Regione Veneto - ULSS 6
Dep. of Nephrology, Dialysis and Renal Transplantation
International Renal Research Institute Vicenza - IRRIV
San Bortolo Hospital - Vicenza - Italy

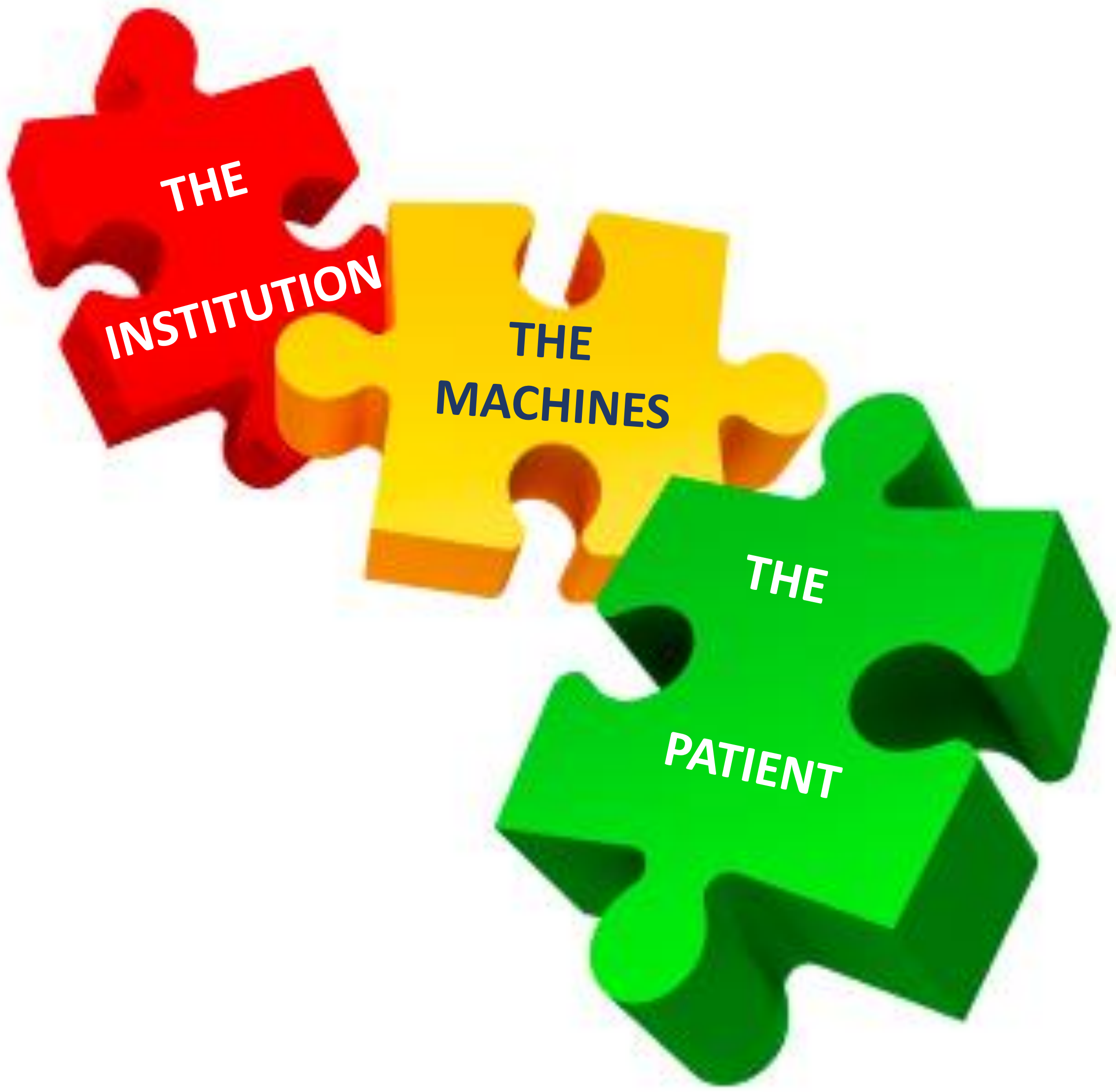
34th Vicenza Course on AKI & CRRT

MODALITIES of Renal Replacement Therapy in AKI

Jorge Cerdá, MD, MS, FACP, FASN
Clinical Professor of Medicine
Albany Medical College
Albany, NY, USA

