Supportive Therapies: Intermittent Hemodialysis, Continuous Renal Replacement Therapies, and Peritoneal Dialysis

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Over the last decade, significant advances have been made in the availability of different dialysis methods for replacement of renal function. Although the majority of these have been developed for patients with end-stage renal disease, more and more they are being applied for the treatment of acute renal failure (ARF). The treatment of ARF, with renal replacement therapy (RRT), has the following goals: 1) to maintain fluid and electrolyte, acid-base, and solute homeostasis; 2) to prevent further insults to the kidney; 3) to promote healing and renal recovery; and 4) to permit other support measures such as nutrition to proceed without limitation. Ideally, therapeutic interventions should be designed to achieve these goals, taking into consideration the clinical course. Some of the issues that need consideration are the choice of dialysis modality, the indications for and timing of dialysis intervention, and the effect of dialysis on outcomes from ARF. This chapter outlines current concepts in the use of dialysis techniques for ARF.

CHAPTER

19

Dialysis Methods

DIALYSIS MODALITIES FOR ACUTE RENAL FAILURE

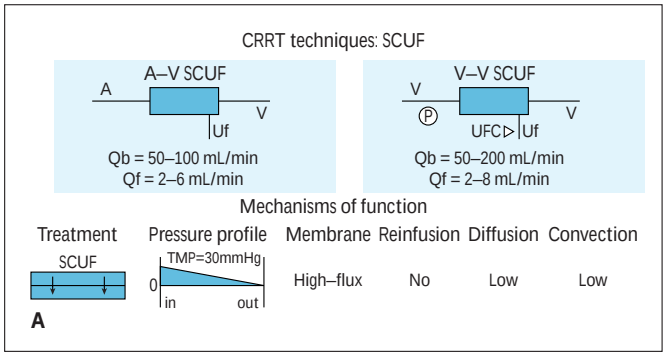
Intermittent therapies	Continuous therapies
Hemodialysis (HD)	Peritoneal (CAPD, CCPD)
Single-pass	Ultrafiltration (SCUF)
Sorbent-based	Hemofiltration (CAVH, CVVH)
Peritoneal (IPD)	Hemodialysis (CAVHD, CVVHD)
Hemofiltration (IHF)	Hemodiafiltration (CAVHDF, CVVHDF)
Ultrafiltration (UF)	CVVHDF

FIGURE 19-1

Several methods of dialysis are available for renal replacement therapy. While most of these have been adapted from dialysis procedures developed for end-stage renal disease several variations are available specifically for ARF patients [1] .

Of the intermittent procedures, intermittent hemodialysis (IHD) is currently the standard form of therapy worldwide for treatment of ARF in both intensive care unit (ICU) and non-ICU settings. The vast majority of IHD is performed using single-pass systems with moderate blood flow rates (200 to 250 mL/min) and countercurrent dialysate flow rates of 500 mL/min. Although this method is very efficient, it is also associated with hemodynamic instability resulting from the large shifts of solutes and fluid over a short time. Sorbent system IHD that regenerates small volumes of dialysate with an in-line Sorbent cartridge have not been very popular; however, they are a useful adjunct if large amounts of water are not available or in disasters [2]. These systems depend on a sorbent cartridge with multiple layers of different chemicals to regenerate the dialysate. In addition to the advantage of needing a small amount of water (6 L for a typical run) that does not need to be pretreated, the unique characteristics of the regeneration process allow greater flexibility in custom tailoring the dialysate. In contrast to IHD, intermittent hemodiafiltration (IHF), which uses convective clearance for solute removal, has not been used extensively in the United States, mainly because of the high cost of the sterile replacement fluid [3]. Several modifications have been made in this therapy, including the provision of on-line preparation of sterile replacement solutions. Proponents of this modality claim a greater degree of hemodynamic stability and improved middle molecule clearance, which may have an impact on outcomes.

As a more continuous technique, peritoneal dialysis (PD) is an alternative for some patients. In ARF patients two forms of PD have been used. Most commonly, dialysate is infused and drained from the peritoneal cavity by gravity. More commonly a variation of the procedure for continuous ambulatory PD termed continuous equilibrated PD is utilized [4]. Dialysate is instilled and drained manually and continuously every 3 to six hours, and fluid removal is achieved by varying the concentration of dextrose in the solutions. Alternatively, the process can be automated with a cycling device programmed to deliver a predetermined volume of dialysate and drain the peritoneal cavity at fixed intervals. The cycler makes the process less labor intensive, but the utility of PD in treating ARF in the ICU is limited because of: 1) its impact on respiratory status owing to interference with diaphragmatic excursion; 2) technical difficulty of using it in patients with abdominal sepsis or after abdominal surgery; 3) relative inefficiency in removing waste products in "catabolic" patients; and 4) a high incidence of associated peritonitis. Several continuous renal replacement therapies (CRRT) have evolved that differ only in the access utilized (arteriovenous [non-pumped: SCUF, CAVH, CAVHD, CAVHDF] versus venovenous [pumped: CVVH, CVVHD, CVVHDF]), and, in the principal method of solute clearance (convection alone [UF and H], diffusion alone [hemodialyis (HD)], and combined convection and diffusion [hemodiafiltration (HDF)]).



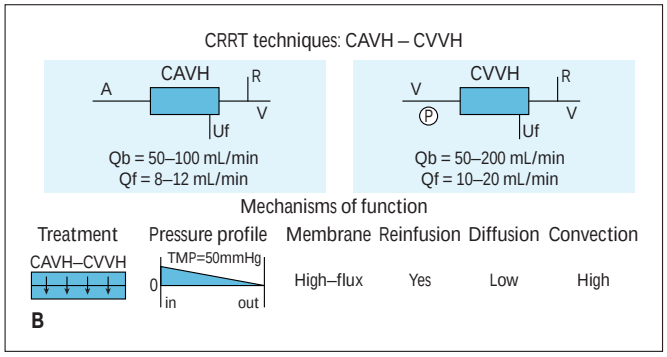


FIGURE 19-2

Schematics of different CRRT techniques. **A**, Schematic representation of SCUF therapy. **B**, Schematic representation of continuous arteriovenous or venovenous hemofiltration (CAVH/CVVH) therapy.

