

Intermittent Hemodialysis for Small Animals

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KEYWORDS

- Hemodialysis • Intermittent • Dialyzer • Acute kidney injury
- Chronic kidney disease

Intermittent hemodialysis (IHD) is a renal replacement modality that is defined by short, efficient hemodialysis sessions with the goal of removing endogenous or exogenous toxins from the bloodstream. Common indications for IHD include drug or toxin ingestion, acute or acute-on-chronic kidney injury, and chronic kidney disease (CKD). Sessions can be performed once, as is common with toxin ingestion, or can be repeated daily or every other day for several days or longer, as is often done for acute kidney injury (AKI). Sessions can be planned 2 or 3 times per week for the duration of the patient's life, as may be selected for CKD. Sessions are traditionally 1 to 6 hours in length, but can be longer depending on stability of the patient and efficiency of the session. IHD is designed as a more efficient modality than continuous renal replacement therapy (CRRT), meaning that IHD sessions remove small dialyzable molecules (including blood urea nitrogen [BUN], creatinine, phosphorus, electrolytes, and certain drugs and toxins) from the bloodstream more rapidly than CRRT. Between treatments (the interdialysis period), these dialyzable molecules may again increase in the bloodstream. IHD is commonly performed in university or private practice specialty referral centers, and cases are most often overseen by Diplomates of the Colleges of Veterinary Internal Medicine or Emergency and Critical Care.

PRINCIPLES OF HEMODIALYSIS

The main forces used during IHD are diffusion, convection, and adsorption. The magnitude of exchange of fluids and solutes is determined by the characteristics of the solute as well as the pore size and structural characteristics of the dialyzer

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membrane. In IHD, diffusion is the most prevalent force for exchange of solutes and fluids; convection and adsorption generally play a minor role.

During diffusion, solutes move from areas of high to low concentration. In moving, solutes leave the blood or dialysate fluid compartment in which they had been dissolved, cross the dialysis membrane, and enter the opposite fluid compartment. Blood solutes such as BUN, creatinine, and electrolytes diffuse across the semipermeable dialyzer membrane into dialysate, which is discarded. Solute in high concentration in dialysate, such as bicarbonate and selected electrolytes, may diffuse across the dialyzer membrane according to their concentration gradient into blood. The rate of solute transfer via diffusion is determined by the concentration gradient of the solutes, kinetic energy in solution (mainly determined by molecular weight), and membrane permeability. Diffusion is best at removing molecules with low molecular weight from the blood, including BUN and creatinine, sodium, potassium, phosphorus, and magnesium (**Box 1**).

During convection, water is removed from the blood along with dissolved solutes. Blood traveling in semipermeable membranes of the dialyzer is exposed to positive transmembrane pressure, which pushes fluid (ultrafiltrate) and dissolved solutes out of blood, across the dialyzer membrane, and into the dialysate, which is discarded. The rate of fluid and solvent transfer via convection is determined by transmembrane hydrostatic pressure between the blood and dialysate, and the surface area of the dialysis membrane. Convection, a prevalent force in CRRT but not IHD, is best at removing molecules with low and middle molecular weight from the blood. Middle

Box 1**Molecular weights of selected uremic toxins***Low molecular weight (<500 Da)*

- Creatinine
- Hydrogen
- Magnesium
- Oxalic acid
- *p*-Cresol
- Phosphate
- Potassium
- Sodium
- Urea (60)

Middle and high molecular weight (>500 Da)

- β_2 -Microglobulin
- Parathyroid hormone
- Carbamylated proteins
- Granulocyte inhibitory proteins
- Other peptides and proteins

Data from Yeun JY, Depner TA. Principles of hemodialysis. In: Owen WF, Pereira BJJ, Sayegh M, editors. Dialysis and transplantation: a companion to Brenner & Rector's the kidney. Philadelphia: WB Saunders; 2000. p. 1–31.

molecules include many inflammatory mediators, as well as uremic toxins (see **Box 1**).

INDICATIONS FOR IHD

Acute and Acute-on-chronic Kidney Injury

AKI occurs as a result of acute damage to the hemodynamic, filtration, or excretory functions of the kidney (**Table 1**). The subsequent acute decrease in glomerular filtration rate leads to accumulation of uremic toxins and metabolic wastes in the blood stream, resulting in dysregulation of fluid, electrolyte, and acid-base balance.

A diagnostic algorithm that includes the following criteria may be used to establish the clinical definition of AKI.

Main criteria for diagnosis of AKI

- Acute onset of clinical signs (<7 days)
- Increased creatinine or increased BUN levels despite fluid correction of prerenal azotemia.

Supportive criteria for diagnosis of AKI

- Known normal creatinine within past 1 month
- Known recent ischemia or nephrotoxicant ingestion
- Morphologic confirmation of acute renal lesions
- Return of creatinine to normal values.

In dogs, the most common causes of AKI include ischemia and toxin ingestion.¹ Ischemic events may be caused by pancreatitis, hypovolemia, sepsis, disseminated intravascular coagulopathy, hospital procedures (general anesthesia), or other causes.^{2,3} The most common ingested nephrotoxicant in dogs is ethylene glycol, though AKI has been reported from many other toxins, including grapes and raisins, aminoglycoside antibiotics, chemotherapy agents such as cisplatin and ifosfamide, and nonsteroidal antiinflammatory medications (NSAIDs).^{1,4,5} Leptospirosis is a common cause of AKI in dogs, and peritoneal or hemodialysis seems to improve outcome in dogs with severe infections.^{6,7}

In cats, the most common causes of AKI include toxic and ischemic insults. The most common ingested nephrotoxicant in cats is the lily plant of the genera *Lilium* and *Heimerocallis*, although AKI has been reported from ethylene glycol, as well as a variety of medications such as aminoglycoside antibiotics, NSAIDs, and chemotherapy agents.^{8,9} Partial or complete ureteral obstruction can lead to acute or chronic kidney injury, most commonly as a result of calcium-based urolithiasis, the incidence of which is rising.^{10,11} Recently, dried solidified blood calculi have been shown to cause ureteral obstruction in cats.¹² Some clinicians define urethral obstruction in cats as an indication for hemodialysis.¹³

