Hemodialysis Treatment Prescription

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9.1 Case: 1

A 16-year-old female with end-stage renal disease due to diabetic nephropathy is scheduled to start hemodialysis next week. She has poorly controlled blood sugars, along with moderate obesity (weight of 42 kg, body mass index of 34 kg/m^2). Her blood pressure and proteinuria have been reasonably well controlled with lisinopril and atenolol. She is moderately hypoalbuminemic (serum albumin of 3.4 g/dL [34 g/L]) and anemic (hemoglobin of 9.6 g/dL [96 g/L]), while her serum potassium and bicarbonate levels have been normal on alkali supplementation. She had dialysis catheter insertion into her right internal jugular vein and a creation of arteriovenous fistula simultaneously this past week, after her blood urea nitrogen level surpassed 94 mg/dL (33.9 mmol/L) the week prior. Factors that need to be considered while writing hemodialysis prescription are summarized in (Table 9.1).

9.1.1 What Is the Principle of Blood Purification via Hemodialysis?

Concentration gradient-driven diffusion process is the main principle underlying blood purification in hemodialysis (HD), which effectively eliminates small

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Table 9.1 Hemodialysis prescription

Dialyzer type	Determined by patient size, clearance, and UF needs
Tubing type	Neonatal tubing—in patients <10 kg blood pump set at 2.6 mm Pediatric tubing—in patients 10–20 kg blood pump set at 6.4 mm
Priming of system	For circuits with extracorporeal volume >10% of patient blood volume (>80 mL/kg), diluted PRBC, or whole blood circuit priming
Dialysate composition	Composition determined on a per-patient basis
Dialysate flow	Flow <200 mL/min for infants/small children
Dialysate temperature	To avoid hypothermia, temperature may be elevated to 37.5 °C To prevent hypotension, temperature may be lowered to 35 °C
Blood flow rate	Gradually increase over first 3–5 treatments First treatment, BF = 2–3 mL/kg/min Second treatment, BF = 3–4 mL/kg/min Third treatment, BF = 4–5 mL/kg/min
Urea reduction	30% reduction in the first session 50% reduction in the second session 70% afterward
UF goals	No >5% of child's body weight removed during 3–4-h session
Anticoagulation	For continuous heparinization of patients <10 kg, consider loading dose of 10–15 units/kg, with a maintenance dose of 10–25 units/kg/h For routine heparinization of all low-risk dialysis patients, consider total heparin dose of 25 units/kg/h of dialysis For patients at slight to moderate risk of bleeding (such as those with recent surgery with low bleeding risk, pericarditis, and/or Coumadin therapy), consider total heparin of 10 units/kg/h of dialysis
Medications	Administered via infusion pump connected to venous port or IV push
Blood transfusion	Transfuse blood during dialysis to reduce volume overload and hyperkalemia risk
Patient monitoring	– Vital signs should be recorded at least every 30 min (q 15 min in PICU patients) in patients <15 kg – Staff members performing dialysis must remain within visual and auditory range of the patient/dialysis machine – Crit-Line monitoring and/or sodium modeling may help prevent intradialytic hypotension

UF ultrafiltration, *PRBC* packed red blood cell, *BF* blood flow, *IV* intravenous

molecules such as urea. The rate of blood flow correlates directly with HD clearance (K_{HD}) [1]. It is a passive transfer of solute across a semipermeable membrane. There is no net transfer of solvent, mainly driven by concentration gradient, much like a tea bag in water. Factors that affect mass transfer are [2]:

- Concentration gradient (*dC*)
- Dialyzer surface area (*A*)
- Dialyzer diffusivity (*KO*) for particular solute
- Sum of resistances (Rb + Rm + Rd) ~ (d*x*/KO) where Rb is mass transfer resistance of blood, Rm is mass transfer resistance of membrane, and Rd is mass transfer resistance of dialysate
- Countercurrent flow
- Time

$$\text{Mass Transfer} = \text{Driving Force} / \text{Resistance} \left(J = KOA \times dC / dx \right)$$

where J is diffusive mass transfer rate (mg/s) and dC/dx is the change in concentration of the solute in relation to distance.

