CHAPTER 176

Nomenclature: Basic Principles

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OBJECTIVES

This chapter will:

1. List the nomenclature related to extracorporeal renal replacement therapies.
2. Provide a detailed description of the performance characteristics of membranes and filters.
3. Define and characterize transmembrane transport of solutes and fluid.
4. Name methods of measurement of prescribed and delivered treatment.

This chapter reports the conclusions of a consensus expert conference on the basic principles and nomenclature of renal replacement therapy (RRT) currently used to manage acute kidney injury (AKI). Common definitions, components, and modalities used to deliver extracorporeal therapies will be discussed, using a "machine-centric" rather than a "patient-centric" approach. A description of the performance characteristics of membranes, filters, transmembrane transport of solutes and fluid, flows, and methods of measurement of delivered treatment are provided, focusing on continuous renal replacement therapies (CRRTs), which are used in the management of critically ill patients with AKI. Devices and operations are classified and defined in detail to serve as guidelines for use of terminology in papers and research.

CHARACTERISTICS OF THE MEMBRANE AND FILTER

Geometric Characteristics

The main one-dimensional geometric characteristics of hollow fiber membranes are length (L), mean inner radius ($\bar{r}_i$), wall thickness (t), and number of pores (N_p). The membrane surface area depends on the number of fibers (N_f). Using these parameters, multidimensional characteristics[1] can be expressed as listed in Table 176.1.

Performance Characteristics

The performance characteristics define the potential applications of each membrane.

Membrane Ultrafiltration Coefficient and Filter Ultrafiltration Coefficient

The membrane ultrafiltration coefficient (K_{UF}) represents the water permeability of the filter membrane per unit of pressure and surface. It depends on the dimensions of the membrane and the number of pores and is measured as

$$K_{UF} = \frac{Q_{UF}}{TMP} \cdot \frac{1}{A}$$

where Q_{UF} is the ultrafiltration flow rate, TMP is the transmembrane pressure, and A is the membrane surface area. The unit of measurement is mL/hr/mm Hg/m^2. Treatment parameters that enhance or reduce pore blockage induce changes in the K_{UF}.

The filter ultrafiltration coefficient (DK_{UF}) is defined as the product of the K_{UF} and membrane surface area (A):

$$DK_{UF} = K_{UF} \cdot A$$

The unit of measurement is mL/hr/mm Hg. Membrane manufacturers measure DK_{UF} as the ratio of the Q_{UF} per unit of applied TMP.

The K_{UF} is used to define "high flux" or "low flux" membranes. Although there is no definitive consensus in the literature about the K_{UF} cutoff value,[2] it generally is assumed that a K_{UF} less than 10 mL/hr/mm Hg/m^2 identifies a low-flux membrane, a K_{UF} of 10 to 25 mL/hr/mm Hg/m^2 identifies middle-flux membranes, and a K_{UF} greater than 25 mL/hr/mm Hg/m^2 identifies high-flux membranes.

The term *high flux* has been used generally to define a membrane with an ultrafiltration coefficient that exceeds 25 mL/hr/mm Hg/m^2. This mainly describes the hydraulic permeability of the membrane (permeability to water). However, hydraulic permeability does not necessarily correspond to the permeability to solutes, which instead depends on the density of pores, the mean size of pores, and the distribution of pores. For this reason the terms *high flux* and *highly permeable membrane* are not interchangeable.

Mass Transfer Area Coefficient

The mass transfer area coefficient (K_oA) represents the overall capacity of the membrane to provide diffusive remove solute

TABLE 176.1

Multidimensional Characteristics of the Membranes

MULTIDIMENSIONAL CHARACTERISTIC	SYMBOL	FORMULA
Surface area	A	$A = 2 \cdot N_f \cdot L \cdot \pi \bar{r}_i$
Filter priming volume	V_b^F	$V_b^F = N_f \cdot L \cdot \pi \bar{r}_i^2$
Total priming volume	V_b^{TOT}	$V_b^{TOT} = V_b^F$ + volume of tubes
Membrane porosity	ρ	$\rho = N_p \cdot \pi \cdot \bar{r}_p^2$

L, Membrane length; N_f, number of fibers in the filter; N_p, number of pores in the filter; $\bar{r}_p$, mean inner radius of the pores); $\bar{r}_i$, mean inner radius of the fibers.

over the entire filter surface. It is defined as the product of the solute flux per unit of membrane area (K_0) and the membrane surface area. The unit of measurement is mL/min. The K_0A value can change during dialysis as a result of changes in membrane permeability or a loss of membrane exchange surface area.

Membrane Sieving Coefficient/Rejection Coefficient

The sieving coefficient (SC) is the ratio of a specific solute concentration in the ultrafiltrate (removed only by a convective mechanism), divided by the mean plasma concentration in the filter:

$$SC = \frac{C_{UF}}{(C_{pi} + C_{po})/2}$$

where C_{UF} is the solute concentration in the ultrafiltrate, and C_{pi} and C_{po} the plasma solute concentrations at the inlet and outlet of the filter, respectively. A true calculation would require to measure solute concentration in plasma water rather than plasma to avoid interference of proteins. Nevertheless, for practical purposes, plasma concentration normally is accepted.