In both dogs and cats, bacterial pyelonephritis, ureteral obstruction, and urinary tract rupture can cause AKI. Bacterial pyelonephritis is commonly caused by ascending lower urinary tract infection, but may be caused by hematogenous spread. Ureteral obstruction is most common in cats and small dogs caused by calcium-based ureteroliths, or less commonly ureteral trauma, neoplasia, or inflammation.¹⁰ Urinary tract rupture may be caused by trauma, pressure necrosis from urolithiasis, or surgery.¹⁴ A combination of melamine and cyanuric acid caused AKI in both dogs and cats during an outbreak of contaminated pet food from China in March of 2007.^{15,16}

Initial management of acute or acute-on-chronic injury includes intravenous fluid administration, correction of hypovolemia, correction of mineral, electrolyte, and acid-base imbalances, supportive care of the clinical signs of uremia, and nutritional

Table 1
Renal indications for hemodialysis in the veterinary literature

Reference	Indication for Hemodialysis
Cowgill and Elliott, ¹⁷ 2000	<p>Acute renal failure</p> <p>When the clinical consequences of the azotemia, fluid, electrolyte, and acid-base disturbances cannot be managed with medical therapy</p> <p>When severe oliguria or anuria in which an effective diuresis cannot be maintained with replacement fluids, osmotic or chemical diuretics, and renal vasodilators</p> <p>Chronic renal failure</p> <p>When severe, chronic uremia (BUN level >90, creatinine level >7) exceeds the efficacy of medical management, and owners wish for short periods of dialytic support to ameliorate the azotemia and other complications of CKI</p> <p>Finite periods of hemodialysis may be indicated for the preoperative management of animals awaiting renal transplantation</p>
Langston, ²⁸ 2002	<p>Acute renal failure</p> <p>Uncontrolled biochemical or clinical manifestations of uremia</p> <p>Life-threatening electrolyte disturbances: hyperkalemia, hyponatremia, hypernatremia</p> <p>Life-threatening fluid overload: pulmonary edema, congestive heart failure, systemic hypertension</p> <p>Severe or refractory azotemia (BUN level >100 mg/dL; creatinine level >10 mg/dL) that is unresponsive to aggressive medical management for 12 to 24 hours</p> <p>Chronic renal failure</p> <p>Refractory uremia (BUN level >100 mg/dL; creatinine level >8 mg/dL)</p> <p>Intractable clinical signs related to uremia</p> <p>Preoperative stabilization for renal transplantation</p>
Elliott, ²³ 2000	<p>Refractory azotemia (BUN level >90 mg/dL, creatinine level >6 mg/dL)</p> <p>Intractable uremic signs</p> <p>Hyperkalemia</p> <p>Fluid overload</p> <p>Severe metabolic acidosis</p> <p>Preoperative conditioning for renal transplantation</p> <p>Postoperative delayed graft function</p> <p>Acute renal graft rejection</p> <p>Acute exacerbations of chronic renal failure</p>
Groman, ¹⁹ 2010	<p>Fluid overload</p> <p>Immune-mediated diseases</p> <p>Removal of inflammatory mediators</p> <p>Apheresis</p> <p>Artificial liver</p>

support. Treatment also includes removal of the inciting cause of renal injury, if possible. Many causes of AKI are potentially reversible; animals may die of complications of uremia before sufficient renal recovery occurs.

IHD may be an appropriate consideration when medical management fails to achieve the goals outlined earlier. Therefore, IHD is indicated in cases of significant or rising azotemia, electrolyte abnormalities, or acidosis unresponsive to medical management. IHD is also indicated in cases of oliguria and anuria in the face of appropriate medical management.

Before IHD is considered, consider the following questions in your patient:

- Have I adequately rehydrated my patient?
- Have I corrected hypovolemia and hypotension using fluid therapy or pressor medications?
- Have I challenged my anuric or oliguric patient with diuretic therapy?

If the answers are yes to these questions and medical management still fails to improve the patient's clinical and clinicopathologic picture, or if the life-threatening severity of disease precludes attention to each question, consideration of IHD is warranted. These questions should be addressed in a matter of hours, not days, because early intervention improves the chance of a successful outcome.^{13,17}

CKD

IHD is commonly used in the management of humans with CKD.¹⁸ IHD is an uncommon but available therapy for management of CKD in veterinary patients. Indications for IHD in patients with CKD include reduction of chronic progressive azotemia, hyperkalemia, and fluid overload, as well as stabilization before renal transplantation.

Future indications for IHD therapy

In the future, IHD may become part of the treatment offered for liver failure via liver dialysis, in which a specialized dialyzer membrane acts as an artificial liver. IHD may become part of a routine treatment of patients with systemic inflammatory response syndrome, sepsis, or other severe inflammatory conditions via filtration and removal of inflammatory mediators, or fluid overload and congestive heart failure via ultrafiltration and removal of excess intravascular fluid volume as well as apheresis.¹⁹

HEMODIALYSIS EQUIPMENT

Venous Access

Hemodialysis removes blood volume from the patient, cleanses it using the extracorporeal dialysis membrane, and returns it to the patient. Therefore, dependable venous access is a cornerstone of IHD success. In veterinary medicine, recirculating blood access and return is generally obtained using a double-lumen intravenous jugular catheter (see the article on vascular access by Chalhoub and colleagues elsewhere in this issue for further exploration of this topic).

When first selecting a dialysis catheter, consider both the lumen width and the catheter length. Select the largest lumen width appropriate for your patient, which enables higher blood flow, increased dialysis efficiency (if desired), and theoretically fewer complications such as blood stasis and clotting. Select the length of your catheter by measuring from the expected insertion point to the junction of the cranial vena cava and right atrium of the patient. Vascular access may be impaired if catheters are too short and are unable to draw blood from the vena cava or right atrium, or if they are too long and result in increased resistance to flow.