cerdaj@mail.amc.edu

In AKI, RRT is a multidimensional task



The components

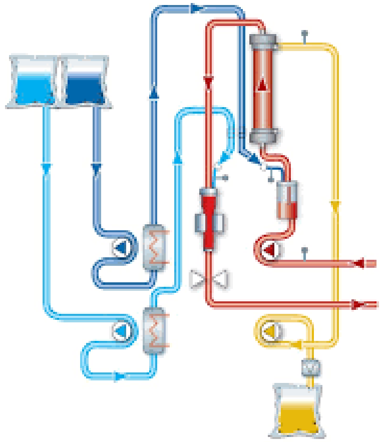
RECOVERY FUNCTION
SURVIVAL
HEMODYNAMIC STABILITY

TIMING
DELIVERED DOSE

OUTCOMES

MODALITY
Diffusion, Convection or both
MEMBRANES/FILTERS
SOLUTIONS
BUFFERS
PRESCRIBED DOSE
MEASURED DOSE

MACHINES



MOF
AKI
COMORBIDITIES
RENAL OR NON RENAL
INDICATIONS
FLUID STATUS
HEMODYNAMICS
ACID BASE
DYSELECTROLYTEMIAS
CATABOLISM
DRUGS
NUTRITION

PATIENT

NURSING
TECHS
EDUCATION
QUALITY MEASURES
INSTITUTIONAL SUPPORT
COST
TEAM WORK

ENVIRONMENT

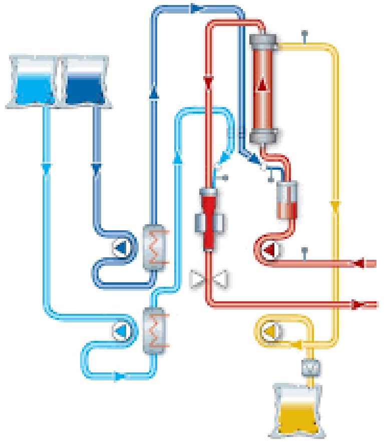
A multi-component system

RECOVERY FUNCTION
SURVIVAL
HEMODYNAMIC STABILITY

TIMING
DELIVERED DOSE

MODALITY

Diffusion, Convection or both
MEMBRANES/FILTERS
SOLUTIONS
BUFFERS
PRESCRIBED DOSE
MEASURED DOSE



MOF
AKI
COMORBIDITIES
RENAL OR NON RENAL
INDICATIONS
FLUID STATUS
HEMODYNAMICS
ACID BASE
DYSELECTROLYTEMIAS
CATABOLISM
DRUGS
NUTRITION

NURSING
TECHS
EDUCATION
QUALITY MEASURES
INSTITUTIONAL SUPPORT
COST
TEAM WORK

Objectives

- Establish the basic components of the CRRT prescription
- Know your CRRT Machines
- Know your Solutions
- What Modality should you use?
- What Dose should you use?
- Writing Prescriptions
- Troubleshooting

What are the characteristics of the “ideal” AKI treatment modality in the ICU?

- Preserves homeostasis
- Does not increase co-morbidity
- Does not worsen patient’s underlying condition
- Is inexpensive
- Is simple to manage
- Is not burdensome for the ICU staff

