apparent on continuous monitors because of the concurrent UF. Hypotension that rapidly responds to small bolus of crystalloid fluid but rapidly recurs may be an indication of ongoing bleeding. An acute onset of dyspnea may denote pulmonary hemorrhage.

The three issues to be addressed in a patient that is actively hemorrhaging is (1) decrease ongoing loss, (2) correct anemia, and (3) support affected organs. Immediate cessation of anticoagulant administration is

intuitive. Protamine can be given to reverse the effects of heparin, at a dose of 1 mg protamine for each 100 units of heparin to be reversed, although an overdose of protamine can cause a coagulopathy. If bleeding is due to systemic diseases associated with coagulation factor deficiency, plasma transfusion may be helpful. A major component of uremic bleeding is thrombocytopathy; platelet transfusion is unlikely to be helpful. Dialysis partially corrects the platelet dysfunction (Kaw and Malhotra 2006). Other treatments to prevent or treat uremic bleeding in people include erythropoietin, desmopressin, cryoprecipitate, and conjugated estrogen (Hedges et al. 2006; Kaw and Malhotra 2006).

Blood transfusion is usually indicated for moderate to severe hemorrhage associated with clinical signs. Although erythropoiesis stimulating agents are commonly necessary in most chronic hemodialysis patients, a significant increase in hematocrit generally takes several weeks to effect. Hemorrhage into critical areas such as the lungs or CNS may cause damage that slowly resolves, but this is frequently a catastrophic fatal event.

Thrombosis

Right atrial thrombosis occurs in 22% of human hemodialysis patients who have a catheter for vascular access (Bolz et al. 1995). The presence of right atrial thrombosis is associated with a 68% chance of concurrent infection and 27% mortality (Negulescu et al. 2003). Right atrial thrombosis detected primarily by echocardiography is common in veterinary patients and can routinely be seen within 2 weeks of catheter placement. Catheter thrombosis is discussed in catheter complications section.

Electrolyte and acid–base disorders

Hyperkalemia (Chapter 62) is usually associated with anuria or severe oliguria. In the chronic dialysis patient, however, hyperkalemia can occur in the nonoliguric patient, but usually only when the GFR is less than 10% of normal (Allon 2005). Patients with acute kidney injury are more likely to develop hyperkalemia than those with chronic disease, because the kidney can compensate by increasing the efficiency of potassium excretion. Factors that contribute to hyperkalemia, in addition to the limited ability of the kidney to excrete potassium, include certain drugs [ACE inhibitors, potassium-sparing diuretics (spironolactone, amiloride, triamterene), prostaglandin inhibitors, heparin, nonspecific beta-blockers (propranolol), high doses of potassium penicillin], aldosterone deficiency, inorganic acidosis, and high dietary intake. Commonly used renal diets are supplemented with potassium.

Potassium is a small molecule that is rapidly removed by dialysis. Use of a potassium-free dialysate will normalize serum potassium. In acute dialysis, using a prescription of short treatments with slow blood flow for the first few treatments, the potassium level will generally normalize by the end of each treatment, but the total body excess of potassium has probably not been removed. After cessation of that dialysis treatment, serum potassium levels will increase. Usually after the second or third dialysis treatment, the potassium rebound is less exaggerated. SLED or CRRT may be used for more sustained potassium control in the first day. EKG abnormalities start to improve within the first 15 minutes of dialysis, even though the potassium concentration has not yet been corrected. It has been the author's clinical experience that treatment of hyperkalemia with agents that translocate potassium intracellularly (i.e., insulin, dextrose, bicarbonate) within the hour or two prior to the dialysis treatment limit the total body removal of potassium in a short initial dialysis treatment. Conceptually, potassium is less available in the bloodstream for diffusive clearance during a short treatment, but starts translocating out of the cells after several hours (after the end of the treatment), potentially leading to symptomatic hyperkalemia in the interdialysis interval. In those settings, SLED or CRRT should be considered.

In patients with chronic hyperkalemia between dialysis treatments, sodium polystyrene resin (Kayexalate, Sanofi-Aventis, Bridgewater, NJ) can be administered orally (or by enema). Sodium is released when potassium binds the resin and potassium is trapped for removal via the GI tract. Side effects include anorexia, nausea, vomiting, constipation, hypokalemia, hypocalcemia, and hypernatremia. Drugs that will transiently decrease potassium concentrations include insulin, dextrose, bicarbonate, and beta agonists (e.g., albuterol) (Allon 2005; Kogika and de Morais 2008).