Dialysis catheters can be temporary or permanent. Temporary catheters are appropriate for treatment of acute intoxications, acute and acute-on-chronic injury, and in patients too unstable to receive a permanent catheter. Temporary catheters are placed using a modified Seldinger technique.^{20,21} All personnel involved in catheter placement should wear a cap, mask, and sterile gloves. The doctor or technician placing the catheter should also wear a sterile gown. First, the patient is lightly sedated; we often use butorphanol 0.2 mg/kg intravenously. Comatose patients should not be sedated. Next, clip and drape the area in a sterile manner, and perform a sterile preparation of the area using a chlorhexidine scrub and alcohol. The temporary dialysis catheter is then placed as follows.

The vessel is punctured with a trocar or 16 G over-the-needle catheter, using a cut-down technique if appropriate. The guidewire is advanced through the lumen of the trocar, and the trocar is withdrawn. The dilator sheath is placed over the guidewire into the vessel, and the guidewire is withdrawn. The catheter is placed through the dilator sheath into the vessel, the sheath is withdrawn, and the catheter is sutured into place. Alternatively, the dilator sheath can be removed before placement of the catheter over the guidewire. A lateral radiograph of the thorax is always taken to make sure the catheter is placed appropriately and the tip is at the level of the right atrium. The catheter is wrapped in a sterile manner, and is used only for hemodialysis. The catheter is locked with heparin (1000 units/mL) when not in use, to prevent clotting.

Permanent dialysis catheters that are surgically placed are recommended for those patients who receive chronic IHD. Permanent catheters are also chosen based on lumen width and catheter length, as explained earlier. Both types of catheters are heparin locked when not in use, are used exclusively for hemodialysis, and are always handled in a sterile manner. Differences between temporary and permanent catheters include the following^{17,22}:

- Material
 - Temporary catheters can be polyurethane or silicone
 - Permanent catheters should be silicone, which is softer and less reactive than polyurethane
- Placement
 - Temporary catheters are placed percutaneously in a clean room using the modified Seldinger technique
 - Permanent catheters are placed surgically, and the catheter is tunneled subcutaneously from insertion site to the skin exit site to reduce motion, decrease infection risk, and keep the catheter in place
- Cuffing
 - Temporary catheters do not contain cuffs
 - Permanent catheters may contain cuffs to help keep the catheter in place for long periods; the cuff is placed in the subcutaneous tunnel.

THE DIALYZER OR ARTIFICIAL KIDNEY

The hemodialyzer is a compact, disposable extracorporeal unit that acts as an artificial kidney. The dialyzer unit is a sealed compartment with connections on either end to allow for flow of blood and dialysate through the unit (**Fig. 1**). Within the most common type of dialyzer are thousands of hollow straws (called hollow fiber design). Blood flows within the straws, whereas dialysate flows around the straws, in a concurrent or countercurrent direction. The surface of the straw acts as both a physical barrier separating the blood and dialysate compartments, and as a semipermeable

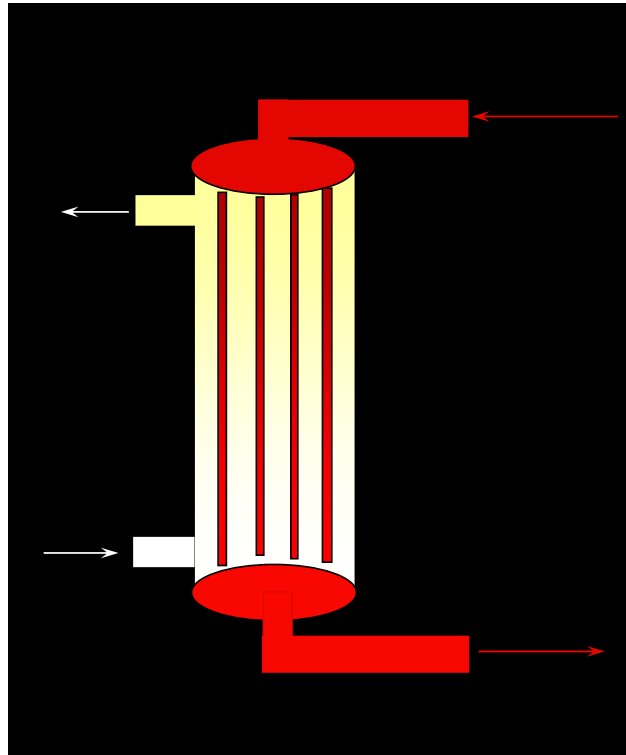


Fig. 1. A dialyzer. (Courtesy of Dr Cathy Langston, New York.)

membrane allowing transfer of fluid and solutes according to the principles of diffusion and convection (**Fig. 2**).

When first selecting a dialyzer unit, consider the membrane type, and the size of the dialyzer unit. Membranes come in a wide variety of types, and both the membrane material and the pore size are important. At our dialysis center, we generally use dialyzer membranes made of polysulfone, a synthetic material. Synthetic dialyzer membranes are less reactive, and are less likely to induce complement activation than the older, cellulose-based dialyzer membranes. Dialyzers are classified broadly by pore size as low flux (small pore size that allows passage of small solutes), or high flux (larger pore size that allows passage of water and small and middle molecules).