N. Lameire et al, NDT 1999;14:2570-2573

Considerations in Renal Replacement Therapy for AKI

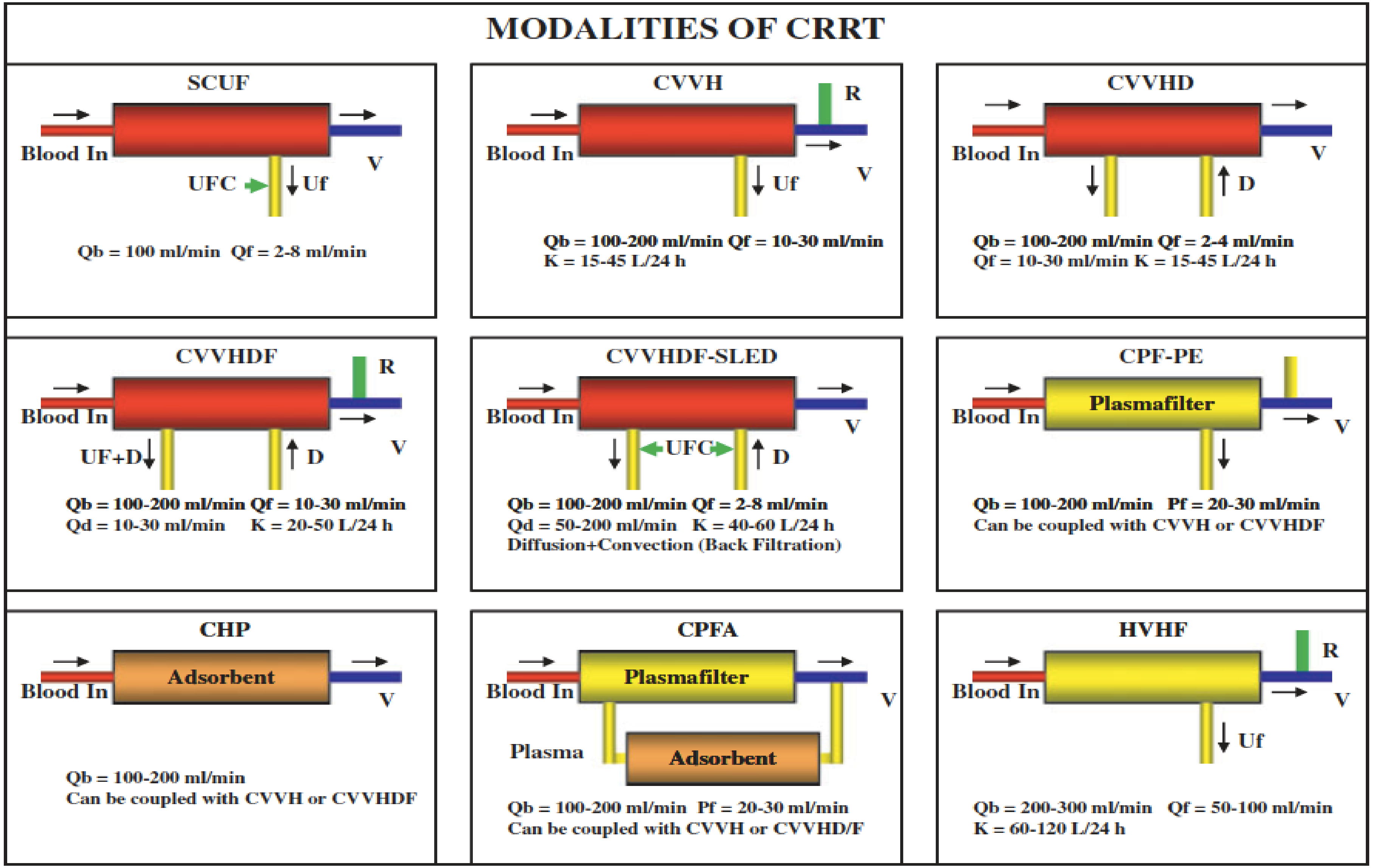
Consideration	Components	Varieties
Dialysis Modality		
	Intermittent Hemodialysis	Daily, Every other day, SLED
	Continuous renal replacement therapies	AV, VV
	Peritoneal dialysis	
Dialysis Biocompatibility	Membrane characteristics	
Dialyzer Performance		
	Efficiency	
	Flux	
Dialysis Delivery		
	Timing of initiation	Early, Late
	Intensity of dialysis	Prescription vs. Delivery
	Adequacy of dialysis	Dialysis dose

Cerdá and Ronco Semin Dialysis 2008

How Do We Choose a Specific RRT Modality?

Therapeutic Goal	Hemodynamics	Preferred Modality
Fluid Removal	Stable	Intermittent Isolated UF
	Unstable	Slow Continuous UF
Urea Clearance	Stable	Intermittent Hemodialysis
	Unstable	CRRT
		Convection: CAVH, CVVH
		Diffusion: CAVHD, CVVHD
		Both: CAVHDF, CVVHDF
Severe Hyperkalemia	Stable/Unstable	Intermittent Hemodialysis
Severe Metabolic Acidosis	Stable	Intermittent Hemodialysis
	Unstable	CRRT
Severe Hyperphosphoremia	Stable/Unstable	CRRT
Brain Edema	Unstable	CRRT

Cerdá and Ronco Semin Dialysis 2008



Cerdá and Ronco Semin Dialysis 2008

Components of the RRT prescription

- Treatment Modality: SCUF, CVVHDF, CVVH, CVVHD
- Blood flow rate
- Ultrafiltration rate
- Replacement fluid: Type of fluid, Rate, Type of dilution
- Dialysate fluid: Type of fluid, Rate
- Labs
- Type of anticoagulation: Citrate, Heparin, None

Anticoagulation

- Is Anticoagulation required?
    - *Almost always!*
- Systemic, or regional citrate anticoagulation?