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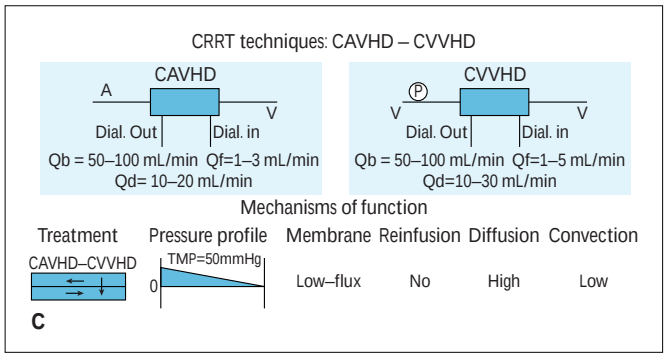


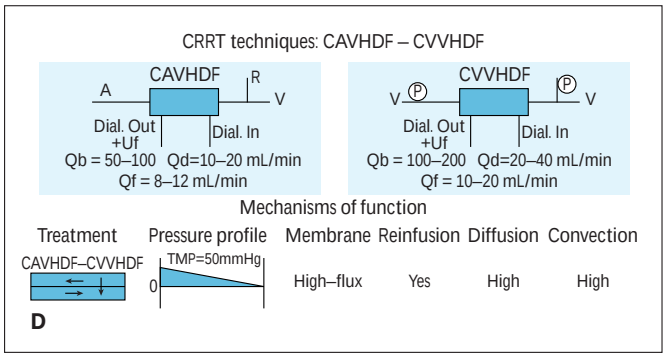


FIGURE 19-2 *(Continued)*

C, Schematic representation of continuous arteriovenous/venovenous hemodialysis (CAVHD-CVVHD) therapy. **D**, Schematic representation of continuous arteriovenous/venovenous hemodiafiltration (CAVHDF/CVVHDF) therapy. A—artery; V—vein; Uf—ultrafiltrate; R—replacement fluid; P—peristaltic pump; Qb—blood flow; Qf—ultrafiltration rate; TMP—transmembrane pressure; in—dilyzer inlet; out—dialyzer outlet; UFC—ultrafiltration control system; Dial—dialysate; Qd—dialysate flow rate. (*From* Bellomo *et al.* [5]; with permission.)

CONTINUOUS RENAL REPLACEMENT THERAPY: COMPARISON OF TECHNIQUES

	SCUF	CAVH	CVVH	CAVHD	CAVHDF	CVVHD	CVVHDF	PD
Access	AV	AV	VV	AV	AV	VV	VV	Perit. Cath.
Pump	No	No	Yes	No	No	Yes	Yes	No†
Filtrate (mL/h)	100	600	1000	300	600	300	800	100
Filtrate (L/d)	2.4	14.4	24	7.2	14.4	7.2	19.2	2.4
Dialysate flow (L/h)	0	0	0	1.0	1.0	1.0	1.0	0.4
Replacement fluid (L/d)	0	12	21.6	4.8	12	4.8	16.8	0
Urea clearance (mL/min)	1.7	10	16.7	21.7	26.7	21.7	30	8.5
Simplicity*	1	2	3	2	2	3	3	2
Cost*	1	2	4	3	3	4	4	3

* 1 = most simple and least expensive; 4 = most difficult and expensive

† cycler can be used to automate exchanges, but they add to the cost and complexity

FIGURE 19-3

In contrast to intermittent techniques, until recently, the terminology for continuous renal replacement therapy (CRRT) techniques has been subject to individual interpretation. Recognizing this lack of standardization an international group of experts have proposed standardized terms for these therapies [5]. The basic premise in the development of these terms is to link the nomenclature to the operational characteristics of the different techniques. In general all these techniques use highly permeable synthetic membranes and differ in the driving force for solute removal. When arteriovenous (AV) circuits are used, the mean arterial pressure provides the pumping mechanism. Alternatively, external pumps generally utilize a venovenous (VV) circuit and permit better control of blood flow rates. The letters AV or VV in the terminology serve to identify the driving force in the technique. Solute removal in these techniques is achieved by convection, diffusion, or a combination of these two. Convective techniques include ultrafiltration (UF) and hemofiltration (H) and depend on solute removal by solvent drag [6].

Diffusion-based techniques similar to intermittent hemodialysis (HD) are based on the principle of a solute gradient between the blood and the dialysate. If both diffusion and convection are used in the same technique the process is termed hemodiafiltration (HDF). In this instance, both dialysate and a replacement solution are used, and small and middle molecules can both be removed easily. The letters UF, H, HD, and HDF identify the operational characteristics in the terminology. Based on these principles, the terminology for these techniques is easier to understand. As shown in Figure 19-1 the letter C in all the terms describes the continuous nature of the methods, the next two letters [AV or VV] depict the driving force and the remaining letters [UF, H, HD, HDF] represent the operational characteristics. The only exception to this is the acronym SCUF (slow continuous ultrafiltration), which remains as a reminder of the initiation of these therapies as simple techniques harnessing the power of AV circuits. (*Modified from* Mehta [7]; with permission.)

Operational Characteristics

Anticoagulation

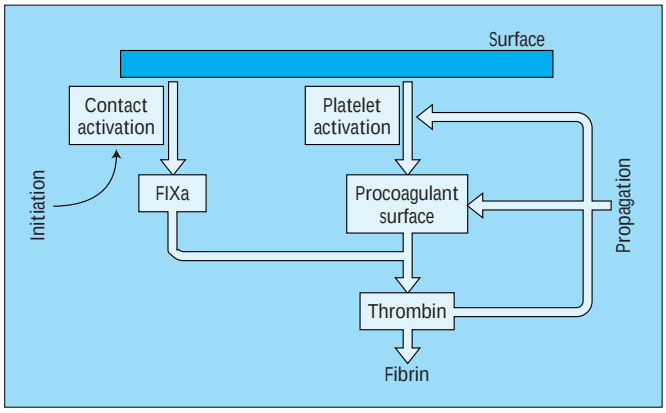


FIGURE 19-4

Pathways of thrombogenesis in extracorporeal circuits. (*Modified from* Lindhout [8]; with permission.)

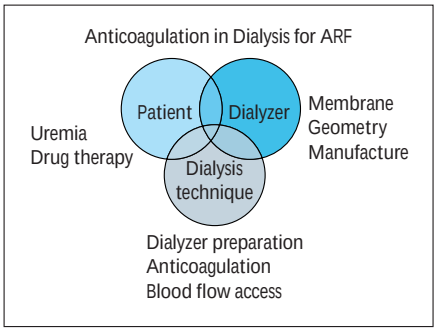
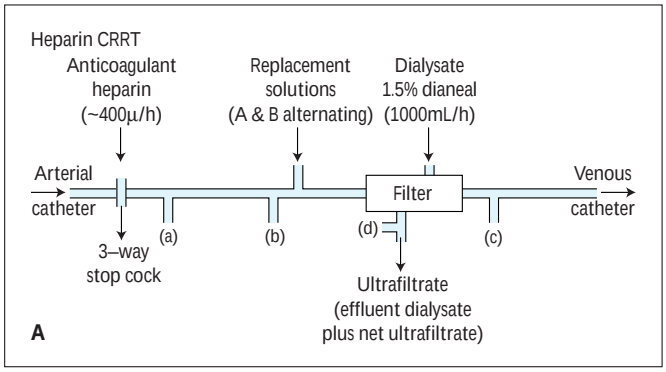


FIGURE 19-5

Factors influencing dialysis-related thrombogenicity. One of the major determinants of the efficacy of any dialysis procedure in acute renal failure (ARF) is the ability to maintain a functioning extracorporeal circuit. Anticoagulation becomes a key component in this regard and requires a balance between an appropriate level of anticoagulation to maintain patency of the circuit and prevention of complications. Figures 19-4 and 19-5 show the mechanisms of thrombus formation in an extracorporeal circuit and the interaction of various factors in this process. (*From* Ward [9]; with permission.)