The larger the dialyzer unit, the greater the membrane surface area for exchange of water and solutes, and, potentially, the more efficient the dialysis session. However, with larger dialyzer units comes greater extracorporeal blood volume, meaning that



Fig. 2. Close-up of hollow fiber design.

more blood is outside the patient's body during the dialysis session. Therefore, the size of the dialyzer unit must be carefully chosen to maximize efficiency and minimize excessive extracorporeal blood volume. In addition, each dialyzer unit comes with a set of blood tubing. The dialyzer unit plus the associated blood tubing is called the blood circuit, and each blood circuit has a predetermined, consistent, and labeled blood volume that fills the circuit. Therefore, when choosing a dialyzer unit, consider the volume of the blood circuit, which equals the total extracorporeal blood volume. The total extracorporeal blood volume should be less than 10% of the patient's blood volume to minimize patient hypotension and hypovolemia.^{17,23} The smallest blood circuits that are commonly used in veterinary medicine are neonatal circuits, which necessitate an extracorporeal blood volume of at least 50 mL. For small patients less than 7.0 kg, this circuit contains more than 10% of the patients' blood volume, and it is advantageous to prime the circuit with type-matched whole blood, colloidal fluids, or other volume-expanding fluids to minimize hypotension and hypovolemia.¹⁷

THE IHD MACHINE

The IHD machine is the foundation of the dialysis session (**Fig. 3**). The machine allows the doctor or technician to control the following parameters:

- Blood flow rate
- Dialysate flow rate
- Direction of blood flow with respect to dialysate flow (concurrent vs countercurrent)
- Dialysate composition
- Treatment length

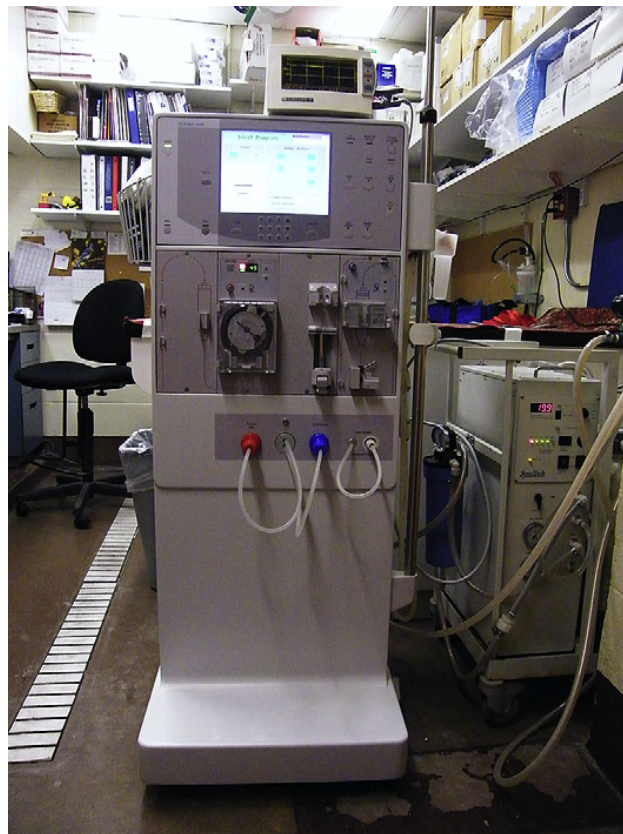


Fig. 3. IHD machine.

- Sodium profiling, a method to regulate plasma osmolality and stabilize fluid shifts
- Anticoagulant administration rate, including bolus and continuous rate infusion (CRI) capabilities
- Temperature of returning blood
- Fluid removal from the bloodstream.

Careful attention to these parameters allows you to control the efficiency of the dialysis session and maximize the safety and stability of the patient. The IHD machine manufactures dialysate during each session, according to your prescription. The basic ingredients include a concentrated solute solution, a concentrated bicarbonate solution, and purified water. The concentrated solute solution may contain sodium, potassium, and calcium, as well as dextrose, chloride, and magnesium in amounts that approximate plasma concentrations. Solute solutions are available without potassium for use with hyperkalemic patients. Solute solutions are also available with different calcium concentrations and even without calcium, for use with hypercalcemic patients or patients anticoagulated with citrate, as discussed later. Most modern IHD machines allow you to sodium profile during the session. The most commonly used method of sodium profiling keeps dialysate sodium slightly higher than patient plasma sodium at the start of the session, with a gradual decrease in dialysate sodium during the session. The high dialysate/plasma sodium ratio allows sodium to diffuse from dialysate into patient plasma early in the dialysis session, when diffusion of urea out of patient plasma into dialysate is most rapid.²² Using the equation for plasma osmolality

$$2 (\text{Na}^+ + \text{K}^+) + \text{BUN}/2.8 + \text{BG}/18$$

we see that increasing plasma sodium during times of rapid decrease in plasma urea can help stabilize patient plasma osmolality, which lowers the risk of a serious IHD side effect called dialysis disequilibrium syndrome (DDS), as discussed later. As the session progresses, dialysate sodium is lowered to avoid patient plasma hypernatremia.²²

The bicarbonate solution is initially separate from the concentrated solute solution to avoid precipitation with calcium and magnesium, and is mixed by the IHD machine in diluted states to avoid precipitation.¹⁷ Acetate, an alternative to bicarbonate, is more stable in solution but is not recommended, because it can cause vasodilation, hypotension, and reduced cardiac contractility in veterinary patients.¹⁷

The blood path is defined by the path of the extracorporeal circuit (**Fig. 4**). Blood is pulled from one of the 2 ports of the dialysis catheter, and travels through the

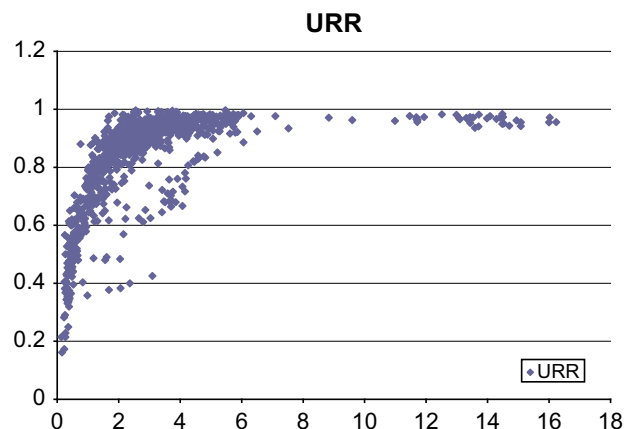


Fig. 4. Graph of URR to determine dialysis prescription. (Courtesy of Dr Cathy Langston, New York.)

extracorporeal circuit being pulled (prepump) and then pushed (postpump) by the clockwise circling of the blood pump. Blood then enters the straws of the dialyzer and runs the length of the dialyzer, separated from the dialysate by the semipermeable dialyzer membrane. Filtered blood is then returned to the patient via the second port of the dialysis catheter. IHD can be performed with a single-lumen catheter if needed; the IHD machine alternates pull and return of blood, and the session is less efficient.²² Along the extracorporeal circuit are instruments to detect air and leaks, a filter to catch thrombi, pressure pods for measuring occlusion or disconnection in the circuit, and sampling ports from which blood may be drawn and medications given.

