Hemodiafiltration (HDF)

The Physics, the Practice, and the Patient Impact

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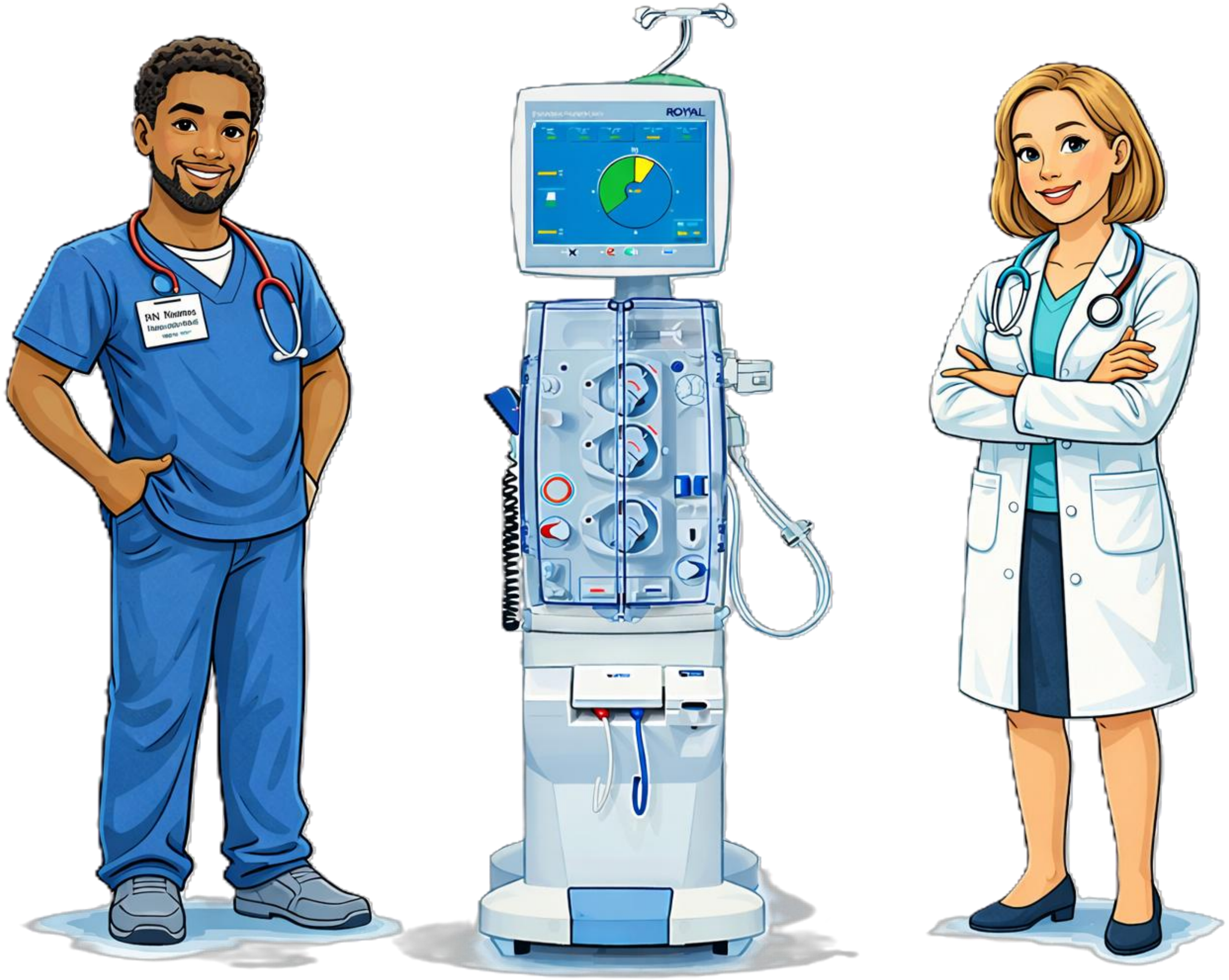
Objectives

Describe	Describe the physiologic principles of hemodiafiltration
Explain	Explain how fluid balance is achieved during hemodiafiltration
Identify	Identify the factors that limit effective hemodiafiltration
Apply	Apply hemodiafiltration concepts to clinical scenarios



HOW HDF WORKS

- Convection
- Fluid
- Math

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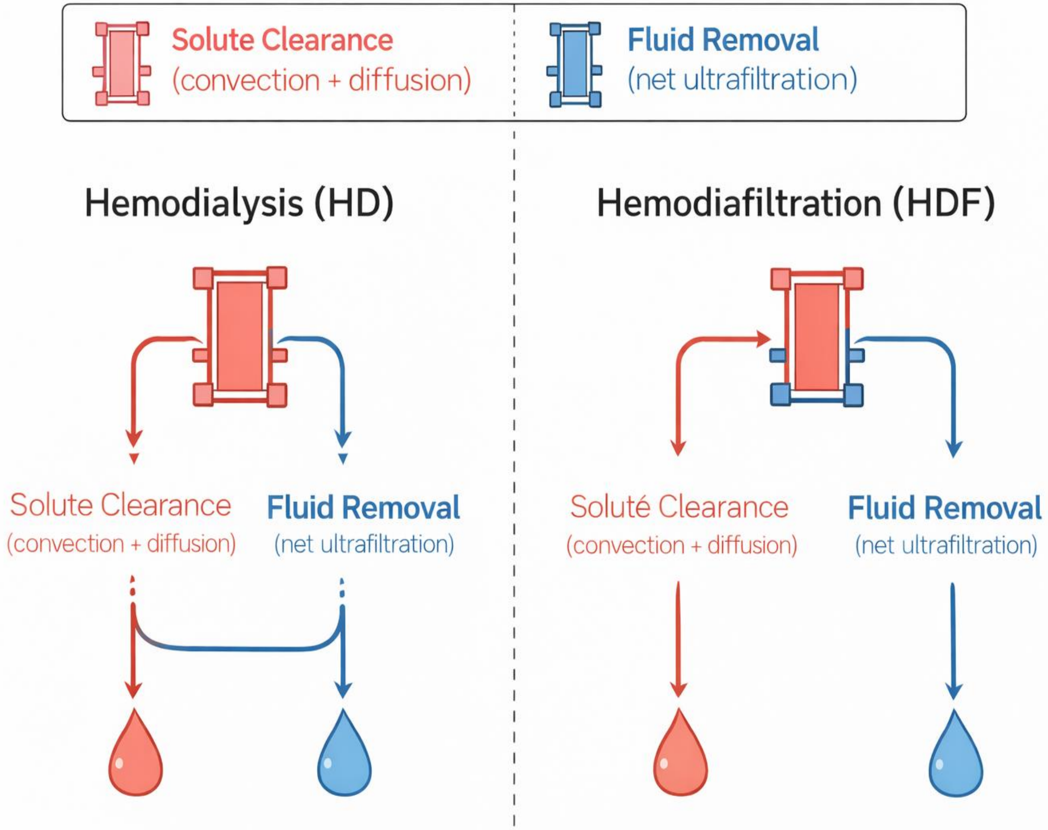
What Makes HDF Fundamentally Different from HD?