- Why would anyone use anything but Citrate regional anticoagulation?

    - Does not affect patient’s coagulation
    - Safe if protocols are in place
    - Helps manage acid base disorders
    - May have a positive impact on recovery

CRRT Machines

NexStage

B.Braun

Fresenius

Prismaflex

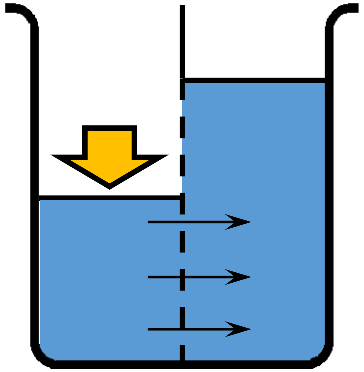
CRRT Modalities

Molecular Transport Mechanisms

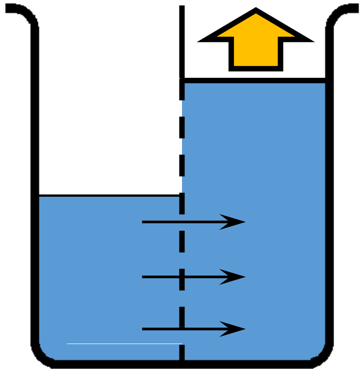
- Ultrafiltration $\longrightarrow$ Fluid Transport
- Diffusion
- Convection
- Adsorption

Solute Transport

Ultrafiltration



positive pressure

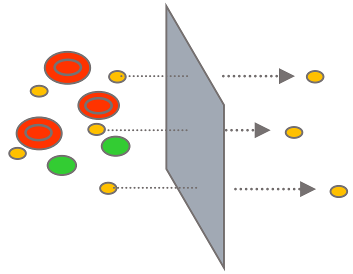


negative pressure

- The movement of fluid through a membrane caused by a pressure gradient.

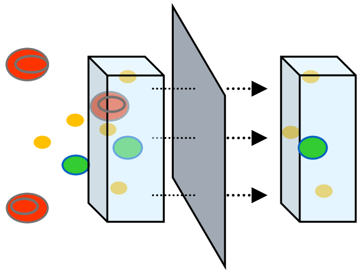
Diffusion vs. Convection

•Diffusion is solute transport across a semi-permeable membrane - molecules move from an area of higher to an area of lower concentration



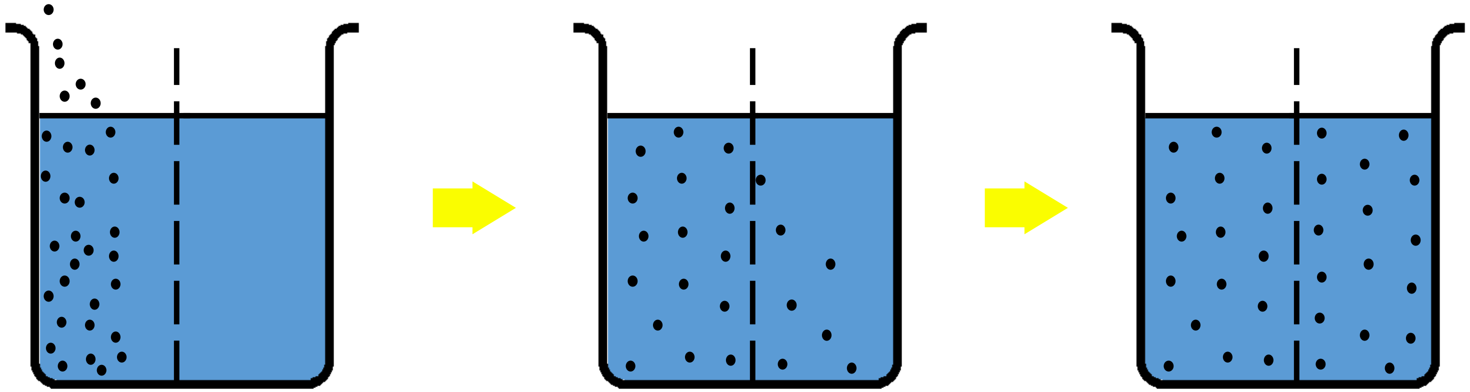
Best for small molecule clearance

•Convection is a process where solutes pass across the semi-permeable membrane along with the solvent ("solvent drag") in response to a positive transmembrane pressure