Other monitoring equipment helpful or essential to an IHD session include a continuous electrocardiogram, activated clotting time (ACT) machine, blood warmer cuff to warm the returning blood line, pulse oximeter, blood pressure monitoring, and supplemental oxygen. In-line blood-volume profiling equipment monitors hematocrit and oxygen saturation, and is a helpful adjunct to pulse oximetry and indirect blood pressure monitoring in the vigilance against hypotension and hypoxemia, 2 complications of IHD. It is essential to have equipment and staff capable of initiating cardiopulmonary cerebral resuscitation in the event of an arrest.

Patients should be positioned and lightly restrained on a cushioned, comfortable table, with a heating pad positioned under the patient. We generally keep a harness on our patients, and restrain them lightly to the table. Cats sit in the well-cushioned bottom half of a cat carrier. Absorbent pads help keep the patient clean and dry.

ANTICOAGULATION

Extracorporeal blood must be anticoagulated when processing through the dialysis tubing and dialyzer unit. The dialyzer membrane initializes the contact activation pathway of the coagulation cascade^{24,25}; therefore, IHD is a prothrombotic procedure, and anticoagulation is almost always used during each session. The 2 most common methods of anticoagulation are unfractionated heparin and citrate. Unfractionated heparin inhibits coagulation by binding antithrombin; together, this complex binds and inactivates multiple coagulation factors, including IIa (thrombin), IXa, Xa, XIa, and XIIa.²⁶ Unfractionated heparin is infused directly into the blood of the extracorporeal circuit before the filter, and is often given as a bolus followed by a CRI. The initial bolus is given at 25 to 50 units/kg, and the heparin CRI is adjusted based on ACT readings.²² The goal is to keep the ACT 1.6 to 2 times more than normal, or approximately 160 to 200 seconds.²² Heparin CRI is discontinued 30 minutes before the end of the IHD session, and the patient is considered heparinized for at least 6 to 8 hours after the session. If intervals between dialysis sessions are short the patient is considered heparinized in the interdialytic period. Citrate inhibits coagulation by binding calcium, which is an important cofactor in the amplification and propagation phases of the cell-based model of coagulation.²⁵ Citrate anticoagulation differs from heparin because citrate anticoagulation is considered regional; the extracorporeal circuit is anticoagulated, but the patient ideally is not. Citrate is infused directly into the blood of the extracorporeal circuit before the filter, and anticoagulates the extracorporeal circuit. The citrate infusion is adjusted based on the postfilter ionized calcium in the extracorporeal blood.²² Before the filtered and citrated blood returns to the patient, calcium is infused into the patient's blood, binding and inactivating the citrate.

STAFFING

IHD sessions last from 1 to 6 hours; sessions may be extended for increased efficiency in certain cases. At our dialysis center, IHD takes place in a quiet, dedicated room

directly across the hall from the intensive care unit (ICU). At least 2 dedicated hemodialysis personnel work on each IHD case: at least one is in the dialysis room monitoring the patient at all times, whereas the other is in the dialysis room or immediately accessible. If not in the same room, personnel are in contact via walkie-talkie. ICU staff, although separate from dialysis staff, are alerted that there is a dialysis session and are available to assist if needed.

Our dialysis staff consists of a dedicated day and evening dialysis technician, whose primary allegiance is the hemodialysis unit, in which they are highly trained in both IHD and CRRT. One dialysis technician helps run nearly every dialysis session. Between session and patients, they run the IHD machine daily, oversee water purification and testing, stock and organize the dialysis room, and participate in continuing education with the dialysis team. One technician is on call at all times; therefore, dedication and dependability of technicians are essential to running a dialysis unit. Between dialysis duties, our technicians work with in- and outpatients, and both are employed full time by the university.

The second part of our hemodialysis team is the clinicians: all internal medicine residents, plus interested interns and emergency and critical care residents, are trained in IHD and CRRT. They participate in a rotating on-call schedule to assist referring veterinarians, clients, and house doctors in deciding whether to pursue hemodialysis on a given case, and plan and run each session. Dialysis plans, prescriptions, and sessions are overseen by 2 dedicated faculty members who specialize in renal medicine. A small team of interested veterinary students are trained to assist during hemodialysis sessions. Building a dialysis unit takes the dedication, training, continuing education, and commitment of many.

FORMULATING AN IHD PRESCRIPTION

The dialysis prescription refers to the parameters that are set for each session to deliver a particular dose of dialysis to a patient. The prescription is different for each patient and for each session; however, some general principles apply. Choosing a dialysis prescription includes consideration of the following parameters such as uremia, the hemodialyzer, blood flow rate, length of session and frequency of sessions (**Box 2**).²³

Box 2

Decision parameters for creating a dialysis prescription

- Severity of uremia
- Expected frequency of IHD sessions
- Choice of hemodialyzer
- Volume of extracorporeal circuit
- Dialysate composition
- Dialysate flow rate
- Blood flow rate
- Length of dialysis session
- Anticoagulant dosage
- Choice of priming solution
- Ultrafiltration rate
- Ultrafiltration volume

BLOOD FLOW RATE AND LENGTH AND FREQUENCY OF DIALYSIS SESSIONS

For acute and acute-on-chronic kidney injury, initial BUN level is often markedly increased. Although IHD is capable of lowering BUN level quickly, a rapid decrease in BUN and/or sodium levels leads to marked decreases in plasma osmolality. Consequent rapid fluid shifts can result in DDS. Therefore, initial sessions are designed to be less efficient.²⁷ Methods to decrease diffusion efficiency include shorter sessions, slower blood flow rates, and concurrent (rather than countercurrent) flow of blood and dialysate.