Hemodiafiltration intentionally separates two goals:

1. **Solute clearance** (via convection + diffusion)
2. **Patient fluid removal** (net ultrafiltration)

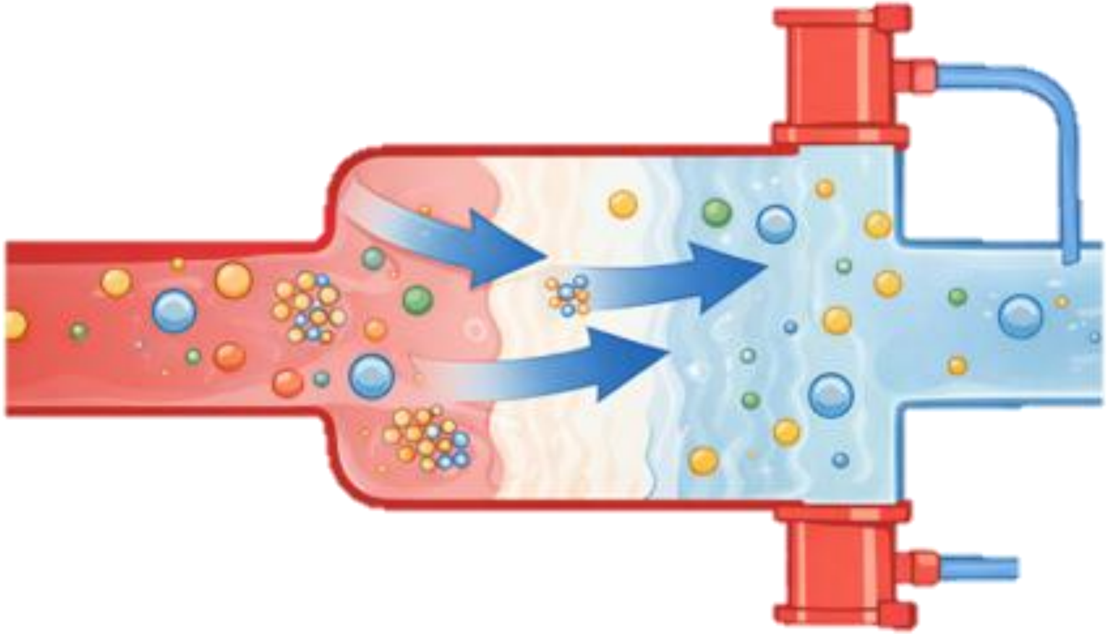
These are linked in HD — but **decoupled** in HDF.



Convection Is Intentional Plasma Water Removal

Convection = bulk plasma water movement across the membrane

- Plasma water is forced across the dialyzer
- Solutes move with it via **solvent drag**
    - Especially Middle and Large Molecules
- Clearance depends on **volume**, not gradients

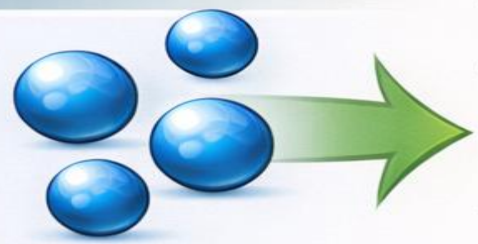


Bigger molecules require convection to move

Uremic Toxins and Their Health Effects

Small Molecules (<500 Da)

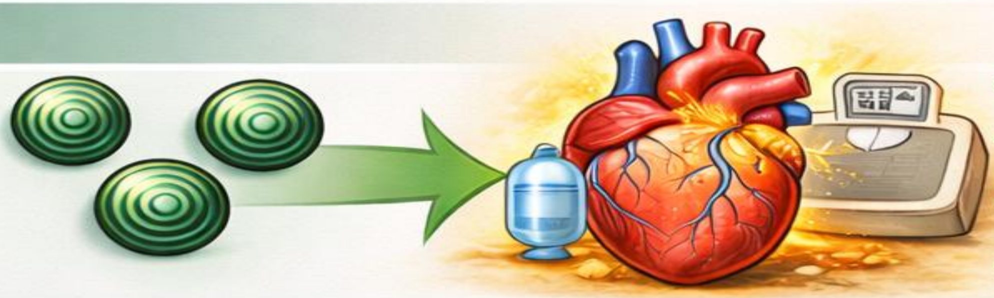
- Urea
- Creatinine
- β-Lipoprotein
- Uric acid



- ✓ Uremic toxicity
- ✓ Fatigue
- ✓ Nausea
- ✓ Neurologic issues

Middle Molecules (500–25 kDa)