Life-threatening ventricular arrhythmia is the most serious complication of hyperkalemia. EKG abnormalities are usually not seen at potassium concentration of less than 6.5 mEq/L. The earliest EKG changes include peaked T wave. Above 6.5 mEq/L, PR interval prolongation and widened QRS complex may be seen. Above 8–9 mEq/L, a sinoventricular rhythm may occur and P waves are not apparent. Above 10 mEq/L, the classic sine-wave EKG pattern appears, and ventricular fibrillation and asystole are imminent (Parham et al. 2006). In the author's clinical experience, acute elevations in potassium are more likely to induce symptomatic EKG changes, whereas patients with chronic renal disease and chronic hyperkalemia may sustain higher potassium concentrations without obvious signs.

Sodium disorders are commonly encountered and include both hyponatremia and hypernatremia. Sodium is readily diffusible, and the sodium dialysate composition can be used to normalize patient sodium concentration.

Metabolic acidosis (Chapter 66) occurs due to a failure of the kidney to excrete an adequate amount of acid and to reabsorb bicarbonate. Dialysis corrects acidosis by two methods. First, it removes organic and inorganic acid solutes. Second, bicarbonate in the dialysate diffuses into the blood to buffer retained acids. Standard dialysate bicarbonate concentration in veterinary medicine is 30 mEq/L, which loads the patient with bicarbonate during dialysis, to delay the reoccurrence of metabolic acidosis in the interdialysis interval.

Magnesium (Chapter 63) is a divalent cation that is excreted by the kidney. Hypermagnesemia may occur with renal failure, but is corrected by dialysis.

Anemia

Anemia is almost a universal problem in patients on dialysis, even those with acute kidney injury. There are several sources of blood loss, including gastrointestinal bleeding, diagnostic blood sampling, and blood loss in the dialyzer. About 5–10 mL of blood remains in the dialyzer after even the most complete blood rinseback at the end of the treatment, and substantially more blood can be lost if there is any dialyzer clotting. In addition, anticoagulation necessary for dialysis can increase the risk of hemorrhage. Red cell survival times are shortened with uremia. Hemolysis is unlikely to occur in the blood pump segment with the gentle roller pumps employed currently, but can be a problem if excessive negative pressure (from inadequate access flow) occurs. ERRT patients are unable to produce sufficient replacement red blood cells primarily due to lack of erythropoietin production. Additionally, uremic toxins and inflammation inhibit erythropoiesis. Iron, vitamin B, and other nutritional deficiencies may contribute. Myelofibrosis from renal osteodystrophy related to renal secondary hyperparathyroidism has been reported in humans. Aluminum toxicity, which can occur chronically from aluminum-containing phosphate binders and inadequate dialysate water treatment, or acutely from dialysate water contamination, can cause anemia.

Treatment of anemia in dialysis patients in the acute setting generally involves blood transfusion. Oxyglobin can be used in emergency settings. Most patients receiving dialysis for more than a few weeks will benefit from administration of an erythropoiesis stimulating agent such as darbepoetin, although there is a risk of pure red cell aplasia from antibody formation. Iron supplementation is of paramount importance in obtaining an adequate response, as iron losses in the dialysis patient are 3–6 times higher than in the normal patient (Schmidt and Besarab 2008).

Bone and mineral

Approximately 60% of ingested phosphorus is absorbed from the GI tract normally, and up to 80% is absorbed in the presence of active vitamin D. The bulk of the body's phosphorus (85%) is located in bones and teeth. Approximately 14% is located in the soft tissues, 0.5% in interstitial fluid, and 0.02% is in the plasma compartment. Phosphorus (Chapter 65) that is removed during dialysis comes from the intracellular pool. The main determinant of phosphate removal during the first 60–90 minutes of dialysis is the serum phosphate concentration. After the phosphate gradient between blood and the dialysate is decreased, the slow diffusion rate of phosphate out of cells determines the rate of phosphate removal during dialysis. There is a large rebound effect after dialysis, with phosphate values returning to 80% of predialysis values. The kinetics of phosphate removal with hemodialysis make thrice weekly hemodialysis relatively ineffective at controlling hyperphosphatemia. Phosphate removal during short daily dialysis treatments (1.5–3 hours for 6 days a week) is dependent on predialysis phosphate concentration. Nocturnal dialysis (6–10 hours six nights a week) removes twice as much phosphate weekly as conventional thrice weekly hemodialysis. Patients on short daily or nocturnal dialysis have better control of phosphate despite higher phosphate intake and lower phosphate binder doses (Kooienga 2007).