9.1.2 What Is the Terminology Used to Decide the Prescription?

The low-flux and high-flux F-series Fresenius Polysulfone membrane dialyzers are available with a very good performance, larger endotoxin retention capability, and superb hemocompatibility. These hemodiafilters are manufactured specifically for high-volume hemodiafiltration (HDF) to handle more than 15 L of fluid exchange per treatment [3]. These hemodiafilters use new variant of the Helixone membrane with sophisticated housing design and enable [3]:

- Increased fluid exchange rates during HDF (>15 L/treatment)
- Increased elimination of low-molecular-weight substances such as phosphate
- Better elimination of middle molecules

The benefit of high-flux steam dialyzer is the integration of safe sterilization technique with blood-compatible membrane [3]. Its advantages are:

- Exceptional compatibility with blood.
- Best performance.
- Broad range of the products (0.7–2.4 m^2).
- Good for HD, hemofiltration (HF), and HDF.
- Efficient elimination of β_2-microglobulin.
- Enhanced capability for endotoxin retention.
- Exclusive steam sterilization in-line (without sterilization of by-products/residues and dry).
- Rinsing is not required prior to treatment.

Factors to keep in mind during the blood flow rate prescription for a HD are the relation between the specific solute clearance rate, dialysis membrane type, and rate of the blood flow [4]. Clearance of small solutes such as urea (molecular weight, 60) is highly flow dependent as linear relationship is observed between urea clearance and blood flow rates. Furthermore, property of the dialysis membrane is the limiting factor as clearance rates gradually reduce at higher blood flow rates [4]. The dialyzer efficacy in urea elimination (KoA) is dependent on the surface area of dialyzer, pore size, and membrane thickness. By increasing the rate of blood flow, clearance rate of urea can be augmented further by using high-efficiency membrane (KoA >600 mL/min). On the contrary, there is no notable difference in urea clearance between high-efficiency and conventional membranes at low blood flow rates since the rate of blood flow is the main factor affecting clearance, not the membrane [4].

Dialysis Clearance Clearance is a function of dialyzer efficiency. Clearances are routinely reported for urea (small solutes), β_2-microglobulin (middle molecule), and vitamin B12 (large solute).

Flux Flux is a measure of ultrafiltration capacity. The coefficient of ultrafiltration (Kuf) differentiates low flux from high flux. Kuf less than 10 mL/h/mm Hg is considered as low flux, whereas Kuf greater than 20 mL/h/mm Hg is considered as high flux [5].

Permeability Permeability is the capability of the dialyzer to eliminate middle molecular weight substance such as β_2-microglobulin (middle molecule clearance). With usual clinical flow and ultrafiltration, the correlation between permeability and flux is; permeability is low when the clearance of β_2-microglobulin is <10 mL/min (*low-flux membrane*), whereas the permeability is high when the clearance of β_2-microglobulin is >20 mL/min (*high-flux membrane*) [6, 7].

Efficiency It is the dialyzer's capability to remove urea (urea clearance). Low-efficiency dialyzer has KoA less than 500 mL/min, whereas high-efficiency dialyzer has KoA greater than 600 mL/min [6].

Surface Area Larger surface area dialyzer usually has higher clearance for urea, but the dialyzer efficiency (KoA) is vital in attaining optimal urea clearance, independent of a dialyzer's surface area.

The Mass Transfer Area Coefficient of the Dialyzer for Urea (KoA) KoA is the measure of dialyzer efficiency in removing urea and other small molecular weight solutes. At infinite dialysate and blood flow rates for a particular solute, KoA of the dialyzer is the highest theoretical clearance measured in milliliters/minute. Usually the surface area of any given dialyzer membrane will be proportional to KoA; however, drop in KoA occurs when the surface area becomes very large [8]. Small patients should be dialyzed with low-efficiency dialyzers with KoA <500 mL/min. Routine treatments are done with moderate-efficiency dialyzers with KoA of 500–700 L/min. Large-size patients with the need for >4-h dialysis session should be dialyzed with high-efficiency dialyzers of KoA >700 mL/min. KoA increases with increase in flow rate of the dialysate from 500 to 800 mL/min because of good dialysate penetration into hollow-fiber bundle at higher dialysate flow resulting in higher efficacy of dialysis due to expansion of effective surface area of the dialyzer [9, 10]. However, change in blood flow rates does not affect KoA.