Effectiveness less dependent on molecular size

Diffusion



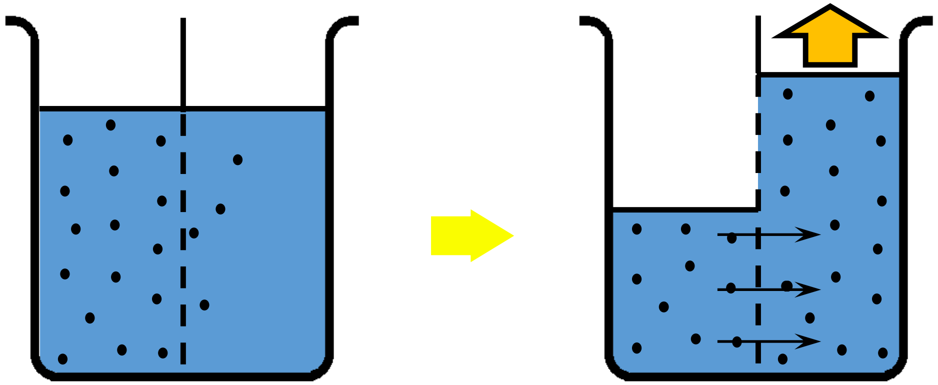
- The movement of solutes from an area of higher concentration to an area of lower solute concentration.

Diffusion

- Random movement of molecules across a semi-permeable membrane
- *Fick's Law of Diffusion* $J_d = - D \cdot \left(\frac{dc}{dx}\right)$
- Where diffusivity coefficient D:
- $$D = \frac{k_B T}{6\pi\mu R}$$

Effective radius of molecule

Convection



- The movement of membrane-permeable solutes with a water-flow, ultrafiltered water.

Membrane Sieving Coefficient

- Ratio of a specific solute concentration in the ultrafiltrate (removed by *convection*) to pre- and post-filter solute concentration:

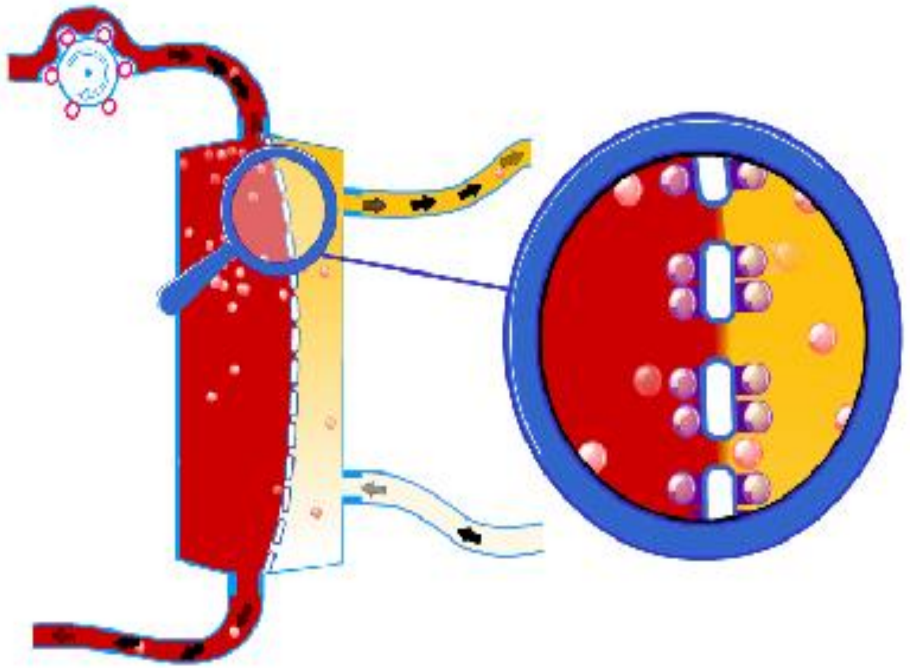
$$SC = 2 \cdot \frac{C_{UF}}{C_{Pi} + C_{Po}}$$