Parathyroid hormone (PTH) is considered a uremic toxin. Concentrations of PTH are elevated in patients with renal disease because of variety of factors, including hyperphosphatemia, inadequate calcitriol formation, and alterations in parathyroid gland sensitivity. PTH is considered a middle molecule, and removal is limited during conventional dialysis. Use of a high-flux dialyzer and convective clearance help remove this substance.

Ionized calcium concentration (Chapter 64) must be regulated within a narrow range to preserve appropriate neurologic and muscular function. The ionized fraction of calcium is available for diffusive transfer; complexed or protein-bound calcium does not diffuse with dialysis. Acute hypocalcemia is suspected as a contributor to intradialytic hypotension, because of an inability of the vasculature to constrict in the absence of calcium. Various dialysate calcium concentrations are available to suit the individual patient's needs.

Water balance

Maintaining water balance can be a significant challenge in patients who require dialysis. Volume overload is common, as the kidneys are not able to excrete water appropriately, and even modest fluid administration rates may cause fluid accumulation in patients with anuria, oliguria, or relative oliguria. Additionally, many patients with acute kidney injury are hypoalbuminemic or have a vasculitis, leading to interstitial fluid accumulation, which complicates assessment of hydration status by physical examination. The traditional veterinary end-stage chronic kidney disease patient is polyuric with a tendency to develop dehydration. Most of these patients die or are euthanized due to uremia prior to (or at the time of) development of oliguria, unless maintained with dialysis. Volume overload, frequently exacerbated by nutritional support via an enteral feeding tube, is common in this group. These patients may need some degree of UF at each dialysis treatment.

Nutrition

Malnutrition is a significant concern in the dialysis patient. Both enteral and parenteral feeding involves an obligate water load, which many patients cannot excrete. The administered water can be removed via UF, with either intermittent or continuous therapies. Acute kidney injury is a highly catabolic disease. Provision of adequate protein can ameliorate (although not eliminate) the negative nitrogen balance that occurs with AKI, and protein restriction, a standard recommendation for patients with chronic kidney disease, may not be appropriate for patients with AKI (Druml 2001).

Standard diets for chronic kidney disease may not be appropriate for chronic dialysis patients. With each dialysis treatment, amino acids are lost into the dialysate, and the protein restriction of renal diets may be insufficient to replenish these losses. Most renal diets are potassium rich, because hypokalemia may occur in the pre-dialysis CKD patient, but these diets induce hyperkalemia in the dialysis patient that has extremely limited renal potassium excretory capability. Supplementation with carnitine and taurine, amino acids that may be lost in the dialysate, is recommended for patients on dialysis for over a month (Fischer 2006).

Infection

Infection is the second most common cause of mortality in human dialysis patients, accounting for 14% of deaths (Evers 1995; Tokars et al. 2005; Katneni and Hedayati 2007). In one study, bacterial infection is responsible for more than 30% of all causes of morbidity and mortality in human patients, with vascular access infection being the culprit in 73% of all bacteremias (Ponce et al. 2007). Bacteremia occurs in human hemodialysis outpatients at a rate of 0.6–1.7% of patients per month, and vascular access infections occur in 1.3–7.2% of patients per month (Tokars et al. 2005). Data is not available in animals, but appears to be similar or higher. Most infections in human dialysis patients are catheter related (28–33% in one study) (Tokars et al. 2005).

Catheter-related infections include exit site infections, catheter infections, and bacteremia. Catheter exit site infections are characterized by erythema, warmth, induration, swelling, tenderness, breakdown of skin, loculated fluid, or purulent exudates (Tokars et al. 2005).