SC is correctly measurable only in the absence of a gradient for diffusion (no concentration gradient through the membrane). Measurement of the SC varies during treatment because the characteristics of the membrane change. SC is specific for each solute and for every membrane (Fig. 176.1). The formula is simplified commonly to the ratio between the concentration in the ultrafiltrate and the concentration in prefilter plasma. The rejection coefficient (RC) is defined as

$$RC = 1 - SC$$

Cutoff

For a specific membrane, the cutoff represents the molecular weight of the smallest solutes retained by the membrane. Taking into account the normal distribution of membrane pore size, the statistical cutoff value is identified as the molecular weight of a solute with a SC of 0.1. For a specific membrane, the retention onset (cutoff 90% or 0.9) represents the molecular weight of a molecule with a SC of 0.9. For a complete understanding of the performance characteristics of a membrane, the cutoff value and the retention onset both must be taken into account, allowing evaluation of the profile of the SC curve for each membrane (see Fig. 176.1).[3,4]

Clinically, the expression "high cutoff membranes" describes membranes with a cutoff value that approximates the molecular weight of albumin (before exposure to blood or plasma).

MECHANISMS OF SOLUTE AND FLUID TRANSPORT

Solute transport occurs mainly by two phenomena: convection and diffusion. Fluid transport across semipermeable membranes is driven by ultrafiltration. Adsorption influences removal of hydrophobic (lipid-soluble) compounds by attachment of solute to the membrane. When solute removal rate (mass/time) is normalized by the concentration of blood/plasma entering the filter (mass/volume), the correct term is *solute clearance,* which is expressed in mL/min and describes the volume of blood completely purified by the solute in the unit of time.

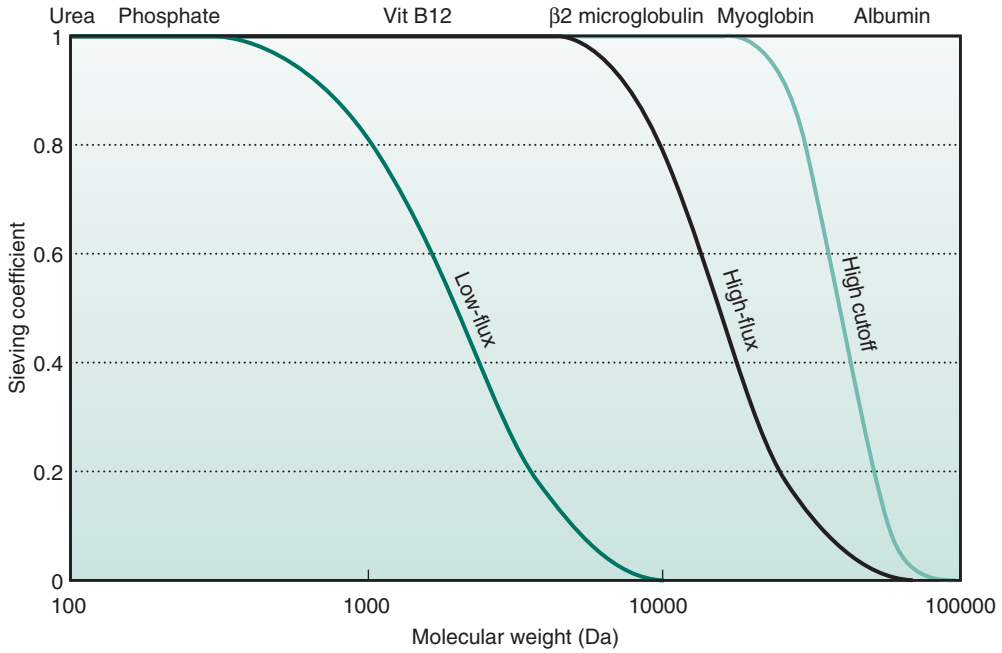

FIGURE 176.1 Schematic diagram of sieving coefficient profiles for low-flux, high-flux, and high cutoff membranes. (Modified from Neri M, Villa G, Garzotto F, et al. Nomenclature for renal replacement therapy in acute kidney injury: basic principles. *Crit Care.* 2016;20:318.)

Ultrafiltration and Convection

Ultrafiltration describes the transport of plasma water (solvent, free of cells and colloids) through a semipermeable membrane, driven by a pressure gradient between blood and dialysate/ultrafiltrate compartments. It is influenced by the intrinsic properties of the filter, such as the DK_{UF}, and the operating parameters (e.g., TMP).[5] Quantitatively, ultrafiltration is defined by the ultrafiltration rate (Q_{UF}):

$$Q_{UF} = DK_{UF} * TMP$$

The term *ultrafiltration* requires some specifications, depending on the context in which it is used. When ultrafiltration is applied to a circuit or a CRRT treatment, specifications should be made using terms such as total ultrafiltration (UF, overall ultrafiltration volume produced during treatment) and net ultrafiltration (UF^{NET}, net ultrafiltrate volume removed from the patient by the machine). In the first case, the overall volume can be replaced completely, partially replaced, or not replaced at all. UF^{NET} is the difference between UF and the volume replaced in the circuit (Table 176.2).

When techniques are discussed, ultrafiltration may be isolated (no other mechanism is used in the treatment and only volume control is achieved), be used as part of hemofiltration (the ultrafiltrate is replaced partially or completely achieving volume and solute control), or combined with diffusion in treatments such as hemodialysis (HD) or hemodiafiltration (HDF). Different membranes are used for different techniques.

Convection is the process in which solutes pass through membrane pores, dragged by fluid movement (ultrafiltration) caused by a hydrostatic and/or osmotic transmembrane pressure gradient.