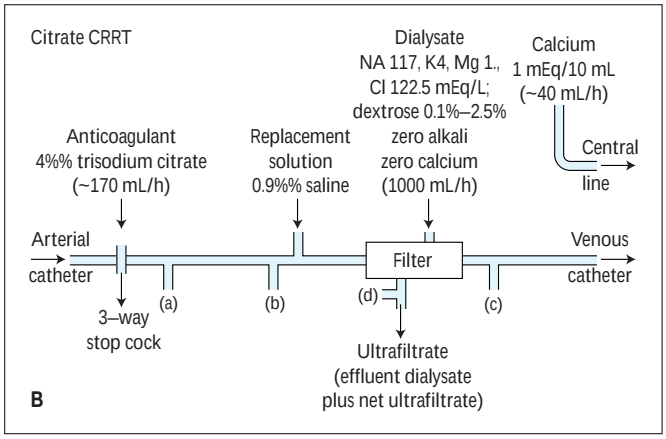
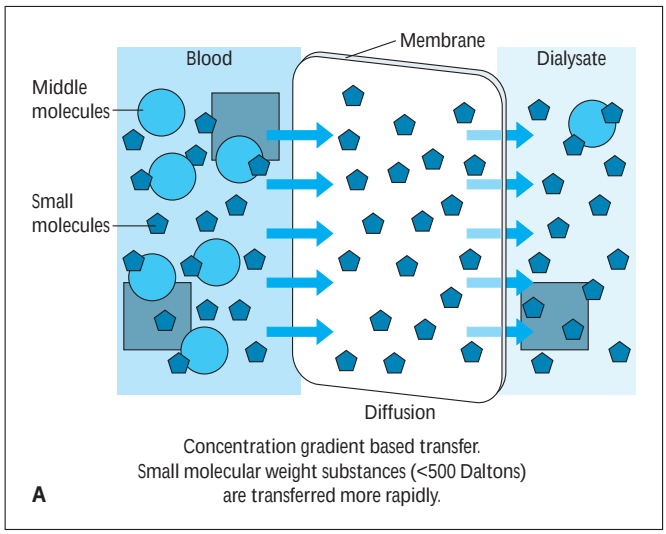


FIGURE 19-6

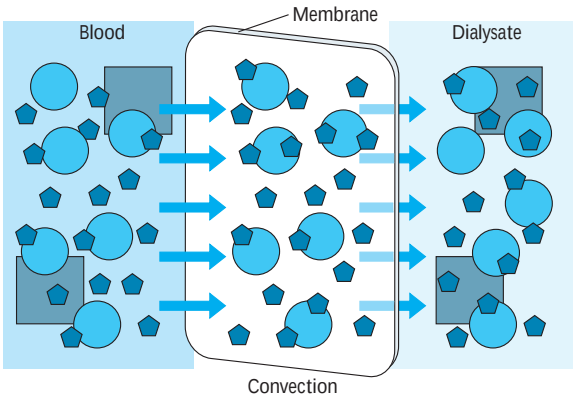
Modalities for anticoagulation for continuous renal replacement therapy. While systemic heparin is the anticoagulant most commonly used for dialysis, other modalities are available. The utilization of these modalities is largely influenced by prevailing local experience. Schematic diagrams for heparin, **A**, and citrate, **B**, anticoagulation techniques for continuous renal replacement therapy (CRRT). A schematic of heparin and regional citrate anticoagulation for CRRT techniques. Regional citrate anticoagulation minimizes the major complication of bleeding associated with heparin, but it requires monitoring of ionized calcium. It is now well-recognized that the longevity of pumped or nonpumped CRRT circuits is influenced by maintaining the filtration fraction at less than 20%. Nonpumped circuits (CAVH/HD/HDF) have a decrease in efficacy over time related to a decrease in blood flow (BFR), whereas in pumped circuits (CVVH/HD/HDF) blood flow is maintained; however, the constant pressure across the membrane results in a layer of protein forming over the membrance reducing its efficacy. This process is termed concentration repolarization [10]. CAVH/CVVH—continuous arteriovenous/venovenous hemofiltration. (*From* Mehta RL, *et al.* [11]; with permission.)

Solute Removal



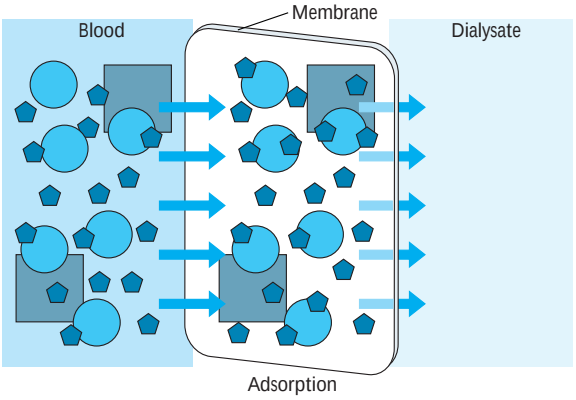
Concentration gradient based transfer.
Small molecular weight substances (<500 Daltons) are transferred more rapidly.

A



Movement of water across the membrane carries solute across the membrane.
Middle molecules are removed more efficiently.

B



Several solutes are removed from circulation by *adsorption* to the membrane. This process is influenced by the membrane structure and charge.

C

FIGURE 19-7

Mechanisms of solute removal in dialysis. The success of any dialysis procedure depends on an understanding of the operational characteristics that are unique to these techniques and on appropriate use of specific components to deliver the therapy. Solute removal is achieved by diffusion (hemodialysis), **A**, convection (hemofiltration), **B**, or a combination of diffusion and convection (hemodiafiltration), **C**.