One way to calculate desired efficiency of the initial session based on severity of uremia is via the urea reduction ratio (URR) to determine the volume of blood that needs to be processed through the dialyzer to achieve a certain percent reduction in BUN level.²² URR and the corresponding blood flow rate (L/kg body weight) needed to achieve that particular URR have been determined for dogs and cats using empirical data from the Companion Animal Hemodialysis Unit at the Veterinary Medical Teaching Hospital at the University of California-Davis. In IHD, blood flow rate is the primary determinant of small molecule clearance, including BUN and potassium clearance.²² Therefore, one way to begin a dialysis prescription is to determine a desired URR (**Box 3**), determine the volume of blood per kilogram body weight the machine must process to achieve that desired URR (see **Fig. 4**), and determine the desired length of the session, which is often 1.5 to 2 hours for the first session, 3 hours for the second session, and 4 hours (cats) to 5 hours (dogs) for the third or fourth sessions.²⁸ Using the patient's body weight, desired blood volume to be processed, and desired length of the session, you can set your blood flow rate in mL/kg/min accordingly. Blood flow rate is often set low at

Box 3

A simplified method built on the URR criteria

- First session

Blood flow rate 5 mL/kg/min

Note: Cowgill and Elliott¹⁷ recommend blood flow rates as low as 1 to 2 mL/kg/min for animals with predialysis BUN level greater than 180 mg/dL

Length of session approximately 1 to 2 hours

Note: Cowgill and Elliott¹⁷ recommend prolonged, slow treatment sessions of up to 8 hours for small patients with severe uremia (BUN level >250 mg/dL), using blood flow rates less than 2 mL/kg/min

- Second session

Blood flow rate 10 mL/kg/min

Length of session approximately 3 hours

- Additional sessions

Blood flow rate 15 to 20 mL/kg/min

Length of session

Cats approximately 4 hours

Dogs approximately 5 hours

Data from Cowgill LD, Elliott DA. Hemodialysis. In: DiBartola SP. Fluid therapy in small animal practice. 3rd edition. Philadelphia: WB Saunders; 2000. p. 528–47; and Langston C. Hemodialysis in dogs and cats. Compendium 2002;24:540–9.

the start of the session and is slowly increased to the prescribed blood flow rate in the first 30 minutes of the session, to avoid hypotension or nausea.²³

For IHD of patients with CKD, sessions are performed 2 or preferably 3 times per week, with twice-weekly sessions appropriate only for those patients with sufficient residual renal function to avoid significant rebound solute accumulation between dialysis sessions.²⁹ Blood flow rate targets can be set at 15 to 25 mL/kg/min if the patient's starting BUN level and vascular access can tolerate this high rate. Targets for length of session are 4 hours in cats and 5 hours in dogs, again, if well tolerated by the patient.^{28,29} For acute and chronic IHD, longer sessions may be both feasible and desirable, depending on treatment goals.

Between dialysis sessions, solutes do reaccumulate. Therefore, bloodwork must always be taken at the start and end of the dialysis session and between dialysis sessions, so that appropriate dialysis prescriptions and interdialysis treatments are optimized for each individual patient.

PRIMING SOLUTION

Priming solution is often saline, but colloids can be used for patients whose extracorporeal blood volume approaches or exceeds the 10% blood volume guideline, or for patients who are anemic or hypovolemic at the start of the session. Useful colloids include typed whole blood and Hetastarch diluted 50% with saline.²²

DIALYSATE FLOW RATE

Dialysate flow rate is, by convention, 500 mL/min. This rate can be altered if needed. A faster dialysis flow rate provides a modest increase in clearance, whereas a slower dialysis flow rate provides a modest decrease in clearance.^{17,22}

ULTRAFILTRATION

Much of the discussion of hemodialysis focuses on removal of solutes, such as urea, creatinine, and potassium, from the uremic patient's bloodstream. However, during IHD, fluid can also be removed from the bloodstream. This process is called ultrafiltration, and is of great benefit to overhydrated patients. The amount of fluid to remove during an IHD session can be calculated as follows²²: % overhydration × kilograms body weight × 10 = milliliters of fluid to remove during the dialysis session.

Once you know the milliliters of excess patient fluid you wish to remove and the length of the session, you can calculate the number of milliliters of plasma fluid your machine should remove, which is programmed in milliliters per hour. The rate of patient fluid removal should not exceed 20 mL/kg/h.²² Ultrafiltration can be modeled to remove more plasma fluid toward the end of the dialysis session, when dialysis efficiency has decreased and the patient is at less risk for solute and corresponding fluid shifts.²⁷

MEASURING EFFICACY

URR, which was estimated before the start of the dialysis session, can be measured after the session using the following equation:

$$\text{URR} = (\text{BUN}_{\text{pre}} - \text{BUN}_{\text{post}}) / \text{BUN}_{\text{post}}$$

If the URR is higher than anticipated, the session has been more efficient than expected, and you may wish to change your dialysis prescription for the next session.

If the URR is lower than anticipated, there may be clotting or clogging of the dialysis membrane, causing reduced efficiency. It is also possible that there is catheter recirculation, meaning that a significant portion of the returned blood is rapidly removed again for filtration, rather than joining the body blood pool. This situation can happen with dual-lumen catheters with staggered ends in which blood is being drawn from the distal lumen and returned through the proximal lumen; such reduced efficiency can be ameliorated if the direction of blood flow is reversed.²² Target URRs should be no greater than 0.1 URR per hour.