The convective flux (J_c) of a solute depends on the Q_{UF}, the membrane surface area (A), the solute concentration in plasma (C_{Pi}), and the solute SC:

$$J_c = \frac{Q_{UF}}{A} \cdot C_{pi} \cdot SC$$

Compared with diffusive transport, convective transport permits the removal of higher molecular weight solutes at a higher rate.[6]

Transmembrane Pressure

In hollow fiber filters, the TMP is the pressure gradient across the membrane. The terms that define this gradient are the hydrostatic pressure in the blood compartment (P_B), the hydrostatic pressure in the dialysate/ultrafiltrate compartment (P_D), and the blood oncotic pressure (π_B). The TMP value varies with length (l) along the whole filter length:

$$TMP(l) = P_B(l) - P_D(l) - \pi_B(l)$$

Generally, TMP is expressed using a simplified formula:

$$TMP* = \frac{P_{Bi} + P_{Bo}}{2} - \frac{P_{Di} + P_{Do}}{2} - \frac{\pi_{Bi} + \pi_{Bo}}{2}$$

where P_{Bi} is the blood inlet pressure, P_{Bo} the blood outlet pressure, P_{Di} the dialysate/ultrafiltrate inlet pressure, P_{Do} the dialysate/ultrafiltrate outlet pressure, π_{Bi} the oncotic

TABLE 176.2

Fluids and Flows in Continuous Renal Replacement Therapy

FLOW RATE	SYMBOL	UNIT OF MEASURE	DEFINITIONS AND COMMENTS
Blood flow rate	Q_B	mL/min	Depends on: • Modality • Vascular access • Hemodynamic stability of the patient
Plasma flow rate	Q_P	mL/min	Approximated as: $Q_P = (1–HCT) \cdot Q_B$ where HCT: hematocrit
Ultrafiltration flow rate	Q_{UF}	mL/hr	Total volume of fluid removed in the filter by positive TMP per unit of time: $Q_{UF} = Q_{UF}^{NET} + Q_{R.}$ Depends on: • Blood flow rate • Filter and membrane design • Transmembrane pressure (TMP) • Membrane ultrafiltration coefficient and surface area
Net ultrafiltration flow rate (Δ weight flow rate) (weight loss flow rate)	Q_{UF}^{NET}	mL/hr	Net volume of fluid removed from the patient by the machine per unit of time
Plasma ultrafiltration flow rate	$Q_{P\text{-}UF}$	mL/hr	Total volume of plasma removed in the plasma filter by positive transmembrane pressure (TMP) per unit of time
Replacement flow rate (or substitution flow rate or infusion flow rate)	Q_R^{PRE} Q_R^{POST} $Q_R^{PRE/POST}$	mL/hr	Sterile fluid replacement can be • Upstream of filter (prereplacement, preinfusion, or predilution): reduced depurative efficiency but better filter life • Downstream of filter (postreplacement, postinfusion, or postdilution): higher depurative efficiency but lower filter life • Both upstream and downstream of filter (prepostreplacement, prepostinfusion or prepostdilution): compromise between the two modalities
Replacement plasma flow rate	$Q_{P\text{-}R}$	mL/hr	Replacement of plasma downstream of the plasma filter
Dialysate flow rate	Q_D	mL/hr	Volume of dialysis fluid running into the circuit per unit of time
Effluent flow rate	Q_{EFF}	mL/hr	Waste fluid per unit of time coming from the outflow port of the dialysate/ultrafiltrate compartment of the filter: $Q_{EFF} = Q_{UF} + Q_D = Q_{UF}^{NET} + Q_{R+} Q_D$

pressure of the inlet blood, and π_{Bo} the oncotic pressure of the outlet blood. It must be stressed that the TMP* is a positive, averaged value along the length of filter, and does not reflect the true local pressure profile in the filter. In other words, a positive TMP* does not imply a positive TMP (l) at each point in the filter.

Furthermore, CRRT machines do not usually measure directly the P_{Di} or the oncotic pressure, so the TMP is *estimated* using an even simpler formula:

$$TMP^* = \frac{P_{PRE} + P_{OUT}}{2} - P_{EFF}$$

where P_{PRE} is the prefilter pressure, P_{OUT} the postfilter pressure, and P_{EFF} the pressure measured in the effluent line (all three measured by the machine). In the most common configuration, as blood flows down the filter, plasma water is removed and eliminated with the spent dialysate (if present), which flows in a countercurrent direction (see later). This ultrafiltration, called *direct (or internal) filtration,* identifies the one-directional movement of plasma water from the blood-side to the dialysate/ultrafiltrate compartment of the filter resulting from a local positive TMP (l):

$$P_B(l) > P_D(l) + \pi_B(l)$$

At a critical point on the filter, where $P_B(l) = P_D(l) + \pi_B(l)$, equilibrium is achieved. After this point, the TMP (l) may become negative (even if TMP* is positive), allowing dialysate fluid to flow back into the blood compartment, resulting in so-called backfiltration.[7] Backfiltration describes the movement of fluid from the dialysate compartment to the blood compartment.