DETERMINANTS OF SOLUTE REMOVAL IN DIALYSIS TECHNIQUES FOR ACUTE RENAL FAILURE

	IHD	CRRT	PD
Small solutes (MW <300)	Diffusion: Q_b Membrane width Qd	Diffusion: Q_d Convection: Q_f	Diffusion: Q_d Convection: Q_f
Middle molecules (MW 500–5000)	Diffusion Convection: Q_f SC	Convection: Q_f SC	Convection: Q_f SC
LMW proteins (MW 5000–50,000)	Convection Diffusion Adsorption	Convection Adsorption	Convection
Large proteins (MW >50,000)	Convection	Convection	Convection

FIGURE 19-8

Determinants of solute removal in dialysis techniques for acute renal failure. Solute removal in these techniques is achieved by convection, diffusion, or a combination of these two. Convective techniques include ultrafiltration (UF) and hemofiltration (H) and they depend on solute removal by solvent drag [6]. As solute removal is solely dependent on convective clearance it can be enhanced only by increasing the volume of ultrafiltrate produced. While ultrafiltration requires fluid removal only, to prevent significant volume loss and resulting hemodynamic compromise, hemofiltration necessitates partial or total replacement of the fluid removed. Larger molecules are removed more efficiently by this process and, thus, middle molecular clearances are superior. In intermittent hemodialysis (IHD) ultrafiltration is achieved by modifying the transmembrane pressure and generally does not contribute significantly to solute removal. In peritoneal dialysis (PD) the UF depends on the osmotic gradient achieved by the concentration of dextrose solution (1.55% to 4.25%) utilized the number of exchanges and the dwell time of each exchange. In continuous arteriovenous and venovenous hemodialysis in most situations ultrafiltration rates of 1 to 3 L/hour are utilized; however recently high-volume hemofiltration with 6 L of ultrafiltrate produced every hour has been utilized to remove middle– and large–molecular weight cytokines in sepsis [12]. Fluid balance is achieved by replacing the ultrafiltrate removed by a replacement solution. The composition of the replacement fluid can be varied and the solution can be infused before or after the filter.

Diffusion-based techniques (hemodialysis) are based on the principle of a solute gradient between the blood and the dialysate. In IHD, typically dialysate flow rates far exceed blood flow rates (200 to 400 mL/min, dialysate flow rates 500 to 800 mL/min) and dialysate flow is single pass. However, unlike IHD, the dialysate flow rates are significantly slower than the blood flow rates (typically, rates are 100 to 200 mL/min, dialysate flow rates are 1 to 2 L/hr [17 to 34mL/min]), resulting in complete saturation of the dialysate. As a consequence, dialysate flow rates become the limiting factor for solute removal and provide an opportunity for clearance enhancement. Small molecules are preferentially removed by these methods. If both diffusion and convection are used in the same technique (hemodiafiltration, HDF) both dialysate and a replacement solution are used and small and middle molecules can both be easily removed.

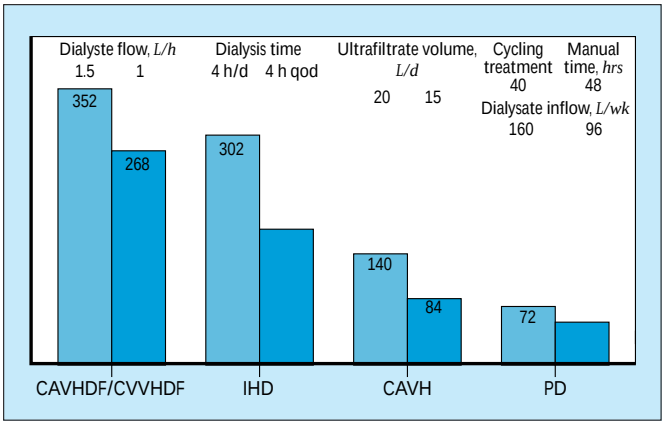


FIGURE 19-9

Comparison of weekly urea clearances with different dialysis techniques. Although continuous therapies are less efficient than intermittent techniques, overall clearances are higher as they are utilized continuously. It is also possible to increase clearances in continuous techniques by adjustment of the ultrafiltration rate and dialysate flow rate. In contrast, as intermittent dialysis techniques are operational at maximum capability, it is difficult to enhance clearances except by increasing the size of the membrane or the duration of therapy. CAV/CVVHDF—continuous arteriovenous/venovenous hemodiafiltration; IHD—intermittent hemodialysis; CAVH—continuous arteriovenous hemodialysis; PD—peritoneal dialysis.

COMPARISON OF DIALYSIS PRESCRIPTION AND DOSE DELIVERED IN CRRT AND IHD

Dialysis Prescription

	IHD	CRRT
Membrane characteristics	Variable permeability	High permeability
Anticoagulation	Short duration	Prolonged
Blood flow rate	≥200 mL/min	<200 mL/min
Dialysate flow	≥500 mL/min	17–34 mL/min
Duration	3–4 hrs	Days
Clearance	High	Low

Dialysis Dose Delivered

	IHD	CRRT
Patient factors		
Hemodynamic stability	+++	+
Recirculation	+++	+
Infusions	++	+
Technique factors		
Blood flow	+++	++
Concentration repolarization	+	+++
Membrane clotting	+	+++
Duration	+++	+
Other factors		
Nursing errors	+	+++
Interference	+	++++

FIGURE 19-10

Comparison of dialysis prescription and dose delivered in continuous renal replacement (CRRT) and intermittent hemodialysis (IHD). The ability of each modality to achieve a particular clearance is influenced by the dialysis prescription and the operational characteristics; however, it must be recognized that there may be a significant difference between the dialysis dose prescribed and that delivered. In general, IHD techniques are limited by available time, and in catabolic patients it may not be possible to achieve a desired level of solute control even by maximizing the operational characteristics.

DRUG DOSING IN CRRT*

Drug	Normal Dose (mg/d)	Dose in CRRT (mg)
Amikacin	1050	250 qd–bid
Netilmycin	420	100–150 qd
Tobramycin	350	100 qd
Vancomycin	2000	500 qd–bid
Ceftazidime	6000	1000 bid
Cefotaxime	12,000	2000 bid
Ceftriaxone	4000	2000 qd
Ciprofloxacin	400	200 qd
Imipenem	4000	500 tid–qid
Metronidazole	2100	500 tid–qid
Piperacillin	24,000	4000 tid
Digoxin	0.29	0.10 qd
Phenobarbital	233	100 bid–qid
Phenytoin	524	250 qd–bid
Theophylline	720	600–900 qd

* Reflects doses for continuous venovenous hemofiltration with ultrafiltration rate of 20 to 30 mL/min.