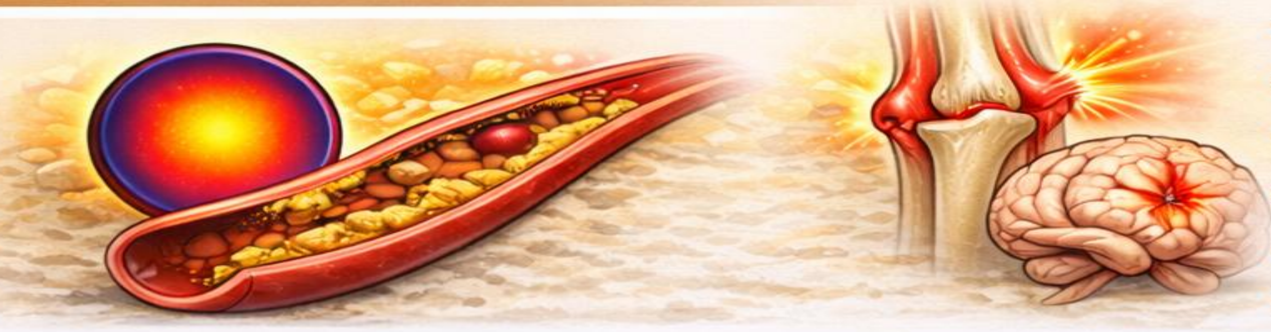
- β-2-Microglobulin
- Leptin
- κ-FLC



- ✓ Amyloidosis
- ✓ CV disease
- ✓ Malnutrition
- ✓ Inflammation
- ✓ Toxicity

Large Molecules (25–45 kDa)

- Interleukin-6
- TNF-alpha
- Pentraxin-3
- YKL-40
- FGF-23



- ✓ Atherosclerosis
- ✓ CV disease
- ✓ Inflammation
- ✓ Sepsis
- ✓ Secondary immunodeficiency
- ✓ Stroke
- ✓ Endothelial inflammation

The Immediate Problem Convection Creates

Removing large volumes of plasma water is not physiologically tolerated

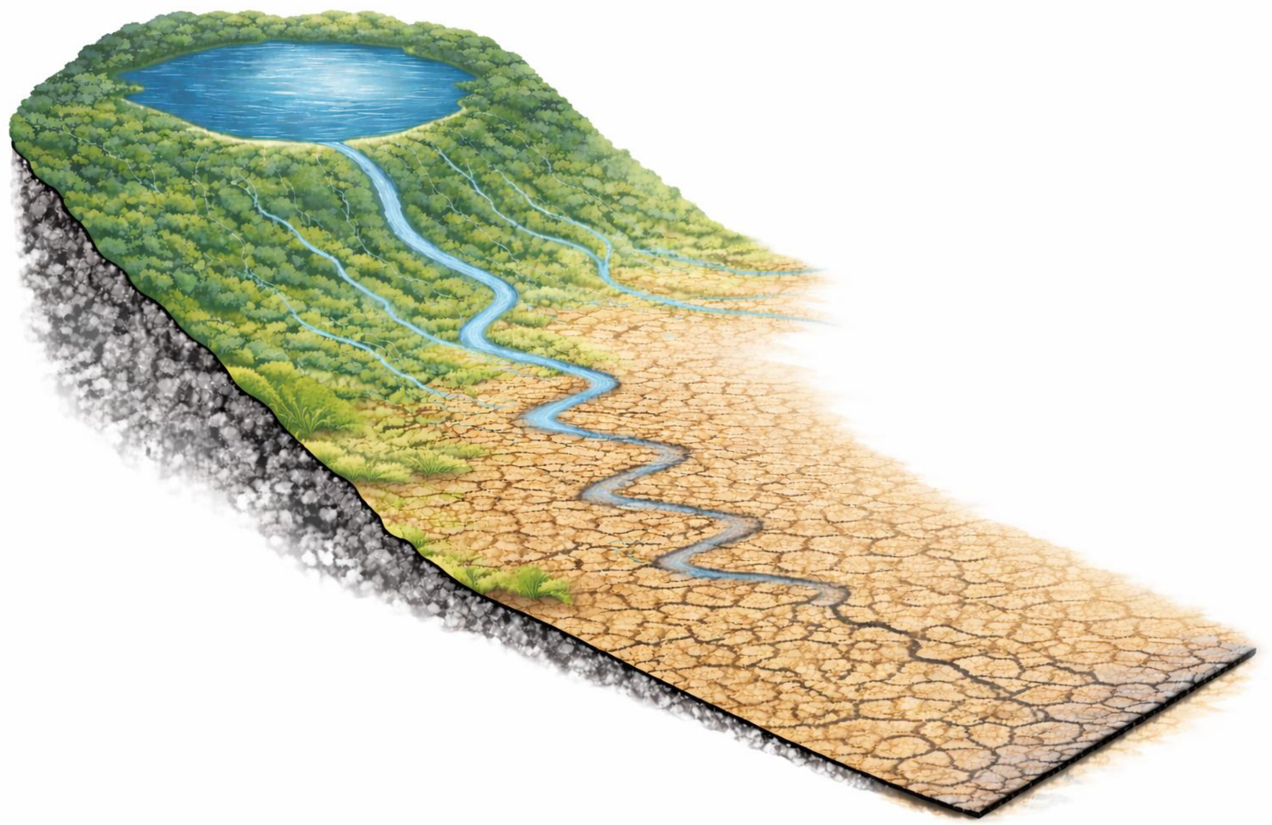
Without replacement:

•Intravascular volume collapse

•Severe hypotension

•Treatment failure

Replacement of fluid is mandatory



Substitution Fluid: What It Is (and Is Not)

Substitution fluid is:

•Online-generated

•Ultrafiltration-processed

•Infusion-grade sterile fluid

Substitution fluid is NOT:

•Standard Dialysate

•Saline

•A bolus

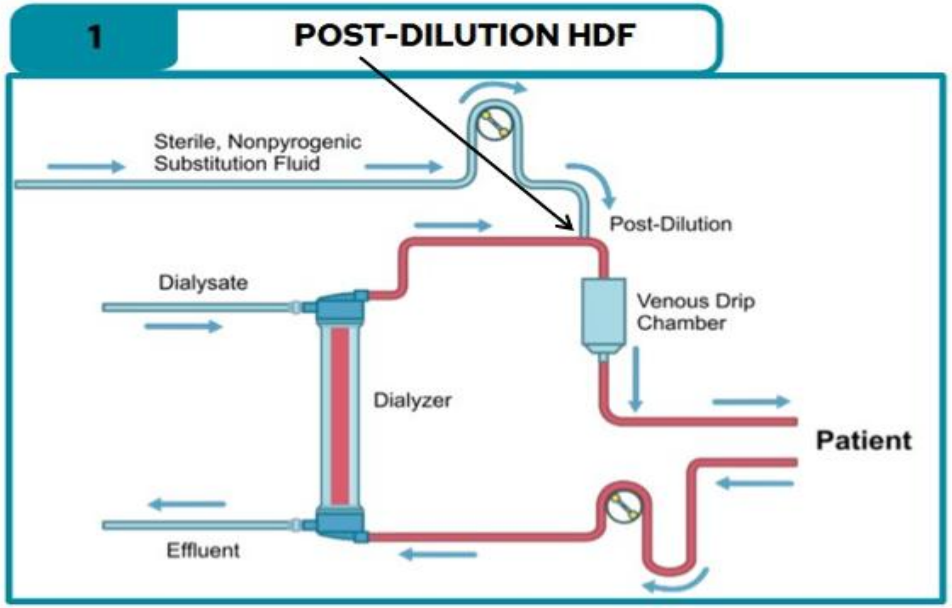
Where Substitution Fluid Is Given Matters