Diffusion

Diffusion is a process in which molecules move randomly across a semipermeable membrane. Solute movement occurs from a more concentrated to a less concentrated area until an equilibrium is reached between the two compartments. The concentration gradient ($C_1 - C_2 = dc$) is the driving force. The unidirectional solute diffusive flux (J_d) through a semipermeable membrane follows Fick's law of diffusion, being directly proportional to the diffusion coefficient (D) of the solute and inversely proportional to the distance between the compartments (dx)[6]:

$$J_d = -D \cdot \left(\frac{dc}{dx}\right)$$

The diffusivity coefficient *D* can be approximated using the Stokes-Einstein equation:

$$D = \frac{k_B T}{6\pi\mu R}$$

in which k_B is the Boltzmann constant, T the absolute temperature, μ the viscosity of the medium, and R the effective radius of the molecules. Assuming that most molecules are globular and their effective radius is proportional to the cube root of their molecular weight, D is higher for smaller molecular weight solutes.[8]

Adsorption

Adsorption is an extracorporeal process in which molecules dissolved in plasma or blood (in particular peptides and proteins) bind to the membrane structure or to other adsorbing substances such as charcoal, resins, or gels. The characteristics that influence molecule-membrane interaction are typical for each molecule (i.e., dimension, charge, and structure) and for each particular membrane (i.e., porosity, composition, hydrophobicity, surface potential). Adsorption cartridges should be evaluated in terms of their device adsorption capability (DAC) and their selectivity. DAC represents the total quantity of a specific molecule that the device is able to adsorb and should be of the same order of magnitude as the blood concentration of that molecule multiplied by the blood volume. Selectivity is a safety parameter: it defines what the device does *not* adsorb.

MODALITIES OF EXTRACORPOREAL RENAL REPLACEMENT THERAPY

Hemodialysis

The main mechanism of solute removal in hemodialysis is diffusion, which is chiefly effective in the removal of small solutes. Hemodialysis involves the use of a *hemodialyzer*, in which blood and dialysate solution circulate countercurrent or co-current. A countercurrent configuration is preferred because the average concentration gradient is kept higher along the whole length of the dialyzer. Conversely, a co-current configuration guarantees better stability and control of hydrodynamic conditions and better air removal during the priming phase.[9] High-flux filters permit achievement of significant convective transport; this modality is called high-flux hemodialysis.[10]

Hemofiltration

Hemofiltration is an exclusively ultrafiltration/convection treatment in which high-flux membranes are used in the absence of dialysis fluid. Infusion of a sterile solution into the blood circuit reconstitutes the reduced plasma volume and reduces solute concentration. Infusion of a sterile solution (replacement fluid) can replace totally or partially the filtered volume. Replacement fluid can be infused prefilter *(predilution)* or postfilter *(postdilution).* In terms of solute clearance, postdilution is more efficient than predilution but can lead more easily to membrane fouling because of hemoconcentration.[5]

Hemodiafiltration

Hemodiafiltration combines hemodialysis and hemofiltration, whereby the mechanisms involved in solute removal are diffusive and convective. Because this modality uses high-flux membranes, adequate amounts volumes of sterile solution must be infused to replace the removed volume (prefilter or postfilter).[11]

Isolated Ultrafiltration

The main goal of ultrafiltration is to remove fluid, using semipermeable membranes without volume replacement, thus achieving volume but not solute control in the patient.[12]

Plasmapheresis

Membrane plasmapheresis filters the plasma through plasma filters and replaces it with plasma-derived products, such as fresh frozen plasma, albumin, or other fluids. Alternatively, plasma can be extracted gravimetrically from whole blood using a centrifuge pump. Plasmapheresis is used to remove hydrophilic and lipophilic high-molecular-weight pathogenic substances.[13]

Hemoperfusion or Plasmaperfusion

In hemoperfusion or plasmaperfusion, blood or plasma circulates through a column containing specific sorbents, with adsorption as the only removal mechanism. Usually combined with other modalities, hemoperfusion and plasmaperfusion are used to remove specific hydrophobic (lipid-soluble) substances, toxins, or poisons.[14]

FLUIDS, VOLUMES, AND FLOWS

Solute transport during extracorporeal treatments strictly depends on the operating conditions including blood flow rate, dialysate, net ultrafiltration, and replacement flow rates, designed to achieve the desired clearance performance. These typical CRRT parameters (fluids and flows) are listed in Table 176.2.

Filtration Fraction and Concentration Ratio

The filtration fraction (FF) is defined as the ratio between the ultrafiltration flow rate (Q_{UF}) and the plasma flow rate (Q_P):

$$FF = \frac{Q_{UF}}{Q_p}$$

Filtration fraction also can be measured by the following equation:

$$FF = \frac{1 - Prot_{IN}}{Prot_{OUT}}$$

where $Prot_{IN}$ is the protein concentration in plasma entering the filter, and $Prot_{OUT}$ is the protein concentration in plasma exiting the filter.

A directly measured FF can be expressed as a fraction:

$$FF = \frac{Q_{UF}}{Q_P} = \frac{Q_{UF}}{Q_{B(1-HCT)+Q_R^{PRE}}}$$

where Q_R^{PRE} is the prereplacement flow rate and Q_B the blood flow rate.

For practical clinical purposes (as often used in CRRT machines) it is useful to define the concentration ratio (CR), which quantifies the magnitude of hemoconcentration inside the filter:

$$CR = \frac{Q_{UF}}{Q_B + Q_R^{PRE}} = \frac{Q_R^{PRE} + Q_{UF}^{NET} + Q_R^{POST}}{Q_B + Q_R^{PRE}}$$

where Q_R^{PRE} is the prereplacement flow rate, Q_{UF}^{NET} is the net ultrafiltration flow rate, and Q_R^{POST} is the postreplacement flow rate (all of which sum to Q_{UF}). Clinically, although filtration fraction should be kept ideally below 30%, the CR should be kept below 20% to 25%[15] depending on initial hematocrit, to reduce hemoconcentration and mitigate protein–membrane interactions.