FIGURE 19-11

Drug dosing in continuous renal replacement (CRRT) techniques. Drug removal in CRRT techniques is dependent upon the molecular weight of the drug and the degree of protein binding. Drugs with significant protein binding are removed minimally. Aditionally, some drugs may be removed by adsorption to the membrane. Most of the commonly used drugs require adjustments in dose to reflect the continuous removal in CRRT. (*Modified from* Kroh *et al.* [13]; with permission.)

NUTRITIONAL ASSESSMENT AND SUPPORT WITH RENAL REPLACEMENT TECHNIQUES

Parameters: Initial Assessment	IHD	CAVH/CVVH	CAVHD/CVVHDF
Energy assessment	HBE x AF x SF, or indirect calorimetry	Same	Same
Dialysate dextrose absorption	Negligible	Not applicable	43% uptake 1.5% dextrose dialysate (525 calories/D) 45% uptake 2.5% dextrose dialysate (920 calories/D) Negligible absorption with dextrose free or dialysate 0.1–0.15% dextrose
Protein assessment			
Visceral proteins	Serum prealbumin	Same	Same
Nitrogen balance: N_2 in–N_2 out	Nitrogen in: protein in TPN +/enteral solutions/6.25	Nitrogen in: same	Nitrogen in: same
	Nitrogen out: urea nitrogen appearance	Nitrogen out: ultrafiltrate urea nitrogen losses	Nitrogen out: ultrafiltrate/dialysate urea nitrogen losses
	UUN†	UUN†	UUN†
	Insensible losses	Insensible losses	Insensible losses
	Dialysis amino acid losses (1.0–1.5 N_2/dialysis therapy)	Ultrafiltrate amino acid losses (1.5–2.0 N_2/D)	Ultrafiltrate/dialysate amino acid losses (1.5–2.0 N_2/D)
Nutrition support prescription: TPN/enteral nutrition	Renal formulas with limited fluid, potassium, phosphorus, and magnesium	Standard TPN/enteral formulations. No fluid or electrolyte restrictions.	Standard TPN/enteral formulations when 0.1–0.15% dextrose dialysate used Modified formulations when 1.5–2.5% dextrose dialysate used TPN: Low-dextrose solutions to prevent carbohydrate overfeeding; amino acid concentration may be increased to meet protein requirements. Enteral: Standard formulas. May require modular protein to meet protein requirements without carbohydrate overfeeding.
Reassessment of requirements and efficacy of nutrition support			
Energy assessment	Weekly HBE x AF x SF*, or indirect calorimetry	Same	Same
Serum prealbumin	Weekly	Same	Same
Nitrogen balance	Weekly	Same	Same

* Harris Benedict equation multiplied by acimity and stress factors

† Collect 24-hour urine for UUN if UOP ≥ 400 ml/d

FIGURE 19-12

Nutritional assessment and support with renal replacement techniques. A key feature of dialysis support in acute renal failure is to permit an adequate amount of nutrition to be delivered to the patient. The modality of dialysis and operational characteristics affect the nutritional support that can be provided. Dextrose absorption occurs form the dialysate in hemodialysis and hemodiafiltration modalities and can result in hyperglycemia. Intermittent dialysis techniques are limited by time in their ability to allow unlimited nutritional support. (*From* Monson and Mehta [14]; with permission.)

Fluid Control

OPERATING CHARACTERISTICS OF CRRT: FLUID REMOVAL VERSUS FLUID REGULATION

	Fluid Removal	Fluid Regulation
Ultrafiltration rate (UFR)	To meet anticipated needs	Greater than anticipated needs
Fluid management	Adjust UFR	Adjust amount of replacement fluid
Fluid balance	Zero or negative balance	Positive, negative, or zero balance
Volume removed	Based on physician estimate	Driven by patient characteristics
Application	Easy, similar to intermittent hemodialysis	Requires specific tools and training

FIGURE 19-13

Operating characteristics of continuous renal replacement (CRRT): fluid removal versus fluid regulation. Fluid management is an integral component in the management of patients with acute renal failure in the intensive care setting. In the presence of a failing kidney, fluid removal is often a challenge that requires large doses of diuretics with a variable response. It is often necessary in this setting to institute dialysis for volume control rather than metabolic control. CRRT techniques offer a significant advantage over intermittent dialysis for fluid control [14,15]; however, if not carried out appropriately they can result in major complications. To utilize these therapies for their maximum potential it is necessary to recognize the factors that influence fluid balance and have an understanding of the principles of fluid management with these techniques. In general it is helpful to consider dialysis as a method for fluid removal and fluid regulation.

APPROACHES FOR FLUID MANAGEMENT IN CRRT

Approaches	Level 1	Level 2	Level 3
UF volume	Limited	Increase intake	Increase intake
Replacement	Minimal	Adjusted to achieve fluid balance	Adjusted to achieve fluid balance
Fluid balance	8 h	Hourly	Hourly Targeted
UF pump	Yes	Yes/No	Yes/No
Examples	SCUF/CAVHD CVVHD	CAVH/CVVH CAVHDF/CVVHDF	CAVHDF/CVVHDF CVVH
Advantages			
Simplicity	+++	++	+
Achieve fluid balance	+	+++	+++
Regulate volume changes	+	++	+++
CRRT as support	+	++	+++
Disadvantages			
Nursing effort	+	++	+++
Errors in fluid balance	+++	++	+
Hemodynamic instability	++	++	+
Fluid overload	+++	+	+

FIGURE 19-14

Approaches for fluid management in continuous renal replacement therapy (CRRT). CRRT techniques are uniquely situated in providing fluid regulation, as fluid management can be achieved with three levels of intervention [16]. In Level 1, the ultrafiltrate (UF) volume obtained is limited to match the anticipated needs for fluid balance. This calls for an estimate of the amount of fluid to be removed over 8 to 24 hours and subsequent calculation of the ultrafiltration rate. This strategy is similar to that commonly used for intermittent hemodialysis and differs only in that the time to remove fluid is 24 hours instead of 3 to 4 hours. In Level 2 the ultrafiltrate volume every hour is deliberately set to be greater than the hourly intake, and net fluid balance is achieved by hourly replacement fluid administration. In this method a greater degree of control is possible and fluid balance can be set to achieve any desired outcome. The success of this method depends on the ability to achieve ultrafiltration rates that always exceed the anticipated intake. This allows flexibility in manipulation of the fluid balance, so that for any given hour the fluid status could be net negative, positive, or balanced. A key advantage of this technique is that the net fluid balance achieved at the end of every hour is truly a reflection of the desired outcome. Level 3 extends the concept of the Level 2 intervention to target the desired net balance every hour to achieve a specific hemodynamic parameter (*eg*, central venous pressure, pulmonary artery wedge pressure, or mean arterial pressure). Once a desired value for the hemodynamic parameter is determined, fluid balance can be linked to that value. Each level has advantages and disadvantages; in general greater control calls for more effort and consequently results in improved outcomes. SCUF—ultrafiltration; CAVHD/CVVHD—continuous arteriovenous/venovenous hemodialysis; CAVH/CVVH—continuous arteriovenous/venovenous hemofiltration; CAVHDF/CVVHDF—continuous arteriovenous/venovenous hemodiafiltration.