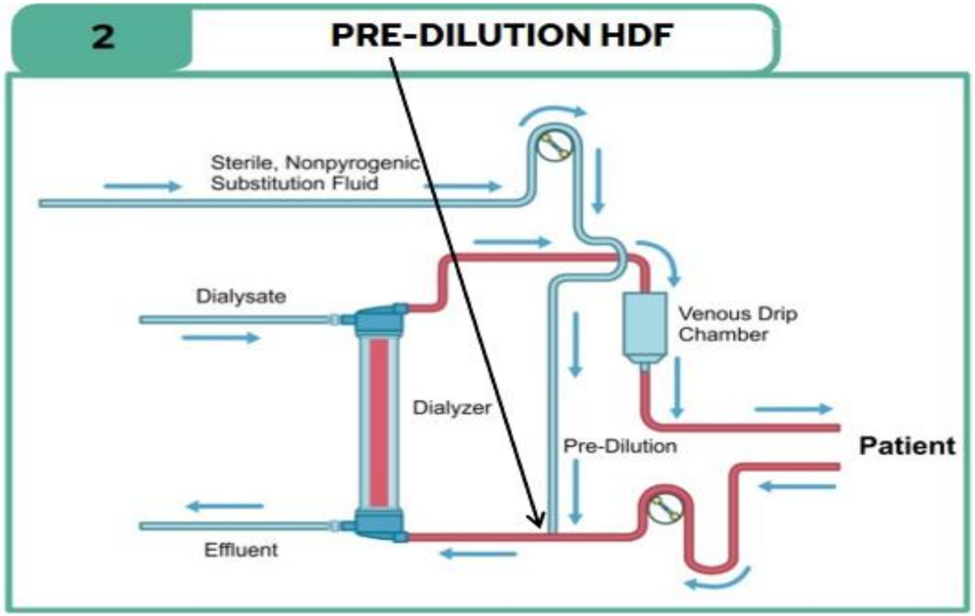
Post-dilution HDF

- Substitution fluid infused **after** the dialyzer
- Highest clearance efficiency
- Requires adequate blood flow

Pre-dilution HDF

- Fluid infused **before** the dialyzer
- Safer at low blood flow
- Lower clearance efficiency





Fluid Balance in HDF

Two independent fluid processes occur simultaneously

Convective Ultrafiltration

•Large volume

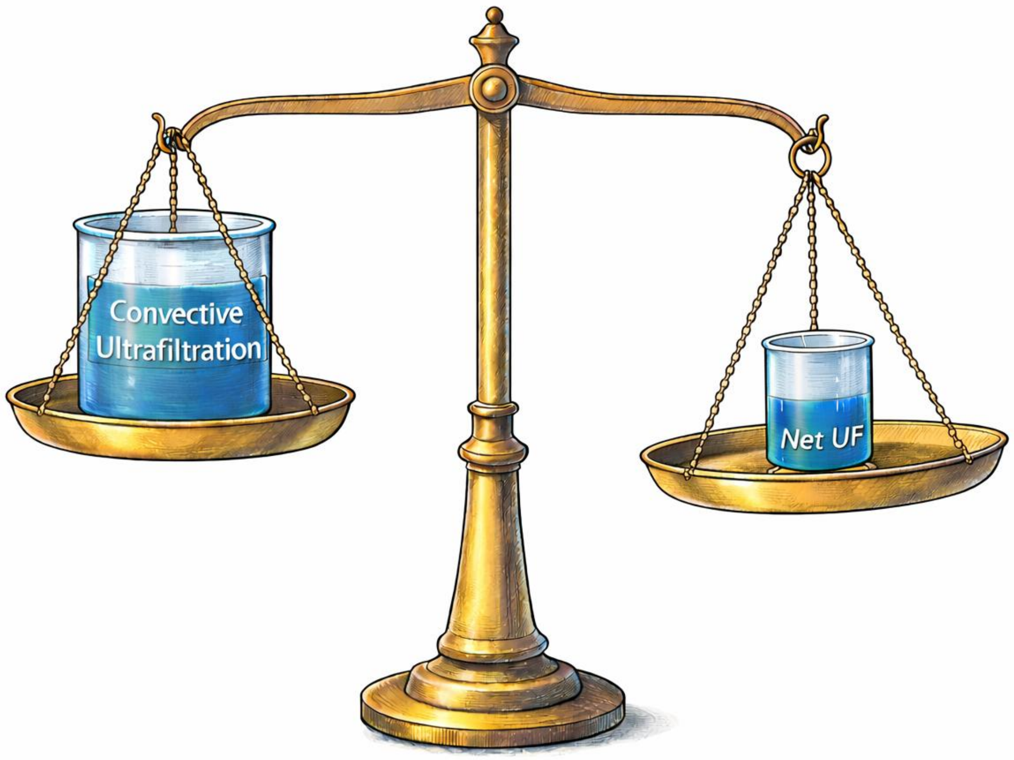
•Purpose: solute clearance

•Does NOT represent patient fluid loss

Net Ultrafiltration

•Prescribed UF goal

•Determines weight loss



The machine balances these in real time.