TREATMENT EVALUATION METHODS: THE "DOSE" OF RENAL REPLACEMENT THERAPY

Although the most appropriate dose has not been established for specific patients, large studies have demonstrated in the general population a direct relationship between dose and survival for intermittent and CRRT modalities.[16–22] Today a growing body of evidence suggests the use of precision CRRT, which is characterized by the need to pay great attention to the balance between demand (of blood purification) and capacity (of the native kidney). In these circumstances, personalized prescription and monitoring of treatment dose is recommended highly.[23–26] Although treatment adequacy should be considered more appropriately as a composite of different elements rather than an index based solely on urea kinetics, in CRRT, a treatment efficiency equal or higher than 25 mL/kg/hr commonly is considered adequate. This will result approximately in a daily standardized Kt/V = 1, which describes the efficacy of treatment for a specific patient.

Dose identifies the volume of blood cleared of waste products and toxins by the extracorporeal circuit per unit time. In practice, it is measured as the rate of removal of a representative solute. Urea is the solute most commonly used to quantify dose[27] because it is an indicator of protein catabolism and is retained in kidney failure.[8] Originally, this solute-based approach was developed to measure the dose of dialysis prescribed to patients with end-stage renal disease. In these patients, application of this approach is relatively simple and correlates well with patient outcomes.[16] However, when using CRRT to treat critically ill patients, other measures of adequacy and dose also should be considered. One potentially easier and more reproducible means of estimating dose is incorporating the measurement of flow rates provided by the dialysis machine.[28]

Multiple different definitions and formulas to calculate RRT "dose" have been proposed.[29,30] In this section, we try to clarify the concept. During RRT, the definition of dose must include target (patient), target (machine), current, average, projected, current effective delivered, and average effective delivered doses. Starting from these definitions, therapies should be identified by their efficiency, intensity, and efficacy.

Target Dose (Prescribed)

The target dose (prescribed) is the clearance prescribed for a specific patient in his or her specific clinical condition and represents the clearance the prescribing clinician wants to achieve in that patient.

Target Machine Dose (Set)

The target machine dose is the clearance that the prescribing clinician wants to achieve from the machine. It usually is set as a target machine efficiency or by specifying the flow rate settings and RRT modality. The target machine dose can be modified during the treatment, to reduce the

mismatch between the target dose (prescribed) and the average effective delivered dose (measured).

Current Dose (Estimated From Treatment Parameters)

The current dose (estimated from treatment parameters) is the clearance at the present time estimated from the flow rates in the extracorporeal circuit. During downtime, when the machine treatment is stopped, the current dose is zero. Interruptions during the treatment can occur because of machine alarms, circuit clotting, vascular access malfunctions, or interruptions when the patient must leave the intensive care unit (ICU), such as for surgery or radiologic investigations.

Average Dose (Measured/Calculated)

The average dose is the clearance calculated for the current dose applied over the total treatment time. The total time of treatment is defined as the sum of the effective time of treatment and downtime. The effective time of treatment is the cumulative time during which the effluent pump is working. The average dose is usually an overestimate of the average effective delivered dose.

Projected Dose (Calculated/Estimated)

The projected dose is the weighted-mean clearance that theoretically will be obtained at the end of the treatment. If the target machine dose is kept constant during treatment, the projected dose and the average dose will align. If the target machine dose is modified, the projected dose will depend on the average dose obtained until that moment and the new set target machine dose. The projected dose is usually an overestimate of the average effective delivered dose.

Current Effective Delivered Dose (Measured)

The current effective delivered dose (measured) is the clearance observed at every moment during the treatment. Unlike the current dose (estimated from treatment parameters), it is based on blood concentrations. The current effective delivered dose depends mainly on the specific RRT modality, treatment settings, and other technical and clinical issues that qualitatively and quantitatively affect clearance. The major determinants are differences between the displayed and real blood or effluent flow rates, inadequate vascular access, incorrect priming procedure, loss of surface area (clotting, air), loss of permeability (clotting of the membrane, protein cake deposition on the inner surface of membranes, concentration polarization), high blood viscosity and hematocrit, and excessive FF.

Average Effective Delivered Dose (Measured)

The average effective delivered dose (measured) or real dose is the clinically relevant (measured) clearance delivered to the patient. It is calculated on the basis of the weighted-mean of the current effective delivered dose, over the total time of treatment until that specific moment. The average effective delivered dose is the average of the current effective delivered dose during the time of treatment, and not of the current dose, because the latter is plagued by errors during times in which flow may be occurring with no solutes clearance, (e.g., bag changes, recirculation procedures). The largest discrepancies between the target dose and the average effective delivered dose are found in predominantly diffusion-based CRRT (i.e., continuous venovenous hemodialysis and continuous venovenous hemodiafiltration).[29]

In an ideal treatment, during which downtime and technical and/or clinical hindrances do not influence clearance, the target, target machine, current, average, projected, current effective delivered and average effective delivered doses will be equal.

Efficiency, Intensity, and Efficacy

Identified as a clearance (K), the efficiency represents the volume of blood cleared of a solute over a given period of time. It can be expressed as the ratio of blood volume over time (e.g., mL/min, mL/hr, l/hr, l/24 hr) and generally is normalized to ideal patient weight (mL/kg/hr). Efficiency depends on the reference molecules chosen (molecular size), removal mechanisms (diffusion, convection, or both), and circuit operational characteristics (i.e., flow rates and type of filter). Efficiency can be used to compare different RRT treatments applied with the same modality using different settings and operational characteristics. Efficiency can be categorized further and defined as target efficiency, target machine efficiency, current efficiency, average efficiency, projected efficiency, current effective delivered efficiency, and average effective delivered efficiency. In Fig. 176.2, the different categories of efficiency during CRRT are illustrated with examples.