The catheter itself can become infected. Bacteria can produce a biofilm that adheres to the walls of the catheter and protect the bacteria. Blood cultures obtained through the catheter may be positive even if bacteremia is not present. To document bacteriemia, blood for culture must be obtained from a separate venipuncture site.

Signs of catheter-related bacteremia include fever, chills, nausea, headache, hypotension, or elevated white blood cell count. The frequency of catheter-associated bacteremia in humans is 2–4 episodes per 1,000 patient days (0.7–1.5 bacteremias per catheter year) (Himmelfarb et al. 2005). With catheter-related bacteremia, 3 weeks of an appropriate antibiotic and exchange over a guidewire, if minimal signs are present, results in cure in 88% of patients, whereas immediate catheter removal with replacement after defervesence is required in patients with severe septic symptoms (Beathard 1999). One study showed that 51% of catheters could be salvaged without exchange with an antibiotic lock and 3 weeks of systemic antibiotics (Krishnasami et al. 2002). Mupirocin or bacitracin to the catheter exit site may decrease catheter-related bacteremia (Sesso et al. 1998; Johnson et al. 2002; Lok et al. 2003). Thrombosis is correlated with an increased rate of infection (Shah et al. 2004).

The most common bacteria isolated from catheter infections and associated bacteremia in humans is *Staphylococcus aureus* and coagulase negative Staphylococci (Tokars et al. 2005; Katneni and Hedayati 2007). In veterinary patients, half of positive catheter-related cultures (including cultures of blood and/or heparin lock obtained through the catheter and the tip of the catheter) are Staphylococcus spp., and gram-negative organisms comprise 32% of positive catheter-related cultures (unpublished data, Langston 2008).

Although catheter-related infections account for the majority of infections in dialysis patients, other common sites in humans include lung (25%), urinary tract (23%), skin and soft tissue (9%), and other or unknown sites (15%) (Tokars et al. 2005). Gram-negative organisms, predominantly Klebsiella and *E. coli*, account for the majority (77%) of positive urine cultures in veterinary dialysis patients (personal observation).

Respiratory system

Respiratory dysfunction can be caused by a variety of mechanisms. Exposure of blood to the dialysis membrane can activate complement, leading to temporary sludging of activated neutrophils and platelets in pulmonary capillaries, impairing oxygen diffusion. Oxygen pressure can decrease by 5–30 mmHg (Liangos et al. 2005). This effect is most profound within 30–60 minutes of starting the treatment, and resolves within hours. Cellulose and substituted cellulose membranes elicit a stronger reaction; more biocompatible synthetic membranes activate compliment to a lesser degree. Other causes of respiratory impairment can be seen in the dialysis patient. Pulmonary hemorrhage has been noted in dogs with leptospirosis and is a potential complication of excessive anticoagulation (Greenlee et al. 2004). Pulmonary edema can occur as a result of volume overload in the face of oliguria or anuria. Uremia increases pulmonary vascular permeability, similar to that observed in acute respiratory distress syndrome (Rabb et al. 2003). Pulmonary thromboembolic disease is a potential complication of an indwelling catheter.

Gastrointestinal system

Gastrointestinal signs, including vomiting, diarrhea, and anorexia, are pervasive in the dialysis population. With adequate dialysis, these signs may resolve. Aggressive therapy with antiemetic drugs is frequently necessary, but rarely completely resolves vomiting and nausea (Ljutic et al. 2002).

Drug dosing

Drugs that are primarily excreted by the kidneys require dose adjustment with advanced renal failure (Chapter 40). In general, the loading dose does not need to be adjusted unless the volume of distribution is significantly altered, as with patients with large changes in body water. Extending the dosing interval is useful for drugs with a long half-life. Dose reduction while maintaining the interval between doses generally leads to more constant serum levels. A variety of factors affect removal of drugs by dialysis. Drugs with a molecular weight >500 Da are poorly cleared by conventional dialysis, although clearance may be enhanced with synthetic membranes commonly used in veterinary ERRT. Drugs that are highly protein or tissue bound or are highly lipid soluble are not dialyzed to a significant degree due to the high volume of distribution. Drugs that are significantly cleared by dialysis may require supplemental dosing after the dialysis treatment to maintain therapeutic levels. Drug level monitoring is available for some drugs, but may be impractical in many situations. Tables of recommended dose adjustments in dialysis patients are available (Aronoff 2005; Johnson 2008; Olyaei and Bennett 2008). With continuous therapies utilizing convective clearance, molecular size and volume of distribution become less limiting than with IHD, but limited pharmacokinetic data is available (Bugge 2001). Although using specific pharmacokinetic data to adjust dosing is preferred, some suggested guidelines for humans in the absence of necessary data are to presume CRRT is equivalent to a GFR of 10–50 mL/min (normal GFR for humans is >90 mL/min/1.73 m^2) or to increase the dose of nontoxic drugs by 30% over the drug dose estimated for the degree of renal failure (Bugge 2001).