Ultrafiltration Coefficient (Kuf) Kuf is the fluid volume (mL/h) transported through the membrane per mmHg of pressure gradient. It is the measure of dialyzer's permeability relative to water [2]. A low Kuf (near zero) denotes low permeability and low flux, whereas high Kuf (near 1.0) denotes near-complete permeability and high flux. The lower the permeability to water, the higher the transmembrane

pressure (TMP) needed to achieve ultrafiltration. High-flux dialyzers achieve desired ultrafiltration (UF) volumes at lower TMPs. Volumetric machines control TMP based on the desired UF rate.

Kuf-UF Coefficient It is the volume of plasma filtered in mL/h for each mmHg of TMP. UF/h = Kuf × TMP. For example, for 100 ml UF/hr, you need 2 Kuf and 500 mmHg TMP, and for Kuf 8, you need TMP 125 mmHg. Minor error in TMP setting will lead to major error in the UF amount when Kuf is high.

9.1.3 What Is an Ideal Dialyzer?

9.1.3.1 Characteristics of High-Efficiency Dialysis

Both high-flux and high-efficiency membranes are similar with respect to clearance of solutes with low molecular weight (urea) and KoA (>600 mL/min). Larger pore size in high-flux membranes results in remarkably higher clearance rates for solutes with high molecular weight such as β_2-microglobulin, which is not cleared with low-flux membranes (Kuf less than 10 mL/h/mm Hg) [4]. As much as 400–600 mg/week of β_2-microglobulin can be cleared with some high-flux membranes. The following are the typical high-efficiency dialysis characteristics [5–7]:

The rate of urea clearance is normally >210 mL/min.
The dialyzer KoA for urea is normally >600 mL/min.
The Kuf and the clearance of middle-molecular-weight molecules may be high or low.
Cellulosic or synthetic membrane dialyzers can be used for dialysis.

High Flux Kuf >14 mL/min/mmHg (hydraulic or fluid removal)
β_2-Microglobulin clearance >20 mL/min (clearance of large molecules) [11]

High Efficiency KoA > 500 L/min at 500 mL/min of dialysate flow rate (Qd)

9.1.4 What Is Dialysis Adequacy and Why Is *KT/V* >1.4 Important?

The main part of dialysis prescription is providing sufficient amount of dialysis. Sudden decrease in urea levels occurs during dialysis followed by a slow rise during the interdialytic period. The three main factors that drive fall in urea concentration during dialysis are clearance rate of the dialyzer for urea (*K*), duration of dialysis (*t*), and urea distribution volume (*V*) [12]. Dialysis membrane properties (KoA), convective urea flux during ultrafiltration, rate of blood, and dialysate flow influence the dialyzer clearance rate for urea (*K*). In a stable patient, interdialytic urea rise depends on the dietary protein intake, volume of urea distribution, and residual kidney function.

Urea kinetic modeling (UKM) consists of *KT/V* and the urea reduction ratio (URR). *KT/V* is a measure of dialysis sufficiency determined by the dialyzer efficiency, dialysate and blood flow rates, HD frequency and duration, and volume of

body water in which urea is distributed. The goal for *KT/V* is ≥1.4 and an acceptable *KT/V* is ≥1.2 [13]. A value of <1.2 denotes inadequate hemodialysis. The URR is also calculated to assess dialysis adequacy using blood urea nitrogen (BUN) before and after dialysis. Desirable URR is ≥65%. No outcome studies exist for pediatric HD patients and require advanced computational capability, which is not available to many pediatric dialysis units. A simple and reliable *Kt/V* estimation method is needed for month-to-month comparison of *Kt/V* in a single unit and across multiple units.