HDF Fluid Math

$$\frac{d\sigma}{d\Omega} = |f(\theta,\phi)|^2$$
$$a^\dagger|n\rangle = \sqrt{n+1}\,|n+1\rangle$$
$$J_\pm|j,m\rangle = \sqrt{j(j+1)-m(m\pm1)}\,|j,m\pm1\rangle$$
$$A(t) = e^{+iHt/\hbar}Ae^{-iHt/\hbar}$$
$$H = p\dot{q} - L$$
$$ct' = \gamma(ct - \beta x)$$
$$E = (\mathbf{p}^2c^2 + m^2c^4)^{1/2}$$
$$\mathbf{E} = -\dot{\mathbf{A}}/c - \nabla\varphi$$

Example prescription:

•Convective UF: **24 L** (must achieve 23 L or more of Convective UF to obtain HDF benefits)
•Substitution fluid: **21 L**
•Net UF: **3 L**

4-hour treatment (240 minutes) = Recommend for all HDF TXs

•Plasma water crossing membrane: ~100 mL/min
•Substitution fluid infused: ~87.5 mL/min
•Net patient fluid loss: ~12.5 mL/min

Parameter	Potential Prescription
Blood flow rate	350-500 mL/min
Ultrafiltration rate	20-30% of BFR
Substitution fluid flow rate	Post-dilution HDF: ~100 mL/min Pre-dilution HDF: 200 mL/min Automatic control algorithm
Dialysate flow rate	400-500 mL/min (or Qd:Qb of 1.2)

Why HDF Is Often Better Tolerated

- Preserved plasma volume
  - Less “empty tank” sensation and fewer rapid BP drops
- Improved vascular refill
  - With better intravascular stability, the body can more effectively shift fluid from the interstitial space back into the bloodstream
- Reduced intradialytic hypotension
  - Due to less abrupt plasma volume contraction, even during meaningful net UF
- Fewer saline interventions
  - High chloride levels introduced by NS boluses cause metabolic acidosis, which can paradoxically worsen life-threatening hyperkalemia and lead to severe fluid overload

“Same Net UF — Different Plasma Volume Behavior”

- HD: plasma volume drops steeply
- HDF: plasma volume drops more gradually

FILTRATION FRACTION, BFR, & TMP

- Will Explore why HDF sometimes “fails”
- Why TMP rises
- Why access and BFR (Qb) are non-negotiable

Why Blood Flow (Qb) Is the Limiting Factor

Convection is limited by how much plasma water can be delivered

- Plasma water is the vehicle for convection
- Plasma water delivery depends on blood flow
- Blood flow sets the upper ceiling for safe convection

You cannot filter what you cannot deliver, HDF is limited by blood flow physiology.

Plasma Water Flow: The Missing Variable

Plasma water flow ≈ BFR × (1 − hematocrit)

Example:

- BFR = 400 mL/min
- Hct = 33% (Hgb 11)
- Plasma water flow ≈ **268 mL/min**

Example:

- BFR = 275 mL/min
- Hct = 33% (Hgb 11)
- Plasma water flow ≈ **184 mL/min**

Example:

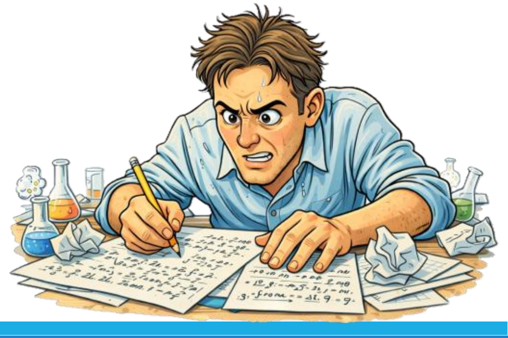
- BFR = 400 mL/min
- Hct = 27% (Hgb 9)
- Plasma water flow ≈ **292 mL/min**

Example:

- BFR = 275 mL/min
- Hct = (Hgb 9)
- Plasma water flow ≈ **274 mL/min**

Hgb → Hct (approx.)

7 → 21%
8 → 24%
9 → 27%
10 → 30%
11 → 33%
12 → 36%
13 → 39%
14 → 42%



Plasma Water Flow of 250 > is the goal to insure HDF Tx

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Filtration Fraction (FF): The Governor

$$\text{Filtration Fraction} = \frac{\textit{Convective UF Rate}}{\textit{Plasma Water Flow}}$$

- FF represents the proportion of plasma water being filtered
- Safe FF ≈ ≤ **25%** (post-dilution)
- Filtration fraction is the **single most important safety limiter** in HDF

Convection Goal: 23L

TX Time: 240 Min

BFR: 450

HCT: 33% (11 Hgb)

$$FF = \frac{95.83}{301.5} = 0.3177 \approx 31.8\%$$

- **Preferred / Safer:** FF ≤ 25%
- **Caution zone:** FF 25–30%
- **Risky:** FF > 30%

Hemoconcentration

What Happens When FF Is Too High

High filtration fraction leads to:

- Hemoconcentration inside fibers
- Increased blood viscosity
- Reduced plasma water refill
- Rising resistance across the membrane

- Preferred / Safer: FF ≤ 25%
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Rising TMP reflects increased resistance to filtration