Kt/V can also be used to calculate session efficiency and is discussed in detail in another article by Cowgill elsewhere in this issue. It is a commonly used measure of urea removal and is a kinetically modeled index reflecting the fractional clearance of urea from its distribution volume during a single dialysis session. This index refers to the delivered dose of dialysis that is equal to delivered clearance. In this index, K is the urea clearance of the dialyzer (mL/min), t is the time of the dialysis session (min), and V is the volume of urea distribution (L) that approximates total body water. Essentially, $Kt/V = \ln(\text{BUN}_{\text{pre}}/\text{BUN}_{\text{post}})$. The higher the Kt/V value, the greater the dose of dialysis and efficacy of the dialysis treatment. Kt/V values between 1.2 and 1.4 are considered adequate hemodialysis doses in human patients, but conventional dialysis prescriptions in animals often result in Kt/V values between 2.5 and 3, reflecting highly effective dialysis treatment.^{17,30} (See the article by Cowgill elsewhere in this issue for further exploration of this topic.)

COMPLICATIONS

Complications of IHD have been widely reported, and include hypotension and hypovolemia; problems with vascular access; and neurologic, respiratory, hematologic, and gastrointestinal complications.^{17,23}

Hypotension and hypovolemia occur during IHD sessions as a result of ultrafiltration and large extracorporeal blood volumes and can persist during or between sessions as a result of blood loss (from bleeding secondary to uremic ulceration, overheparinization, or coagulopathy, or blood loss secondary to filter or line clotting in which not all extracorporeal blood volume can be returned to the patient). Treatments include decreased ultrafiltration, crystalloid or colloid therapy, pressor therapy, or cessation of the IHD session in severe cases. Approximately 50% of feline IHD cases have problems with hypotension and hypovolemia.^{9,31}

Problems with vascular access are common and include thrombosis, failure to provide adequate blood flow, and less commonly bleeding and infection.^{17,29} Thrombosis is countered by filling each catheter lumen with heparin between dialysis sessions; however, incorrect dosage of heparin locks can predispose the patient to bleeding.¹⁷ Failure to provide adequate flow can be countered with careful attention to catheter size choice, as explained earlier. The goal is to choose the largest bore catheter you can safely place in your patient, and to choose the proper length catheter positioned in the right atrium or vena cava.

Neurologic complications can be caused by uremic encephalopathy, intracranial bleeding or thrombosis, or DDS. DDS is caused by rapid shifts in sodium, urea, or bicarbonate, leading to cerebral edema. Clinical signs include agitation, disorientation, vomiting, seizure, coma, and death during or after a dialysis session. We find that dogs often vocalize or become agitated, whereas cats often do not display obvious premonitory signs and may die suddenly. Prevention includes mannitol infusion during the dialysis session, sodium modeling, and limited-efficiency sessions; treatment includes mannitol and diazepam. In a review of IHD in cats, Langston and

colleagues³¹ report DDS in 38% of cats. Clinical signs included disorientation, agitation, vocalization, dilated pupils, acute blindness, or coma. Seventy-eight percent of affected cats responded to treatment with mannitol, whereas 13% did not respond to mannitol, and 8% died despite DDS treatment. Suspected DDS has also been reported in dogs undergoing IHD.⁵

Respiratory signs can occur in IHD patients as a result of underlying disease, complications or IHD, or both. Respiratory complications include uremic pneumonitis and pulmonary hemorrhage, pleural effusion and pulmonary edema, hypoxemia, hypoventilation, and pulmonary thromboembolism (PTE).²³ We suspect that we see pulmonary hemorrhage secondary to leptospirosis infection, as well as because of uremic or iatrogenic coagulopathy. Adin and Cowgill⁷ report that 50% of leptospiremic dogs in one study were thrombocytopenic, likely because of vasculitis. Fluid gain, or failure to correct overhydration, during IHD sessions can lead to pleural effusion and pulmonary edema; cardiac disease can cause or contribute to this complication. Hypoxemia and hypoventilation can be caused by ventilatory failure in the critically ill or neurologically impaired patient; whereas hypoxemia can be caused by diffusion failure as a result of pulmonary hemorrhage, pneumonitis, infectious pneumonia, or edema, or ventilation-perfusion mismatch caused by PTE.³²

Hematologic complications including anemia, thrombocytopenia, and leucopenia are also common in patients with IHD. Again, these complications can be caused by primary disease; anemia is a common sequela of CKD. Anemia and thrombocytopenia result from coagulopathy and vasculitis common with systemic inflammatory response syndrome, and leucopenia can result from infectious or inflammatory processes. Anemia is also common as a result of frequent blood sampling, loss through the extracorporeal circuit, and bleeding, as described earlier. Thrombocytopenia can occur secondary to contact activation with the dialysis membrane, and promotion of the coagulation cascade as a result of disease-specific or iatrogenic coagulopathy, whereas leucopenia can occur transiently as a result of white blood cell interaction with the dialysis membrane.²³ Clinical anemia and thrombocytopenia may be corrected by addressing the underlying cause, and providing compatible colloid, whole-blood, packed red blood cells, or plasma transfusions.

Gastrointestinal complications such as nausea, vomiting, and inappetence are common in uremic animals, and can also be a complication of dialysis-induced hypotension, DDS, dialysate contaminants, and incompatible blood transfusion reactions.²³ Complications can be addressed using histamine-2 receptor blockers or proton-pump inhibitors, antiemetics, and appetite stimulants as appropriate. Many dialysis centers place esophageal feeding tubes at the time of dialysis catheter placement, to help ensure proper nutrition, hydration, and oral medication during interdialysis periods.^{27,33} Parenteral nutrition must be considered when enteral nutrition is not possible.

OUTCOME

Outcome of medical management for AKI in dogs, cats, and humans routinely averages around 50% to 60%.^{1,2,8} Indications to forego continued medical management in favor of hemodialysis include worsening azotemia, worsening hyperkalemia, and anuria or oliguria despite appropriate medical management, as discussed earlier. The cause of AKI can influence the success of both medical and dialytic therapy.