Intensity can be defined by the product "efficiency × time." In practice, intensity represents the blood volume cleared of a solute after a certain period of time; it can be expressed as mL or L. When RRT modalities are compared with different duration times, the use of intensity is more appropriate than the use of efficiency. For example, despite its low efficiency, use of CRRT for a long period of time results in increased treatment intensity.

Renal failure patients frequently require more than a single treatment; therefore frequency of treatment should be considered when assessing dose. Specifically, the product of intensity times frequency (measured as treatment days/week [d/w]) is useful to obtain information beyond a single treatment. Although intensity allows comparison between different treatments, it does not take into account the volume of the solute pool.

Efficacy measures the removal of a specific solute achieved by a given treatment in a given patient. It can be identified as the ratio of the entire volume cleared during the treatment to the volume of distribution of that solute. In practice, efficacy is a dimensionless number and can be defined numerically as the ratio between intensity and the volume of distribution of a specific solute. Definitions of efficiency, intensity, and efficacy, together with the related formulas and abbreviations, are given in Table 176.3.

CONCLUSION

Understanding the basic mechanisms underlying the process of RRT is essential to be able to make appropriate treatment choices for individual patients. Although apparently simple, those choices are in reality complex, and specific

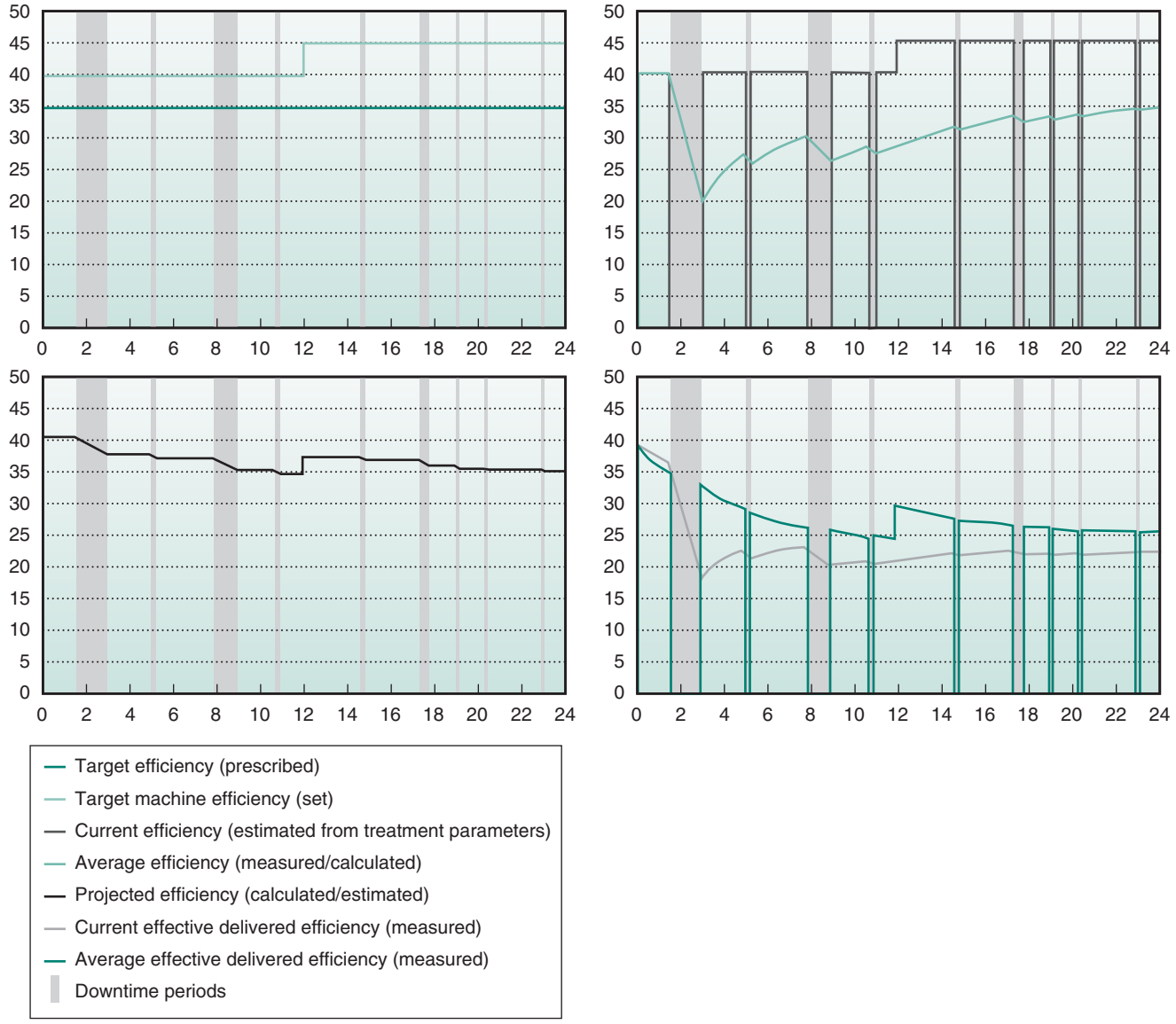

FIGURE 176.2 Practical example showing the different trends in efficiency (mL/kg/hr, Y axis) versus treatment time (h, X axis) during treatment with continuous renal replacement therapy (CRRT). In the example reported, according to the literature, the doctor decides that a target efficiency prescribed of 35 mL/kg/hr is the most adequate for his patient. Taking into account the average downtime in his specific unit, the doctor sets the target machine efficiency of 40 mL/kg/hr, to reach the target dose (prescribed).When the treatment is ongoing, the value of current efficiency (estimated from treatment parameters) equals the target machine efficiency, whereas it is zero during the downtime. The average efficiency measured/calculated) is the efficiency calculated for the current efficiency applied over the total time of treatment. The projected efficiency (calculated/estimated) is the weighted-mean clearance that theoretically will be obtained at the end of the treatment session (24 hr). In this example, as the projected reached efficiency is less than 35 mL/kg/hr (the target prescribed efficiency), the physician can assume that the patient will be undertreated at the end of the treatment and needs to increment the target machine efficiency (set). The last two efficiencies are the current effective delivered and the average effective delivered efficiencies and are based on blood concentrations. They can be measured in specific moments of the treatment to better adjust the target machine efficiency (set). (Modified from Neri M, Villa G, Garzotto F, et al. Nomenclature for renal replacement therapy in acute kidney injury: basic principles. *Crit Care.* 2016;20:318.

to each clinical situation. The aim of this chapter is to standardize the nomenclature used by all parties involved in planning and delivering RRT at any level. It is hoped that the industry will also adopt a standard terminology in the future.