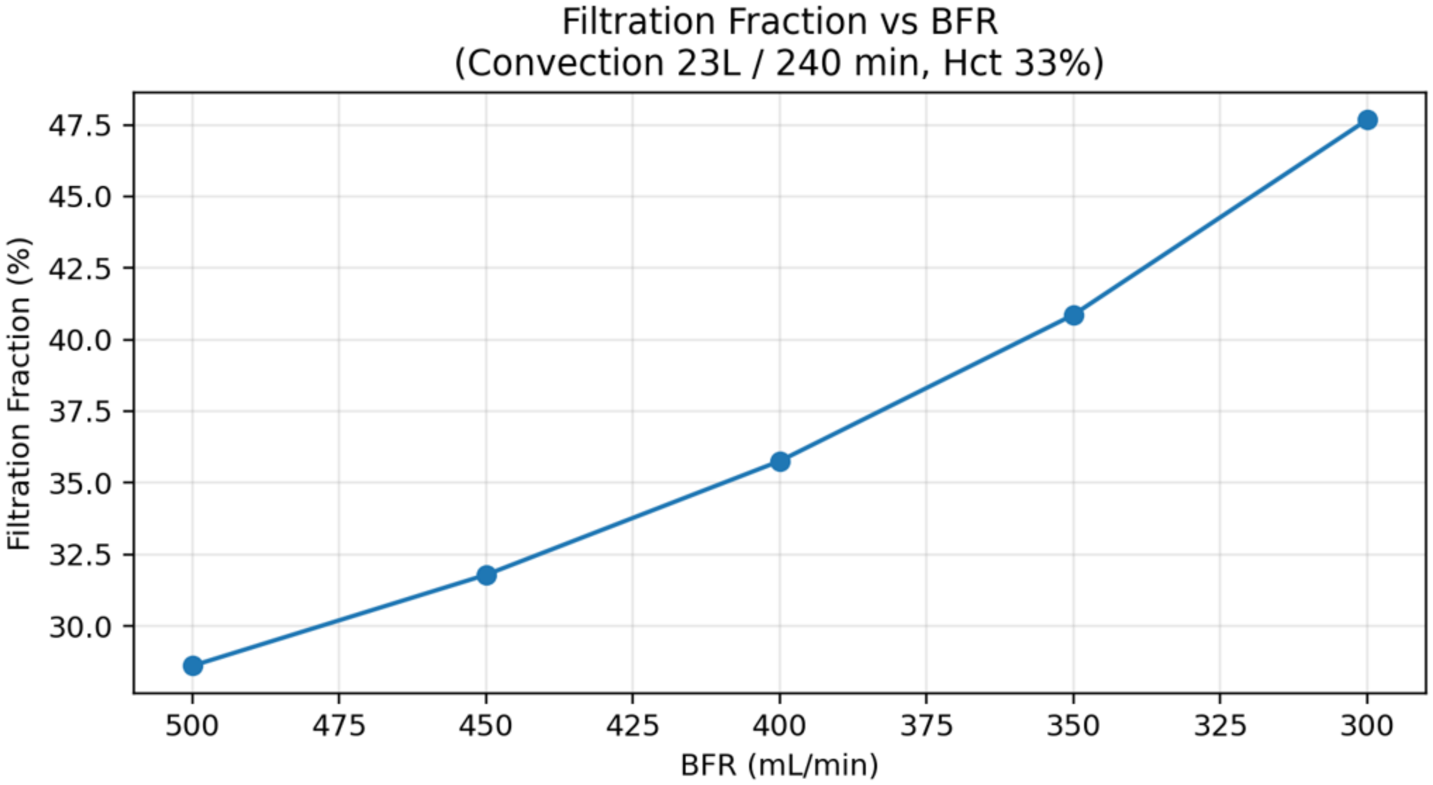
- Hemoconcentration ↑
- Viscosity ↑
- TMP ↑
- Alarms ↑
- Clotting risk ↑

Why High BFR Makes High-Volume HDF Possible

Higher BFR →

- Increased plasma water delivery
- Lower filtration fraction for the same UF rate
- More stable TMP
- Higher achievable convective volumes

Rx Assumptions (Post-dilution HDF):
- Convection Goal: 23 L
- Tx Time: 240 min
- Hct: 33% (Hgb ~11)
- **Access ?**



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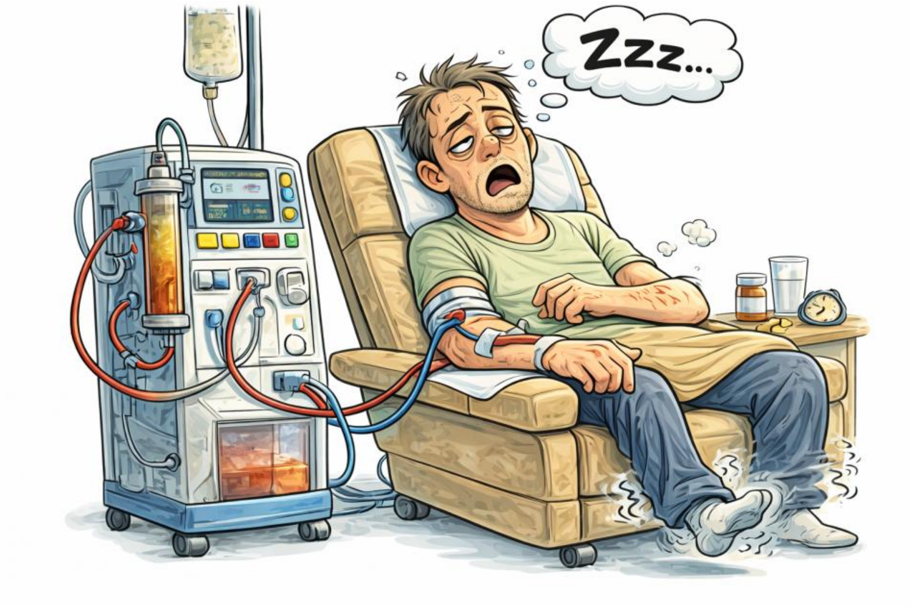
Applying HDF Physics to Real Patients

CASE STUDY 1



Patient Profile
- 54-year-old male
- ESRD: hypertensive nephrosclerosis
- Dialysis: 4 years
- Access: AV fistula
- Qb: 425 mL/min
- Treatment time: 4 hours
- Gains: 3-4L
- Completes all treatments

Symptoms
- Severe fatigue
- Generalized pruritus
- Sleep disturbance
- Restless leg

Recent Labs
- spKt/V: 1.5
- Phosphorus: 4.8 mg/dL
- Albumin: 3.9 g/dL
- K+: 4.9 g/dL

What most likely explains this patient's symptoms?