COMPOSITION OF REPLACEMENT FLUID AND DIALYSATE FOR CRRT

Replacement Fluid

Investigator	Golper [19]	Kierdorf [20]	Lauer [21]	Paganini [22]	Mehta [11]	Mehta [11]
Na^+	147	140	140	140	140.5	154
Cl^-	115	110	—	120	115.5	154
HCO_3^-	36	34	—	6	25	—
K^+	0	0	2	2	0	—
Ca^{2+}	1.2	1.75	3.5	4	4	—
Mg^{2+}	0.7	0.5	1.5	2	—	—
Glucose	6.7	5.6	—	10	—	—
Acetate	—	—	41	40	—	—

Dialysate

Component (mEq/L)	1.5% Dianeal	Hemosol AG 4D	Hemosol LG 4D	Baxter	Citrate
Sodium	132	140	140	140	117
Potassium	—	4	4	2	4
Chloride	96	119	109.5	117	121
Lactate	35	—	40	30	—
Acetate	—	30	—	—	—
Calcium	3.5	3.5	4	3.5	—
Magnesium	1.5	1.5	1.5	1.5	1.5
Dextrose (g/dL)	1.5	0.8	.11	0.1	0.1–2.5

FIGURE 19-15
Composition of dialysate and replacement fluids used for continuous renal replacement therapy (CRRT). One of the key features of any dialysis method is the manipulation of metabolic balance. In general, this is achieved by altering composition of dialysate or replacement fluid . Most commercially available dialysate and replacement solutions have lactate as the base; however, bicarbonate-based solutions are being utilized more and more [17,18].

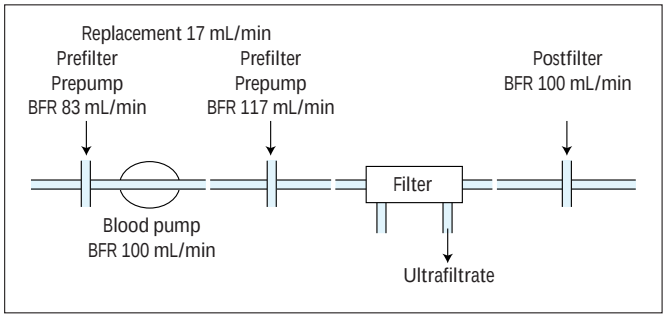


FIGURE 19-16
Effect of site of delivery of replacement fluid: pre- versus postfilter continuous venovenous hemofiltration with ultrafiltration rate of 1 L/hour. Replacement fluids may be administered pre- or postfilter, depending on the circuit involved . It is important to recognize that the site of delivery can influence the overall efficacy of the procedure. There is a significant effect of fluid delivered prepump or postpump, as the amount of blood delivered to the filter is reduced in prepump dilution. BFR—blood flow rate.

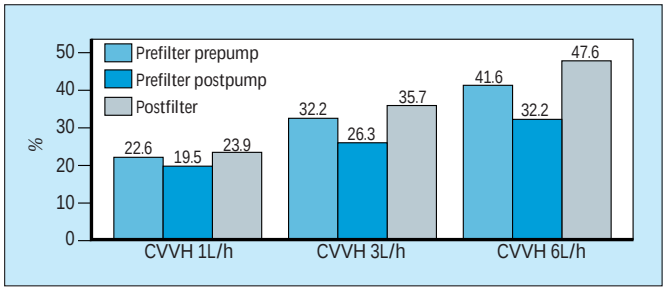


FIGURE 19-17
Pre- versus postfilter replacement fluid: effect on filtration fraction. Prefilter replacement tends to dilute the blood entering the circuit and enhances filter longevity by reducing the filtration fraction; however, in continuous venovenous hemofiltration (CVVH) circuits the overall clearance may be reduced as the amount of solute delivered to the filter is reduced.

Applications and Indications for Dialytic Intervention

INDICATIONS AND TIMING OF DIALYSIS FOR ACUTE RENAL FAILURE: RENAL REPLACEMENT VERSUS RENAL SUPPORT

	Renal Replacement	Renal Support
Purpose	Replace renal function	Support other organs
Timing of intervention	Based on level of biochemical markers	Based on individualized need
Indications for dialysis	Narrow	Broad
Dialysis dose	Extrapolated from ESRD	Targeted for overall support

FIGURE 19-18

Dialysis intervention in acute renal failure (ARF): renal replacement versus renal support. An important consideration in the management of ARF is defining the goals of therapy. Several issues must be considered, including the timing of the intervention, the amount and frequency of dialysis, and the duration of therapy. In practice, these issues are based on individual preferences and experience, and no immutable criteria are followed [7,23]. Dialysis intervention in ARF is usually considered when there is clinical evidence of uremia symptoms or biochemical evidence of solute and fluid imbalance. An important consideration in this regard is to recognize that the patient with ARF is somewhat different than the one with end-stage renal disease (ESRD). The rapid decline of renal function associated with multiorgan failure does not permit much of an adaptive response which characterizes the course of the patient with ESRD. As a consequence, the traditional indications for renal replacement may need to be redefined. For instance, excessive volume resuscitation, a common strategy for multiorgan failure, may be an indication for dialysis, even in the absence of significant elevations in blood urea nitrogen. In this respect, it may be more appropriate to consider dialysis intervention in the intensive care patient as a form of renal support rather than renal replacement. This terminology serves to distinguish between the strategy for replacing individual organ function and one to provide support for all organs.

POTENTIAL APPLICATIONS FOR CONTINUOUS RENAL REPLACEMENT THERAPY

Renal Replacement	Renal Support	Extrarenal Applications
Acute renal failure	Fluid management	Cytokine removal ? sepsis
Chronic renal failure	Solute control	Heart failure
	Acid-base adjustments	Cancer chemotherapy
	Nutrition	Liver support
	Burn management	Inherited metabolic disorders

FIGURE 19-19

Potential applications for continuous renal replacement therapy (CRRT). CRRT techniques are increasingly being utilized as support modalities in the intensive care setting and are particularly suited for this function. The freedom to provide continuous fluid management permits the application of unlimited nutrition, adjustments in hemodynamic parameters, and achievement of steady-state solute control, which is difficult with intermittent therapies. It is thus possible to widen the indications for renal intervention and provide a customized approach for the management of each patient.