List of Abbreviations

A	Membrane surface area
AKI	Acute kidney injury
B.W.	Ideal body weight
C_{Bi}	Prefilter blood concentration of the reference solute
C_{Bo}	Postfilter blood concentration of the reference solute
C_{Pi}	Prefilter plasma concentration of the reference solute immediately before the filter
C_{Po}	Postfilter plasma concentration of the reference solute immediately after the filter
CR	Concentration ratio
CRRT	Continuous renal replacement therapy

TABLE 176.3

Definitions and Formulas for Efficiencies, Intensities, and Efficacies

MEASUREMENT	NAME	SYMBOL	UNIT OF MEASURE	FORMULA
Efficiency	Target (prescribed)	K_T	mL/kg/hr	Assuming that the patient's clinical condition does not change, K_T is a constant value throughout the treatment
Efficiency	Target machine	K_{Tm}	mL/kg/hr	Considering the down time and the reduction in clearance properties of the membranes during treatment, K_{Tm} is usually set at a greater value than K_T
Efficiency	Current	K_{Cr}	mL/kg/hr	$K_{cr} = \frac{(Q_R^{PRE} + Q_D + Q_{UF}^{NET} + Q_R^{POST})}{B \cdot W} \cdot \frac{Q_B}{Q_B + Q_R^{PRE}}$
Efficiency	Average	K_{Am}	mL/kg/hr	$K_{Am} = \frac{1}{t_1} \cdot \int_0^{t_1} KCrdt$
Efficiency	Projected	K_{Pr}	mL/kg/hr	$K_{Pr} = \frac{\int_0^{t_1} K_{Cr}\mathrm{dt} + (t_{tot} - t_1) \cdot K'_{Tm}}{t_{tot}}$ where K'_{Tm} is the new target machine efficiency set
Efficiency	Current effective delivered	K_{Cd}	mL/kg/hr	$K_{Cd} = \left(Q_B \cdot \frac{C_{Bi} - C_{Bo}}{C_{Bi}} + Q_{UF} \cdot \frac{C_{Bo}}{C_{Bi}}\right) \cdot \frac{1}{B \cdot W \cdot}$
Efficiency	Average effective delivered	K_{Aed}	mL/kg/hr	$K_{Aed} = \frac{1}{t_1} \cdot \int_0^{t_1} K_{Cd} dt$
Intensity	Target (prescribed)	I_T	mL/kg	Blood volume that should be cleared applying K_T during the total time of treatment
Intensity	Target machine	I_{Tm}	mL/kg	Blood volume that should be cleared applying K_{Tm} during the total time of treatment
Intensity	Current	I_{Cr}	mL/kg	$I_{Cr} = K_{Cr} \cdot t_{tot}$
Intensity	Average	I_{Am}	mL/kg	$I_{Am} = K_{Cm} \cdot t_1 = \int_0^{t_1} K_{Cr} dt$
Intensity	Projected	I_{Pr}	mL/kg	$I_{Pr} = K_{Pr} \cdot t_{tot} = \int_0^{t_1} K_{Cr} dt + (t_{tot} - t_1) \cdot K'_{Tm}$
Intensity	Current effective delivered	I_{Cd}	mL/kg	$I_{Cd} = K_{Cd} \cdot t_1$
Intensity	Average effective delivered	I_{Aed}	mL/kg	$I_{Aed} = K_{Ced} \cdot t_1 = \int_0^{t_1} K_{Cd} dt$
Efficacy	Target (prescribed)	E_T	Dimensionless	Solute removal obtained applying I_T to the volume of distribution of the solute
Efficacy	Target machine	E_{Tm}	Dimensionless	Solute removal obtained applying I_{Tm} to the volume of distribution of the solute
Efficacy	Current	E_{Cr}	Dimensionless	$E_{Cr} = \frac{I_{Cr}}{V} = \frac{K_{Cr} \cdot t_{tot}}{V}$
Efficacy	Average	E_{Am}	Dimensionless	$E_{Am} = \frac{I_{Cm}}{V} = \frac{1}{V} \int_0^{t_1} K_{Cr} dt$
Efficacy	Projected	E_{Pr}	Dimensionless	$E_{Pr} = \frac{I_{Pr}}{V} = \frac{1}{V} \cdot \left[\int_0^{t_1} K_{Cr} dt + (t_{tot} - t_1) \cdot K'_{Tm}\right]$
Efficacy	Current effective delivered	E_{Cd}	Dimensionless	$E_{Cd} = \frac{I_{Cd}}{V} = \frac{K_{Cd} \cdot t_1}{V} = \frac{1}{V} \cdot \left(Q_B \cdot \frac{C_{Bi} - C_{Bo}}{C_{Bi}} + Q_{UF} \cdot \frac{C_{Bo}}{C_{Bi}}\right) \cdot \frac{1}{B \cdot W \cdot} \cdot t_1$
Efficacy	Average effective delivered	E_{Aed}	Dimensionless	$E_{Aed} = \frac{I_{Ced}}{V} = \frac{K_{Ced} \cdot t_1}{V} = \frac{1}{V} \cdot \int_0^{t_1} K_{Cd} dt$