A. Inadequate dialysis dose

B. Volume overload

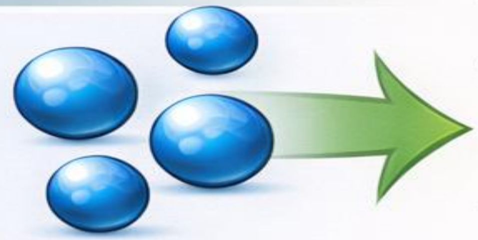
C. Middle-molecule accumulation

D. Nonadherence

Uremic Toxins and Their Health Effects

Small Molecules (<500 Da)

- Urea
- Creatinine
- β-Lipoprotein
- Uric acid



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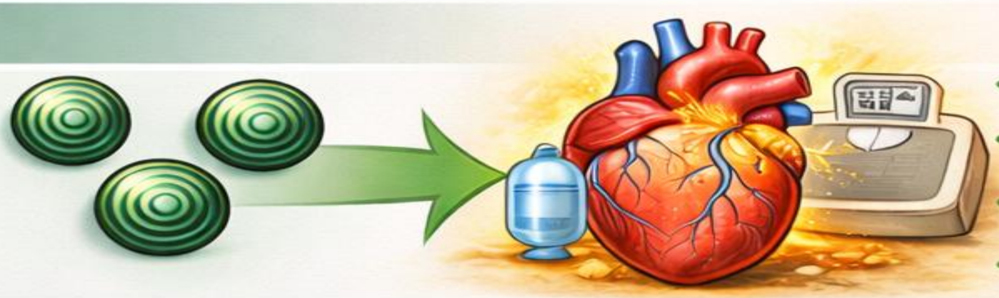

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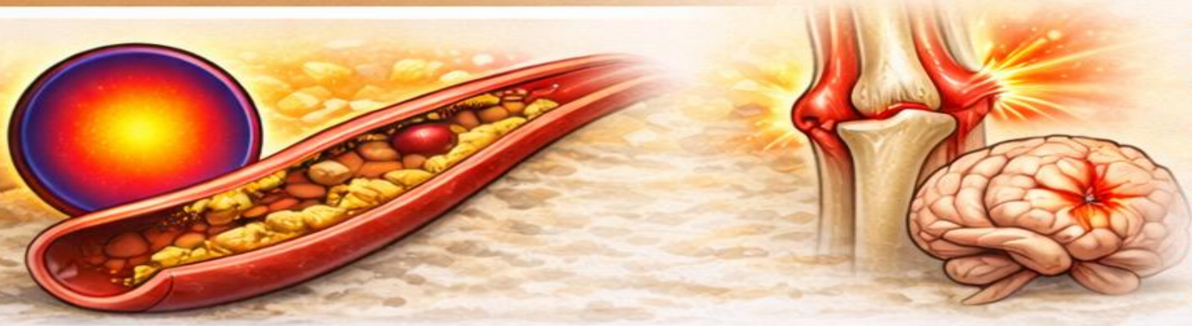

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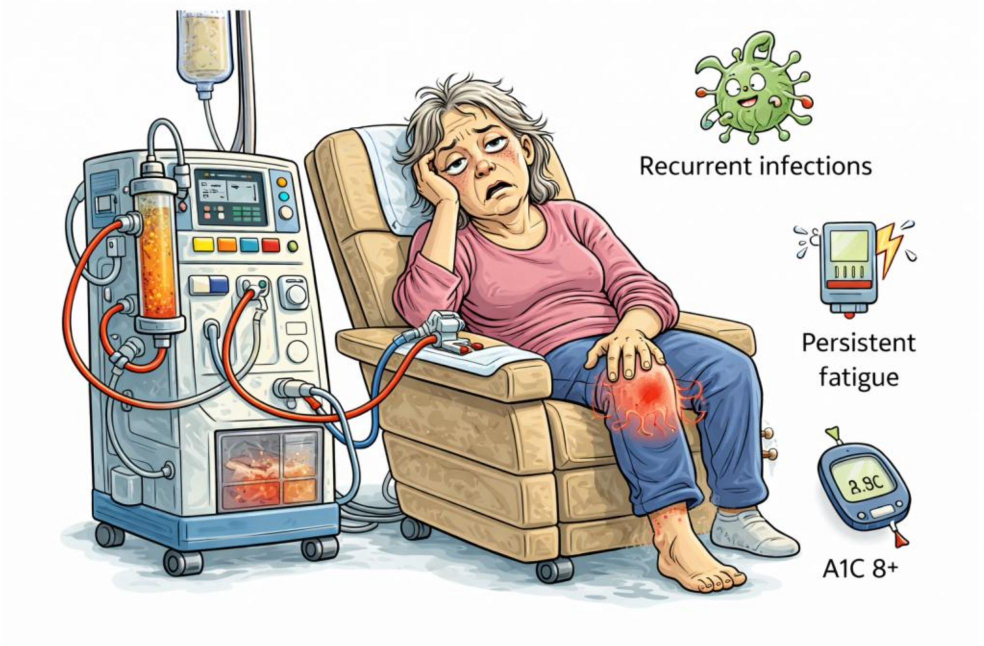
CASE STUDY 2



Patient Profile

- 62-year-old female
- ESRD: diabetic nephropathy
- Dialysis: 6 years
- Access: CVC
- Qb: 350 mL/min
- Treatment time: 4 hours

Clinical History

- Recurrent infections
- Chronic joint pain
- Persistent fatigue
- A1C 8+

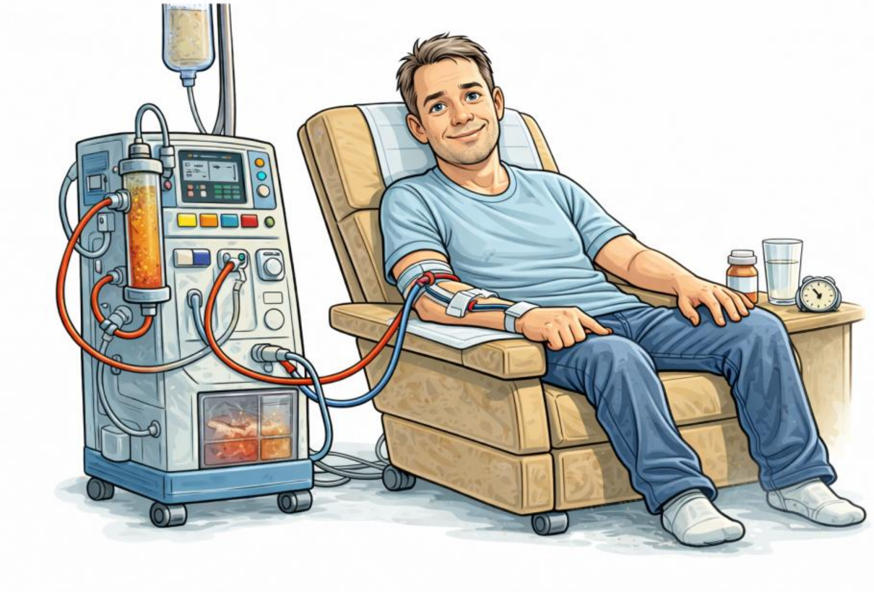
Recent Labs

- spKt/V: 1.4
- Phos: 6.0
- K+: 5.5
- Ferritin: 988
- TSAT: 19
- Albumin: 3.6 g/dL

Which category of toxins is least effectively cleared by conventional HD?