KT/V represents *fractional urea clearance*

K = dialyzer clearance (blood water) in mL/min or L/h
T = time in minutes or hours
V = urea distribution volume in milliliters or liters
Dimensionless

$$\text{URR} = \left(\text{BUN}_{\text{PRE}} - \text{BUN}_{\text{POST}}\right) / \text{BUN}_{\text{PRE}}$$

URR is not precise as urea cleared by ultrafiltration is not taken into account. URR of 65% may have varying sp*Kt/V* (single pool) of 1.1–1.35 based on ultrafiltration volume. Also, URR does not give information about nutrition status (nPCR).

If measurements of dialysis adequacy (*KT/V* and URR) fall below the minimum acceptable levels, the following measures must be taken:

1. Evaluate for errors in prescribed HD dose delivery.
2. Increase the dose of HD prescription:
   - Increase dialyzer size.
   - Increase treatment time.
   - Increase dialysate flow.
   - Increase blood flow.
3. Increase the heparin dose.
4. Correct the dialysis access site if inadequate.

KT/V = 0.5—associated with uremic symptoms, hospitalization, & death

0.7—associated with EEG abnormalities
1.0—associated with good short-term outcome
1.2–1.4—associated with good long-term outcome
>1.4—associated with better outcome

9.1.5 How to Write Initial Prescription in Acute on Chronic Hemodialysis Case?

Equation for Initial HD prescription

$$Kt/V \sim -In\left(C1/C0\right)$$

K = urea clearance of the dialyzer (mL/min)
t = duration of treatment (minutes)

V = total body water estimation (600 mL/kg)
$C0$ = BUN before dialysis (mg/dL)
$C1$ = BUN after dialysis (mg/dL)
ln = natural log

1. Determine the amount of urea to be removed (e.g., 50%).
2. Select dialyzer size appropriately and enter K.
3. Calculate V (600 mL/kg).
4. Get BUN before dialysis ($C0$), perform dialysis for prescribed duration (t), and get BUN after dialysis ($C1$).
5. Estimate V from K, t, and measured $C0$ and $C1$.
6. Repeat steps 1–5 using estimated V.

9.1.5.1 Let's Write Perception?

Desired clearance of urea is 50%.

Choose 1.3 m^2 surface area dialyzer.
(K_{urea} = 210 mL/min at 250 mL/min blood flow rate (Qb))
Weight of the patient is 42 kg before dialysis.
Using the equation: $Kt/V \sim -\ln (C1/C0)$
210 mL/min × t/(42 kg × 600 mL/kg) = −ln (50/100)
Leading to t = 83 min
Example of initial HD prescription and refinement
Hemodialysis performed
BUN before dialysis ($C0$) = 94 mg/dL
BUN after dialysis ($C1$) = 65 mg/dL
HD duration = 83 min
Using the equation: $Kt/V \sim -\ln (C1/C0)$
210 mL/min × 83 min/V = −ln (65/94)
Leading to V = 47.2 L

Acute HD should be delivered in a dialysis center or in pediatric or neonatal ICU with support from the multidisciplinary team that provides integrated and individualized care.

1. *The following must be specified in all pediatric hemodialysis treatment orders:*
   (a) Dialyzer type
   (b) Tubing type (adult, pediatric, or neonatal)
   (c) Priming of system (blood, 5% albumin)/amount to administer
   (d) Dialysate composition
   (e) Dialysate flow
   (f) Dialysate temperature
   (g) Blood flow rate
   (h) Duration of treatment
   (i) Ultrafiltration goal
   (j) Anticoagulation
   (k) Medications
   (l) Blood transfusion
   (m) BP and pulse parameters/management of hypotension