RELATIVE ADVANTAGES (+) AND DISADVANTAGES (−) OF CRRT, IHD, AND PD

Variable	CRRT	IHD	PD
Continuous renal replacement	+	−	+
Hemodynamic stability	+	−	+
Fluid balance achievement	+	−	−
Unlimited nutrition	+	−	−
Superior metabolic control	+	−	−
Continuous removal of toxins	+	−	+
Simple to perform	±	−	+
Stable intracranial pressure	+	−	+
Rapid removal of poisons	−	+	−
Limited anticoagulation	−	+	+
Need for intensive care nursing support	+	−	+
Need for hemodialysis nursing support	±	+	+
Patient mobility	−	+	−

FIGURE 19-20
Advantages (+) and disadvantages (−) of dialysis techniques. CRRT—continuous renal replacement therapy; IHD—intermittent hemodialysis; PD—peritoneal dialysis.

DETERMINANTS OF THE CHOICE OF TREATMENT MODALITY FOR ACUTE RENAL FAILURE

- Patient
  - Indication for dialysis
  - Presence of multiorgan failure
  - Access
  - Mobility and location of patient
  - Anticipated duration of therapy
- Dialysis process
  - Components (*eg*, membrane, anticoagulation)
  - Type (intermittent or continuous)
  - Efficacy for solute and fluid balance
  - Complications
  - Outcome
- Nursing and other support
  - Availability of machines
  - Nursing support

FIGURE 19-21
Determinants of the choice of treatment modality for acute renal failure. The primary indication for dialysis intervention can be a major determinant of the therapy chosen because different therapies vary in their efficacy for solute and fluid removal. Each technique has its advantages and limitations, and the choice depends on several factors. Patient selection for each technique ideally should be based on a careful consideration of multiple factors [1]. The general principle is to provide adequate renal support without adversely affecting the patient. The presence of multiple organ failure may limit the choice of therapies; for example, patients who have had abdominal surgery may not be suitable for peritoneal dialysis because it increases the risk of wound dehiscence and infection. Patients who are hemodynamically unstable may not tolerate intermittent hemodialysis (IHD). Additionally, the impact of the chosen therapy on compromised organ systems is an important consideration. Rapid removal of solutes and fluid, as in IHD, can result in a disequilibrium syndrome and worsen neurologic status. Peritoneal dialysis may be attractive in acute renal failure that complicates acute pancreatitis, but it would contribute to additional protein losses in the hypoalbuminemic patient with liver failure.

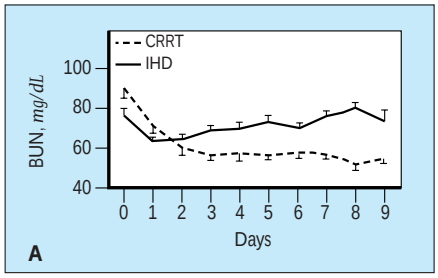
RECOMMENDATION FOR INITIAL DIALYSIS MODALITY FOR ACUTE RENAL FAILURE (ARF)

Indication	Clinical Condition	Preferred Therapy
Uncomplicated ARF	Antibiotic nephrotoxicity	IHD, PD
Fluid removal	Cardiogenic shock, CP bypass	SCUF, CAVH
Uremia	Complicated ARF in ICU	CVVHDF, CAVHDF, IHD
Increased intracranial pressure	Subarachnoid hemorrhage, hepatorenal syndrome	CVVHD, CAVHD
Shock	Sepsis, ARDS	CVVH, CVVHDF, CAVHDF
Nutrition	Burns	CVVHDF, CAVHDF, CVVH
Poisons	Theophylline, barbiturates	Hemoperfusion, IHD, CVVHDF
Electrolyte abnormalities	Marked hyperkalemia	IHD, CVVHDF
ARF in pregnancy	Uremia in 2nd, 3rd trimester	PD

FIGURE 19-22

Recommendation for initial dialysis modality for acute renal failure (ARF). Patients with multiple organ failure (MOF) and ARF can be treated with various continuous therapies or IHD. Continuous therapies provide better hemodynamic stability; however, if not monitored carefully they can lead to significant volume depletion. In general, hemodynamically unstable, catabolic, and fluid-overloaded patients are best treated with continuous therapies, whereas IHD is better suited for patients who require early mobilization and are more stable. It is likely that the mix of modalities used will change as evidence linking the choice of modality to outcome becomes available. For now, it is probably appropriate to consider all these techniques as viable options that can be used collectively. Ideally, each patient should have an individualized approach for management of ARF.

Outcomes



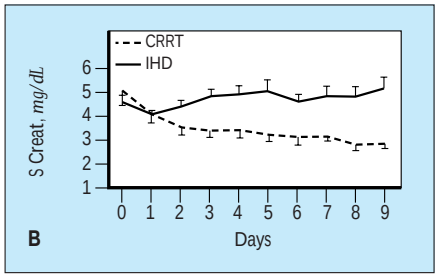


FIGURE 19-23

Efficacy of continuous renal replacement therapy (CRRT) versus intermittent hemodialysis (IHD): effect on blood urea nitrogen, **A**, and creatinine levels, **B**, in acute renal failure.

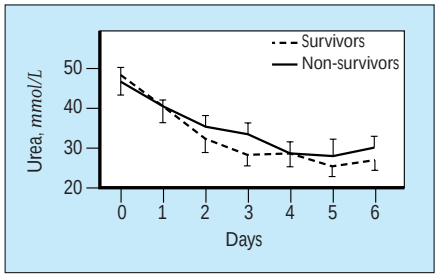


FIGURE 19-24

Blood urea nitrogen (BUN) levels in survivors and non-survivors in acute renal failure treated with continuous renal replacement therapy (CRRT). It is apparent that CRRT techniques offer improved solute control and fluid management with hemodynamic stability, however a relationship to outcome has not been demonstrated. In a recent retrospective analysis van Bommel [24] found no difference in BUN levels among survivors and non-survivors with ARF While it is clear that lower solute concentrations can be achieved with CRRT whether this is an important criteria impacting on various outcomes from ARF still needs to be determined. A recent study form the Cleveland Clinic suggests that the dose of dialysis may be an important determinant of outcome allowing for underlying severity of illness [25]. In this study the authors found that in patients with ARF, 65.4% of all IHD treatments resulted in lower Kt/V than prescribed. There appeared to be an influence of dose of dialysis on outcome in patients with intermediate levels of severity of illness as judged by the Cleveland Clinic Foundation acuity score for ARF (*see* Fig. 19-25). Patients receiving a higher Kt/V had a lower mortality than predicted. These data illustrate the importance of the underlying severity of illness, which is likely to be a major determinant of outcome and should be considered in the analysis of any studies.