Nonrenal uses

Certain toxins can be removed by hemodialysis or a related technique, hemoperfusion. Characteristics of substances that might be removed by dialysis are small molecular weight, minimal protein binding, and a small volume of distribution. Hemoperfusion involves placing a charcoal-filled cartridge in the extracorporal circuit. As blood passes through the cartridge, activated charcoal adsorbs the toxin. Charcoal perfusion can remove substantial amounts of substances that are protein bound. A list of substances that can be removed can be found in Table 28.7 (Fischer et al. 2004a).

Dialytic therapy can be used for other nonrenal indications. Isolated UF can be used for diuretic resistant congestive heart failure. Dialysis removes cytokines and other inflammatory mediators (both proinflammatory and anti-inflammatory) from septic patients, but there is insufficient evidence to support dialysis (specifically, CRRT) as a treatment for sepsis in the absence of acute renal failure. Two separate systems (Molecular Adsorbants Recirculating System and Prometheus) have been developed to treat liver failure with an extracorporeal clearance system. Commonly used dialysis machines (intermittent and continuous) can be used for therapeutic plasmapheresis.

Table 28.7 Substances that can be removed by extracorporeal purification (adapted from Fisher et al. 2004; Cowgill 2008)

Substance	Conventional dialysis	High-flux	Hemoperfusion
Alcohols			
Ethanol	x		
Ethylene glycol	x		
Methanol	x		
Analgesics/anti-inflammatory			
Acetaminophen	x		
Aspirin	x		
Mesalamine (5-ASA)	x		
Morphine		x	
NSAIDs			x
Salicylates	x		x
Pentazocine	x		
Antibacterials			
Amikacin	x		
Amoxicillin (most penicillins)	x		
Cephalexin (most 1st generation cephalosporins)	x		
Cefotetan (many 2nd generation cephalosporins)	x		
Cefoxitin	x		
Ceftriaxone (many 3rd generation cephalosporins)	x		
Chloramphenicol	x		
Enrofloxacin			x
Gentamicin	x		
Imipenem/cilastin	x		
Kanamycin	x		
Linezolid	x		
Nitrofurantoin	x		
Ofloxacin	x		
Metronidazole	x		
Sulbactam	x		
Sulfamethoxazole	x		
Sulfisoxazole	x		
Trimethoprim	x		
Vancomycin		x	
Anticonvulsants			
Gabapentin	x		
Phenobarbital	x		
Phenytoin		x	
Primidone	x		
Antifungals			
Dapsone	x		
Fluconazole	x		
Flucytosine	x		
Antineoplastics			
Busulfan	x		
Carboplatin	x		
Cytarabine		x	
Cyclophosphamide	x		
Fluorouracil (5-FU)	x		
Ifosfamide	x		
Methotrexate	x		
Mercaptopurine	x		
Vincristine			x

(*Continued*)

Table 28.7 (*Continued*)

Substance	Conventional dialysis	High-flux	Hemoperfusion
Antivirals			
Acycylovir	x		
Famciclovir	x		
Valvcyclovir	x		
Zidovudine	x		
Cardiac/vasoactive medications			
Atenolol	x		
Bretylium	x		
Captopril	x		
Enalapril	x		
Esmolol	x		
Lisinopril	x		
Metoprolol	x		
Mexiletine	x		
Nitroprusside	x		
Procainamide	x		
Sotalol	x		
Tocainide	x		
Chelating agents			
Deferoxamine	x		
Ethylendiamine tetraacetic acid (EDTA)	x		
Penicillamine	x		
Immunosuppressive agents			
Azathioprine	x		
Methyl prednisone	x		
Miscellaneous medications			
Allopurinol	x		
Amatoxins			x
Amitriptyline	x		x
Ascorbic acid	x		
Barbiturates			x
Caffeine	x		
Carisoprodol	x		
Chloral hydrate	x		
Chlorpheniramine	x		
Diazoxide	x		
Foscarnet	x		
Iohexol	x		
Iopamidol	x		
Lithium	x		
Mannitol	x		
Metformin	x		
Minoxidil	x		
Octreotide	x		
Ranitidine	x		
Theophylline	x		x