2. *Machine specifications*: Fresenius 2008K machines will be used.
   (a) For blood flow <120 mL/min, use the pediatric mode. If normal mode is used with low blood flows, UF will automatically be set at 70 mL/h.
   (b) Selection: Move arrow on display to MENU, and then push SET. Move arrow to DIALYSIS OPTIONS, and then push SET. Move arrow to PEDIATRIC, and then push SET to change "NO" to "YES." Move arrow to DIALYSIS, and then push SET to go back to DIALYSIS screen.
   (c) To change back to normal mode, move arrow to MENU, and then push SET. Move arrow to DIALYSIS OPTIONS, and then push SET. Move arrow to PEDIATRIC, and then push SET to change "YES" to "NO." Move arrow to DIALYSIS, and then push SET to return to DIALYSIS screen.
3. *Dialyzer*
   (a) Determined by patient's size and the patient's clearance and UF needs.
   (b) Consult the specification sheets for the clearance and UF capacities of specific dialyzers (Table 9.2).
4. *Tubing*
   (a) Patients <10 kg—*neonatal tubing* with blood pump set at 2.6 mm
   (b) Patients 10–20 kg—*pediatric tubing* with blood pump set at 6.4 mm
   (c) Patients >20 kg—*adult tubing* with blood pump set at 8 mm
5. *Priming of system*
   (a) Extracorporeal volume (tubing volume + dialyzer volume) >10% of the estimated blood volume of the patient (>80 mL/kg), blood priming of the circuit should be done especially in patients <10 kg to prevent intradialytic hypotension [2, 14].
   (b) One unit of *diluted packed red blood cells* (PRBCs) (hematocrit 35%) should be ordered which has been typed and crossmatched with the patient.
   (c) Prime the circuit with normal saline.
   (d) Add two units of heparin/mL into the diluted PRBCs.
   (e) Prime the circuit with diluted PRBCs.
   (f) Wait for 5 min to recirculate and heparinize the system and to warm the blood to an adequate level for the patient.

Table 9.2 Specifications of different dialyzers [14]

Dialyzer	Membrane	SA (m^2)	Prime volume (mL)	Kuf	Patient weight (kg)
F3	PS	0.4	28	1.7	10–15
F4	PS	0.7	42	2.8	15–25
F6	PS	1.3	82	5.5	25–35
F160	PS	1.5	83	50	35–80
F180	PS	1.8	99	48	>80
B 190 Xebium	PES	1.9	114	75	
B 150	CET	1.5	95	3.15	(Hypoallergenic)

PS polysulfone, *PES* polyethersulfone, *CET* cellulose triacetate, *SA* surface area, *Kuf* ultrafiltration coefficient of a dialyzer

(g) Entire blood priming should be done by connecting the arterial and venous lines concurrently.
(h) Caution should be exercised in deciding about giving half or the entire prime in children who weigh 10–15 kg or hemodynamically unstable.
(i) No prime is given in children >15 kg who are hemodynamically stable.

6. *Dialysate*
   (a) Dialysate is ordered based on patient's lab reports.
7. *Dialysate flow rate (Qd)*
   (a) Standard Qd of 500 mL/min is adequate for most patients [2].
   (b) In infants and small children during initial HD, decreased flow of <500 mL/min should be considered to prevent disequilibrium syndrome.
   (c) To attain adequate clearance in larger children, higher flow of 800 mL/min may be needed [2].
8. *Dialysate temperature*
   (a) To avoid hypothermia in infants, dialysate temperature is increased to 37.5 °C [2].
   (b) In children with hypotension, dialysate temperature is decreased to as low as 35 °C to improve cardiovascular stability [14].
9. *Blood flow rate (Qb)*
   (a) The rate of blood flow is increased slowly during the initial three to five treatments [2, 14]:
      - First treatment: Qb 2–3 mL/kg/min (start at 200 mL/min in adult-size patients)
      - Second treatment: Qb 3–4 mL/kg/min
      - Third treatment: Qb 4–5 mL/kg/min
   (b) Minimum Qb is 25 mL/min and maximum Qb is 500 mL/min.
   (c) Blood flow may be limited by catheter size/position.
   (d) Monitor for any problems with outflow or high venous resistance.
10. *Duration of treatment*
   (a) First dialysis treatment in uremic patients should be limited to 2 h.
   (b) Subsequent dialysis treatments may be slowly increased to 3–4 h (30–60 min/treatment).
   (c) If serum osmolality >300 mOsm, BUN > 100 mg/dL, or first dialysis in chronic patient, intravenous mannitol 0.25 g/kg/dose should be considered at the beginning of dialysis.
   (d) The duration of treatment is estimated based on serum ammonia levels in children with hyperammonemia or intoxication (in PICU/NICU) as the duration is not known at onset.
11. *Ultrafiltration goal*
   (a) General rule is no >5% of the child's body weight should be removed during a 3–4-h HD session [14].
   (b) Fluid removal is usually better tolerated in a shorter period of time in an isolated UF session.
   (c) UF goal adjustments are done by referring Crit-Line monitoring protocol.