A. Small solutes
B. Electrolytes
C. Cytokines
D. Sodium

CASE STUDY 3



Patient Profile

- 55-year-old male
- ESRD: glomerulonephritis
- Dialysis: 9 years
- Access: AV graft
- Qb: 400 mL/min
- Treatment time: 4 hours

Medical History

- Left ventricular hypertrophy
- Coronary artery disease
- ESA hyporesponsiveness
- Stable pre and post BP

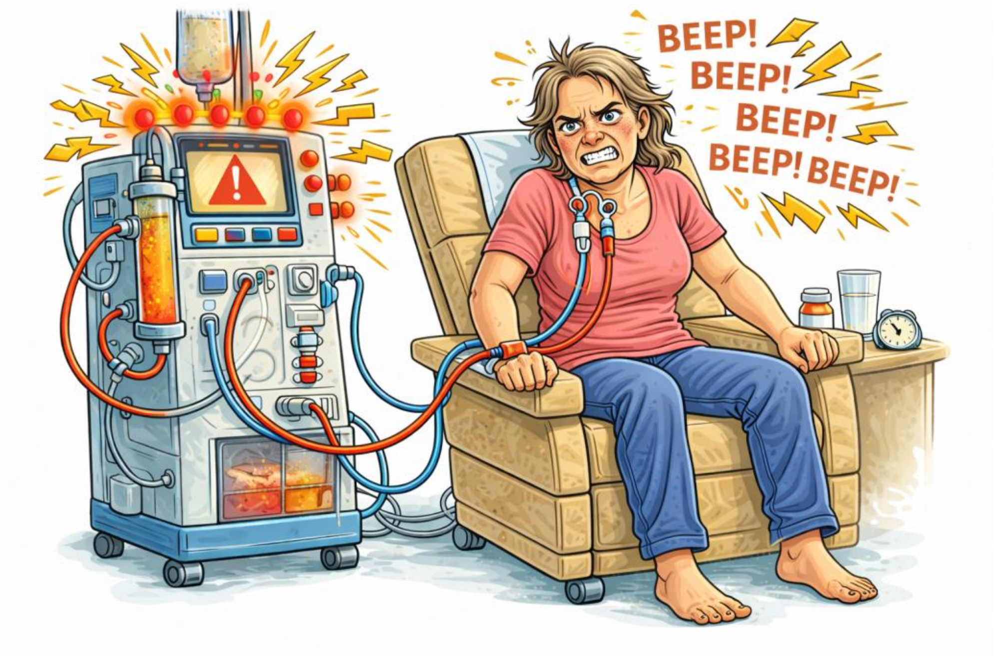
Recent Labs

- spKt/V: 1.6
- Phos: 5.0
- NA: 146
- K+: 4.6
- Albumin: 3.8 g/dL

Which potential HDF benefit is most relevant for this patient?

A. Higher Kt/V
B. Shorter treatment times
C. Reduced inflammatory burden
D. Lower dialysate flow

CASE STUDY 4



Patient Profile

- 68-year-old female
- ESRD: ischemic nephropathy
- Access: tunneled CVC
- Qb: 275 mL/min
- Treatment time: 4 hours

Clinical Issues

- Frequent TMP alarms
- Rising venous pressures
- Unable to achieve convective target
- Clotting episodes despite anticoagulation

What is the primary limitation to effective post-dilution HDF in this patient?

A. Dialyzer surface area
B. Dialysate flow
C. Low blood flow
D. Treatment duration

Mortality Outcomes with High-Volume HDF

What the Evidence Suggests

- Mortality benefit with HDF is **not universal**
- Benefit is **dose- and technique-dependent**
- Observed when:
  - Post-dilution HDF
  - Convective volumes **≥ ~23 L/session**
  - Adequate blood flow and access

When HDF is delivered at high convective doses, a mortality signal emerges. When it is not, that signal disappears.

CONVINCE Trial (Blankestijn et al., 2023, NEJM)

- 23% relative reduction in all-cause mortality with high-dose HDF vs high-flux HD
- Benefit achieved using high-volume post-dilution HDF (target ≥23 L/session)
- Confirms mortality signal is dose/technique dependent (not the "HDF" label alone)

Maduell et al., 2013 (JASN)

- 30% relative reduction in all-cause mortality
- 33% reduction in cardiovascular mortality
- Only in high-volume post-dilution HDF

CONTRAST Trial (Grooteman et al., 2012)

- No overall mortality difference
- Post-hoc: highest convection subgroup showed ~20–25% lower mortality risk

What Mortality Data Does Not Say

- HDF ≠ automatic survival benefit
- Low-volume HDF ≠ high-volume HDF
- Technique matters more than modality label
- Outcomes follow **physics and dose**, not branding.

Why This Matters to the Dialysis Team

Hemodiafiltration: Team-Level Impact

Nurses

- Fewer hypotensive episodes
- Less saline rescue
- More complete treatments
- More predictable machine behavior

Social Workers

- Improved patient engagement
- Fewer symptom-driven missed treatments
- Better quality-of-life conversations

Dietitians

- Improved clearance of phosphorus-adjacent toxins
- Fewer symptoms interfering with intake
- Less reliance on binder escalation alone

Administrators

- Fewer interruptions and alarms
- More consistent chair utilization
- Alignment with future dialysis infrastructure

Final Takeaways

- Adequacy ≠ completeness
- Convection expands clearance
- Fluid balance is controlled, not aggressive
- Blood flow determines feasibility
- Outcomes follow dose and technique
- Net win for the entire Interdisciplinary Team

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