Appendix: Extracorporeal Renal Replacement Therapy Units

United States

Animal Medical Center
510 E. 62nd Street
New York, NY 10065
(212)838-8100 (phone)
(212)329-8618 (hemodialysis unit)
(212)752-2592 (fax)
Dr. Cathy Langston, cathy.langston@amcny.org
hemodialysis@amcny.org
www.amcny.org
IRRT

Advanced Critical Care
City of Angels Veterinary Specialty Center
9599 Jefferson Blvd
Culver City, CA 90232
(310)558-6100 (phone)
(310)558-6199 (fax)
Dr. Richard Mills
Dr. Jon Perlis
www.cityofangelsvets.com
CRRT

Center for Specialized Veterinary Care
609-5 Cantiague Rock Road
Westbury, NY 11590
(516)420-0000 (phone)
(516)420-0122 (fax)
www.vetspecialist.com
CRRT

Companion Animal Hemodialysis Unit
Veterinary Medical Teaching Hospital
University of California-Davis
Davis, CA 95616
(530)752-1393 (phone)
(530)752-8662 (fax)
Dr. Larry Cowgill, ldcowgill@ucdavis.edu
www.vetmed.ucdavis.edu
IRRT

Louisiana State University
Veterinary Medical Teaching Hospital
Baton Rouge, LA 70803
(225)578-9600 (phone)
(225)578-9559 (fax)
Dr. Mark Acierno
www.vetmed.lsu.edu
CRRT

Advanced Critical Care and Internal Medicine
2965 Edinger Avenue
Tustin, CA 92708
(949)654-8950 (phone)
(949)936-0079 (fax)
Dr. Ravi Seshardri
accimvet@aol.com
www.accim.net
CRRT

California Animal Referral And Emergency Hospital
301 Haley St.
Santa Barbara, CA 93101
(805)899-2273 (phone)
(805)965-0070 (fax)
Dr. Andrea Wells
www.carehospital.org
CRRT

Chicago Veterinary Kidney Center
1515 Bush Parkway
Buffalo Grove, IL 60089
(847)459-7535 (phone)
(847)459-3576 (fax)
Dr. Jerry Thornhill, jthornhill@vetspecialty.com
www.vetspecialty.com
CRRT

Companion Animal Hemodialysis Unit
University of California Veterinary Medical Center
10435 Sorrento Valley Road, Suite 101
San Diego, CA 92121
(858)875-7505 (phone) or (858)875-7505 (HD unit)
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Dr. Larry Cowgill
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IRRT

Tufts University Foster Hospital for Small Animals
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(*Continued*)

Appendix: (*Continued*)

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Veterinary Medical Center
2015 SW 16th Ave
Gainesville, FL 32608
(352)392-2235
Dr. Carsten Bandt
www.vetmed.ufl.edu
IRRT

Veterinary Specialists of South Florida
9410 Stirling Road
Cooper City, FL 33024
(954)432-561 (phone)
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CRRT

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Anubi Companion Animal Hospital
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IRRT

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IRRT

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Rio de Janerio – RJ
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renalvet@veterinariaonline.com.br
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IRRT

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IRRT

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IRRT

Tierärztliche Klinik für Kleintiere Kabels
Stieg 41 D-22850
Norderstedt
Germany
(040) 52 98 94-0 (phone)
(040) 52 98 94-55 (fax)
info@tierklinik-norderstedt.de
www.tierklinik-norderstedt.de/page1.aspx?pageid=50
IRRT

IRRT = Intermittent Renal Replacement Therapy (Intermittent Hemodialysis)
CRRT = Continuous Renal Replacement Therapy
Other web-based resources:
www.vetcrrt.net – Home page of the Veterinary CRRT Society
www.queenofthenephron.com – listing of units performing extracorporeal renal replacement therapies and/or renal transplantation

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