12. *Anticoagulation*
    (a) Usually, heparin is given as bolus (patient >10 kg) or by constant infusion (patient <10 kg).
    (b) Monitor machine pressure readings for signs of elevation, which indicates clotting.
    (c) If the pressures increase and the access is patent, stop the dialysis before the system completely clots, and return as much blood as possible to the patient (unless system was primed with blood).
    (d) In children with increased risk for bleeding, non-heparin-based dialysis (normal saline flushes) may be considered [2].
13. *Medications*
    (a) All medications should be given as intravenous push or through infusion pump connected to the venous port.
    (b) Alarm may go on as the venous dialysis bloodline pressure is usually more than that of the infusion pump due to small volume and low infusion rate.
    (c) Medication should be given via a different access if the infusion pump continues to alarm for high pressures.
14. *Blood transfusion*
    (a) Risks of volume overload and hyperkalemia are decreased if blood is transfused during dialysis.
    (b) Order type and crossmatch for 15–20 mL/kg PRBCs (and premedication if needed).
    (c) Transfusion should be done over a period of at least an hour and via blood administration tubing and, if possible, should be extended over the entire duration of the treatment to prevent acute hypertension.
    (d) Only RN should transfuse the blood, and the technician may assist RN about connecting the blood administration line to the saline port of the dialysis tubing and by monitoring vital signs.
    (e) RN should transfuse blood to children in the PICU, including blood verification, control of transfusion rate, and assessment of the patient's response.
    (f) UF goal should include volume of the blood to be transfused.
    (g) Monitor for any transfusion reaction.
    (h) Posttransfusion CBC should be done at the time of the next dialysis treatment to assess response to transfusion.
15. *Patient monitoring/management of hypotension*
    (a) Vital sign parameters are very different in children compared to adults and vary with the age and size of the child.
    (b) Vital signs must be recorded at least every 30 min (every 15 min in PICU or children <15 kg), and the nephrologist should be informed of any significant variations [14].
    (c) Intradialytic hypotension may be prevented by Crit-Line monitoring and/or sodium modeling.
    (d) Before beginning dialysis, orders should be in place for treatment of hypotension unresponsive to adjustment in UF goal per Crit-Line [2]:

- Saline bolus, 5 mL/kg
- 25% albumin 0.25 g/kg, maximum 12.5 g
- Mannitol 0.25 g/kg, maximum 12.5 g

(e) Albumin and mannitol are given no more than every 1 h and should not to be given during the last hour of treatment.
(f) In PICU, vasopressor support may be considered to correct dialysis-associated hypotension.
(g) Dialysate cooling may be considered to increase vascular tone and support BP [14].

16. *Patient monitoring*
    (a) In PICU treatments, the technician performing dialysis must be within visual and auditory range of the patient/dialysis machine.
    (b) If the technician wants to leave the area, even for a few minutes, another staff member must supervise the treatment.
    (c) Patient should be taken off dialysis if another staff member is not available and set up again when the staff member returns.
    (d) To avoid these circumstances, any supplies that might even rarely needed should be taken to the PICU.
17. *Completion of dialysis treatment*
    (a) In children without a blood prime, blood in the system should be returned. Decrease the blood flow rate by 50% when returning the blood to prevent acute hypertension in children <20 kg.
    (b) Discard the entire setup with the blood in it to avoid acute increase in blood volume in whom blood prime was used.
    (c) The nephrologist should be notified of any blood loss.

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