BW, Ideal body weight; C_{Bi}, prefilter blood concentration of the reference solute; C_{BO}, Postfilter blood concentration of the reference solute; *dt,* delta time; Q_R^{PRE}, prereplacement flow rate; Q_D, dialysate flow rate; Q_{UF}^{NET}, net ultrafiltration flow rate; Q_B, blood flow rate; Q_R^{POST}, postreplacement flow rate; Q_{UF}, ultrafiltration flow rate; t_{tot}, total time of treatment; *V,* volume of distribution of the reference solute.

C_{UF}	Concentration of the reference solute in the ultrafiltrate
D	Diffusion coefficient
DAC	Device adsorption capability
dc	Concentration gradient
DK_{UF}	Filter ultrafiltration coefficient
dx	Distance between compartments
E_{Aed}	Average effective delivered efficacy
E_{Am}	Average efficacy
E_{Cd}	Current effective delivered efficacy
E_{Cr}	Current efficacy
E_{Pr}	Projected efficacy
E_{Tm}	Target machine efficacy
E_T	Target efficacy
FF	Filtration fraction
HCT	Hematocrit
I_{Aed}	Average effective delivered intensity
I_{Am}	Average intensity
I_{Cd}	Current effective delivered intensity
I_{Cr}	Current intensity
ICU	Intensive care unit
I_{Pr}	Projected intensity
I_{Tm}	Target machine intensity
I_T	Target intensity
J_c	Convective flux
J_d	Diffusive flux
K	Clearance
K_0	Solute flux per unit of membrane area

K_0A	Mass transfer area coefficient
k_B	Boltzmann constant
K_{Aed}	Average effective delivered efficiency
K_{Am}	Average efficiency
K_{Cd}	Current effective delivered efficiency
K_{Cr}	Current efficiency
K_{Pr}	Projected efficiency
K_{Tm}	Target machine efficiency
K'_{Tm}	New target machine efficiency set at time t_1
K_T	Target efficiency (prescribed)
l	Infinitesimal part of the membrane's length
L	Length of the membrane
K_{UF}	Membrane's ultrafiltration coefficient
N_f	Number of fibers in the filter
N_p	Number of pores in the membrane of the filter
P_B	Hydrostatic pressure in the blood compartment
P_{Bi}	Hydrostatic pressure in the inlet part of the blood compartment
P_{Bo}	Hydrostatic pressure in the outlet part of the blood compartment
P_D	Hydrostatic pressure in the dialysate/ultrafiltrate compartment
P_{Di}	Hydrostatic pressure in the inlet part of the dialysate compartment
P_{Do}	Hydrostatic pressure in the outlet part of the dialysate compartment
P_{EFF}	Pressure in the effluent line
P_{OUT}	Pressure in the outflow line
P_{PRE}	Blood prefilter pressure measured by the machine
$Prot_{IN}$	Protein concentration in plasma entering the filter
$Prot_{OUT}$	Protein concentration in plasma exiting the filter
Q_B	Blood flow rate
Q_D	Dialysate flow rate
Q_{EFF}	Effluent flow rate
Q_P	Plasma flow rate
$Q_{P\text{-}R}$	Replacement plasma flow rate
$Q_{P\text{-}UF}$	Plasma ultrafiltration flow rate
Q_R	Total replacement flow rate
Q_R^{POST}	Replacement flow rate postfilter
Q_R^{PRE}	Replacement flow rate prefilter
Q_{UF}	Ultrafiltration flow rate
Q_{UF}^{NET}	Net ultrafiltration flow rate
RC	Rejection coefficient
R	Radius of the molecules
$\overline{r}_i$	Mean inner radius of the fibers
$\overline{r}_p$	Mean inner radius of the membrane pores
RRT	Renal replacement therapy
SC	Sieving coefficient
T	Absolute temperature
t	Thickness of the fibers
t_1	Treatment elapsed time ($0 < t_1 < t_{tot}$)
TMP	Transmembrane pressure
TMP*	Approximated cumulative pressure gradient across the entire membrane
t_{tot}	Total time of treatment
V	Volume of distribution of the reference solute
V_b^F	Filter priming volume
V_b^{TOT}	Total priming volume
μ	Viscosity
π_B	Oncotic pressure in the blood
π_{Bi}	Oncotic pressure of blood inlet
π_{Bo}	Oncotic pressure of blood outlet
ρ	Membrane porosity

Key Points

1. Standardized definitions regarding renal replacement therapies are important to avoid describing the same modality with different names.
2. Solvents and solutes transport mechanisms, modalities, and dose involved in renal replacement therapies should be known and used appropriately by investigators to describe the nature of the performed therapy accurately.
3. Understanding the terminology and nomenclature explaining basic principles in renal replacement therapies is essential to implement adequate treatment choices to the individual patient.

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A complete reference list can be found online at ExpertConsult.com.

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