Adin and Cowgill⁷ report on the outcome of 14 dogs treated with IHD for AKI secondary to leptospirosis. Twelve of the 14 dogs were oliguric or anuric despite appropriate medical therapy. Survival rate was excellent at 86%, with only one of 14 dogs necessitating chronic hemodialysis. Prognosis for AKI caused by grape or raisin toxicity in

dogs treated medically is 53%, and Eubig and colleagues⁴ and Stanley and Langston⁵ report successful reversal of currant-induced AKI in a dog with progressive azotemia and oliguria despite appropriate medical management. In cats, AKI caused by lily ingestion can be fatal, with recent articles showing 0% survival for anuric lily-intoxicated cats, but that survival after oliguria may be possible with early and aggressive dialysis therapy.^{28,34} Worwag and Langston⁸ discuss successful IHD in 25% (2 of 8) of feline AKI cases but do not specify the criteria for dialysis in these 8 cats; it may be the dialyzed cats were significantly more uremic or more critically ill than the successfully medically managed cats, because overall survival for all cats treated for AKI in this study was 61%. Kyles and colleagues¹⁰ report on the use of IHD to stabilize 13% of cats undergoing surgery for ureteral calculi; although these investigators do not relate IHD to outcome, the outcome of cats that had surgery to correct ureteral obstruction caused by calculi was better than the outcome of cats treated medically for this problem, with 91% of surgically treated cats and 72% of nonsurgically treated cats surviving for 1 month. In a review article on IHD in cats, Langston and colleagues³¹ found that the average survival rate for cats treated with IHD for AKI is 60%, similar to the survival rates in human patients with AKI treated with IHD. Pyelonephritis carried the best prognosis (100% survival), whereas ethylene glycol ingestion had 60% survival but necessitated a more prolonged course of dialysis (mean of 12 ± 7 sessions compared with 3 sessions for cats with pyelonephritis), and resulted in higher BUN and creatinine levels at the termination of dialysis. AKI had better outcomes than acute on CKD (13% or 1 of 8 cats recovered and survived) or CKD (no cats survived).

SUMMARY

IHD is a useful and feasible modality to improve outcome in dogs and cats with kidney injury that do not respond adequately to medical management. The decision to pursue hemodialysis in patients with acute or acute-on-chronic kidney injury should be made as quickly as possible to improve the likelihood of a successful outcome. IHD requires thorough understanding of renal physiology, as well as the principles and machinery involved in dialysis. It also requires a trained and dedicated staff 24 hours a day, 7 days a week, to field questions, identify appropriate cases, develop tailored dialysis prescriptions, perform the technical duties involved during and between dialysis sessions, attend to the patient and client in a holistic and compassionate manner, and be prepared to act in emergency situations that may arise in the care of these often critically ill patients. We encourage readers to become familiar with dialysis facilities near them, and to reach out to these facilities to learn more about dialysis, and indications and preparations to refer. If you are considering referring a patient for hemodialysis, please contact your local dialysis facility to discuss the case ([Appendix](#)); avoid venipuncture of the jugular veins so they remain intact for dialysis catheter placement; and be prepared to address the clients' expectations and financial and emotional investment involved in performing dialysis in our veterinary patients.

APPENDIX: LIST OF IHD FACILITIES

Animal Medical Center, 510 East 62nd Street, New York, NY 10065, USA

Tel: +1 212 329 8618

Dr Cathy Langston: cathy.langston@amcny.org

www.amcny.org/dialysis

AVETS, 4224 Northern Pike, Monroeville, PA 15146, USA

Tel: +1 412 373 4200

Dr Merilee Costello
www.avets.us

Companion Animal Hemodialysis Unit, Veterinary Medical Teaching Hospital,
University of California-Davis, Davis, CA 95616, USA

Tel: +1 530 752 1393

Dr Larry Cowgill: ldcowgill@ucdavis.edu

http://www.vetmed.ucdavis.edu/vmth/small_animal/hemo

Louisiana State University, Veterinary Medical Teaching Hospital, Baton Rouge, LA
70803, USA

Tel: +1 225 578 9600

Dr Mark Acierno

www.dialysis@vetmed.lsu.edu

Tufts University, Cummings School of Veterinary Medicine, Foster Hospital for
Small Animals, 200 Westboro Road, North Grafton, MA 01545, USA

Tel: +1 508 839 5395x84538

Dr Mary Labato

Dr Linda Ross

www.tufts.edu/vet

Aubi Companion Animal Hospital, Strada Genova 299/A, 10024 Moncalieri, Italy

Tel: +39 011 6813033

Dr Claudio Brovida

www.anubi.it

Centro Nefrologico Veterinario, Clinica Veterinaria Citta di Catania, Via Vittorio
Veneto 313, 95126 Catania, Italy

Tel: +39 095 503924

Dr Angelo Basile

www.nefrovet.com

Clinica Veterinaria Roma Sud, Via Pilade Mazza 24, Rome 00173, Italy

Tel: +39 06 72672403

Dr Daniela Mignacca

www.clinicaveterinariaromasud.it

Vetsuisse Faculty University of Berne, Laenggass-Strasse 128, PO Box 8466,
Berne, Switzerland

Tel: +41 (0)31 631 2943

Dr Thierry Francey

www.vetdialyse.unibe.ch

Tierärztliche Klinik für Kleintiere, Kabels Stieg 41, D-22850 Norderstedt, Germany

Tel: +49 (0)40 5298940

www.tierklinik-norderstedt.de

Hospital Veterinario Montenegro, Rua Pereira Reis, 191, 4200-447 Porto, Portugal

Tel: +351 225 089 639/+351 225 089 989

www.hospvetmontenegro.com

Renal Vet Rio de Janeiro, Rua Tereza Guimaraes, 42, Botafogo, Rio de Janeiro -
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Dr David Tan

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