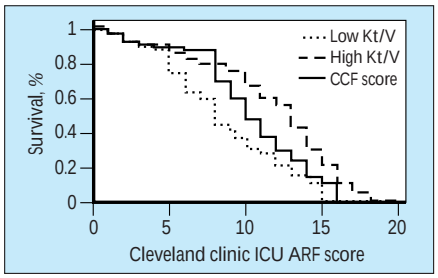


FIGURE 19-25

Effect of dose of dialysis in acute renal failure (ARF) on outcome from ARF.

BIOCOMPATIBLE MEMBRANES IN INTERMITTENT HEMODIALYSIS (IHD) AND ACUTE RENAL FAILURE (ARF): EFFECT ON OUTCOMES

	BCM Group	BICM Group	Probability
Patients, *n*	72	81	
All patients recover of renal function	46 (64%)	35 (43%)	0.001
Survival	41 (57%)	37 (46%)	0.03
Patients nonoliguric before hemodialysis	39	46	
Development of oliguria with dialysis	17 (44%)	32 (70%)	0.03
Recovery of renal function	31 (79%)	21 (46%)	0.0004
Survival	28 (74%)	22 (48%)	0.003
Patients oliguric before hemodialysis	33	35	
Recovery of renal function	15 (45%)	14 (40%)	ns
Survival	12 (36%)	15 (43%)	ns

FIGURE 19-26

Biocompatible membranes in intermittent hemodialysis (IHD) and acute renal failure (ARF): effect on outcomes. The choice of dialysis membrane and its influence on survival from ARF has been of major interest to investigators over the last few years. While the evidence tends to support a survival advantage for biocompatible membranes, most of the studies were not well controlled. The most recent multicenter study showed an improvement in mortality and recovery of renal function with biocompatible membranes; however, this effect was not significant in oliguric patients. Further investigations are required in this area. NS—not significant.

MORTALITY IN ACUTE RENAL FAILURE: COMPARISON OF CRRT VERSUS IHD

		IHD		CRRT			
Investigator	Type of Study	No	Mortality, %	No	Mortality, %	Change, %	P Value
Mauritz [32]	Retrospective	31	90	27	70	−20	ns
Alarabi [33]	Retrospective	40	55	40	45	−10	ns
Mehta [34]	Retrospective	24	85	18	72	−13	ns
Kierdorf [20]	Retrospective	73	93	73	77	−16	< 0.05
Bellomo [35]	Retrospective	167	70	84	59	−11	ns
Bellomo [36]	Retrospective	84	70	76	45	−25	< 0.01
Kruczynski [37]	Retrospective	23	82	12	33	−49	< 0.01
Simpson [38]	Prospective	58	82	65	70	−12	ns
Kierdorf [39]	Prospective	47	65	48	60	−4.5	ns
Mehta [40]	Prospective	82	41.5	84	59.5	+18	ns

FIGURE 19-27

Continuous renal replacement therapy (CRRT) versus intermittent hemodialysis (IHD): effect on mortality. Despite significant advances in the management of acute renal failure (ARF) over the last four decades, the perception is that the associated mortality has not changed significantly [26]. Recent publications suggest that there may have been some improvement during the last decade [27]. Both IHD and peritoneal dialysis (PD) were the major therapies until a decade ago, and they improved the outcome from the 100% mortality of ARF to its current level. The effect of continuous renal replacement therapy on overall patient outcome is still unclear [28] . The major studies done in this area do not show a survival advantage for CRRT [29,30]. Although several investigators have not been able to demonstrate an advantage of these therapies in influencing mortality, we believe this may represent the difficulty in changing a global outcome which is impacted by several other factors [31]. It is probably more relevant to focus on other outcomes such as renal functional recovery rather than mortality. We believe that continued research is required in this area; however, there appears to be enough evidence to support the use of CRRT techniques as an alternative that may be preferable to IHD in treating ARF in an intensive care setting.

Future Directions

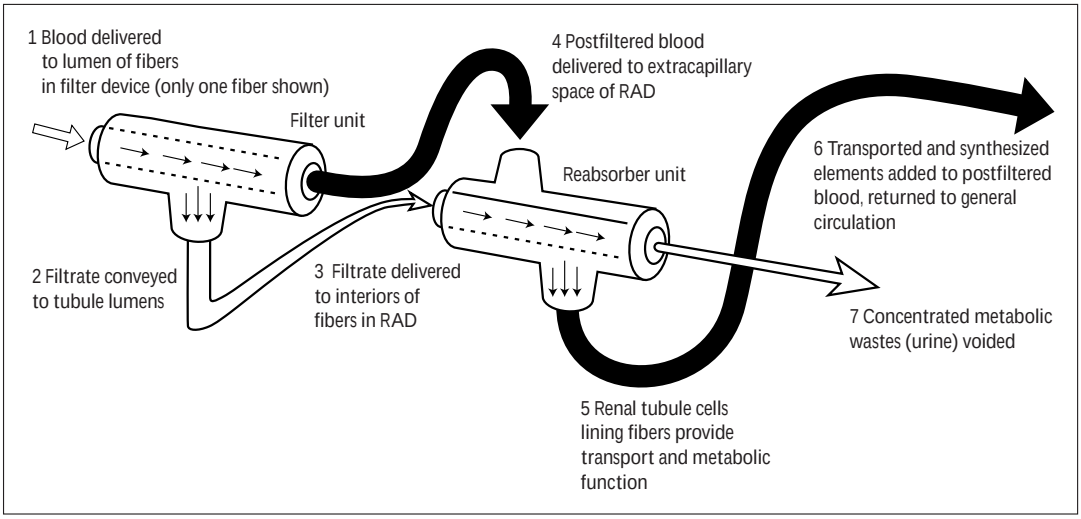


FIGURE 19-28

Schematic for the bioartificial kidney. As experience with these techniques grows, innovations in technology will likely keep pace. Over the last 3 years, most of the major manufacturers of dialysis equipment have developed new pumps dedicated for continuous renal replacement therapy (CRRT). Membrane technology is also evolving, and antithrombogenic membranes are on the horizon [41]. Finally the application of these therapies is likely to expand to other arenas, including the treatment of sepsis, congestive heart failure [42], and multiorgan failure [43]. An exciting area of innovative research is the development of a bioartificial tubule utilizing porcine tubular epithelial cells grown in a hollow fiber to add tubular function to the filtrative function provided by dialysis [44]. These devices are likely to be utilized in combination with CRRT to truly provide complete RRT in the near future. (*From* Humes HD [44]; with permission.)

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