- Convective flow *Jc* of a solute depends on:

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

QUF – magnitude of UF
A – membrane surface area
Cpi – solute concentration plasma water
SC – solute sieving coefficient

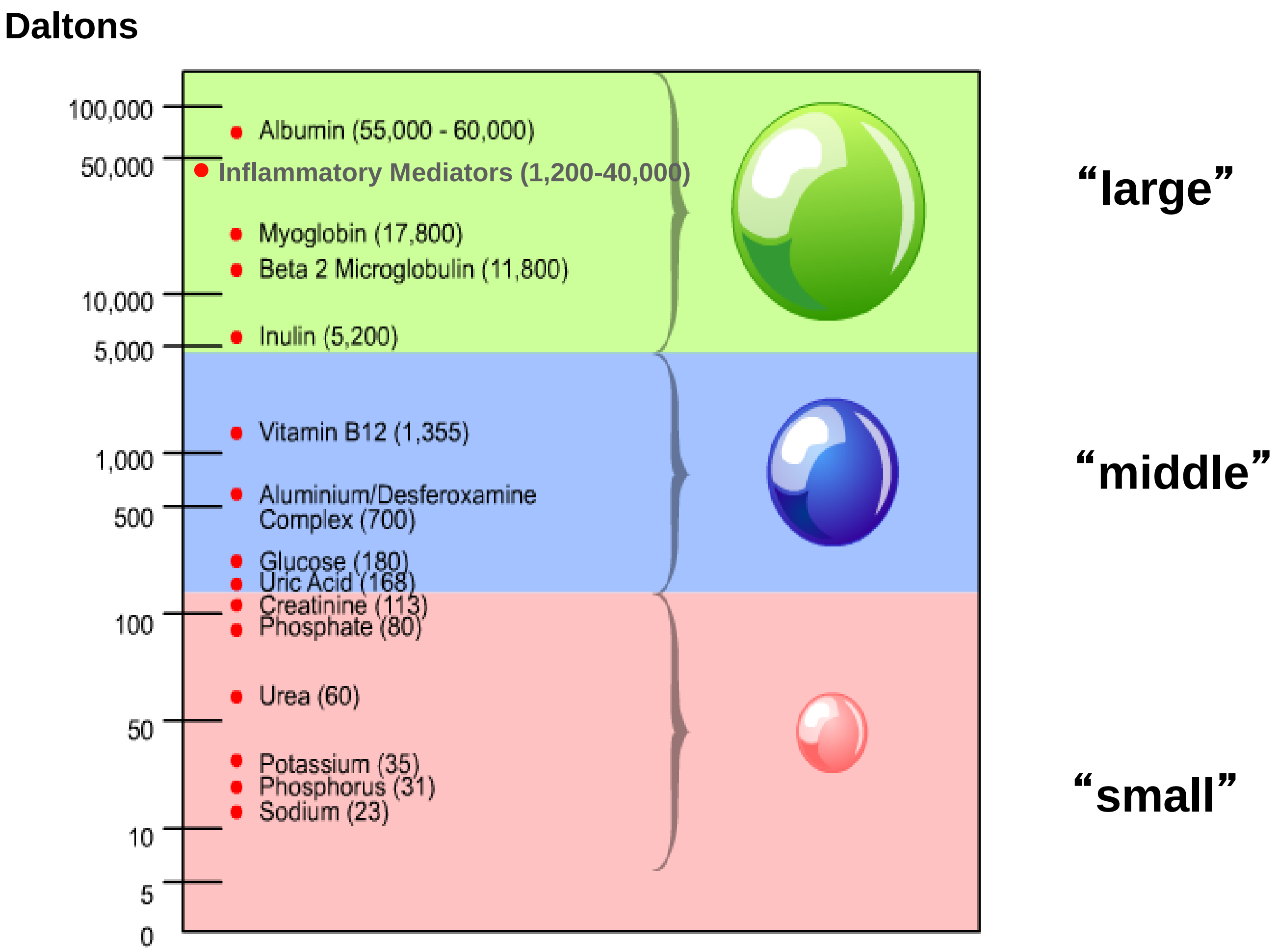
Adsorption



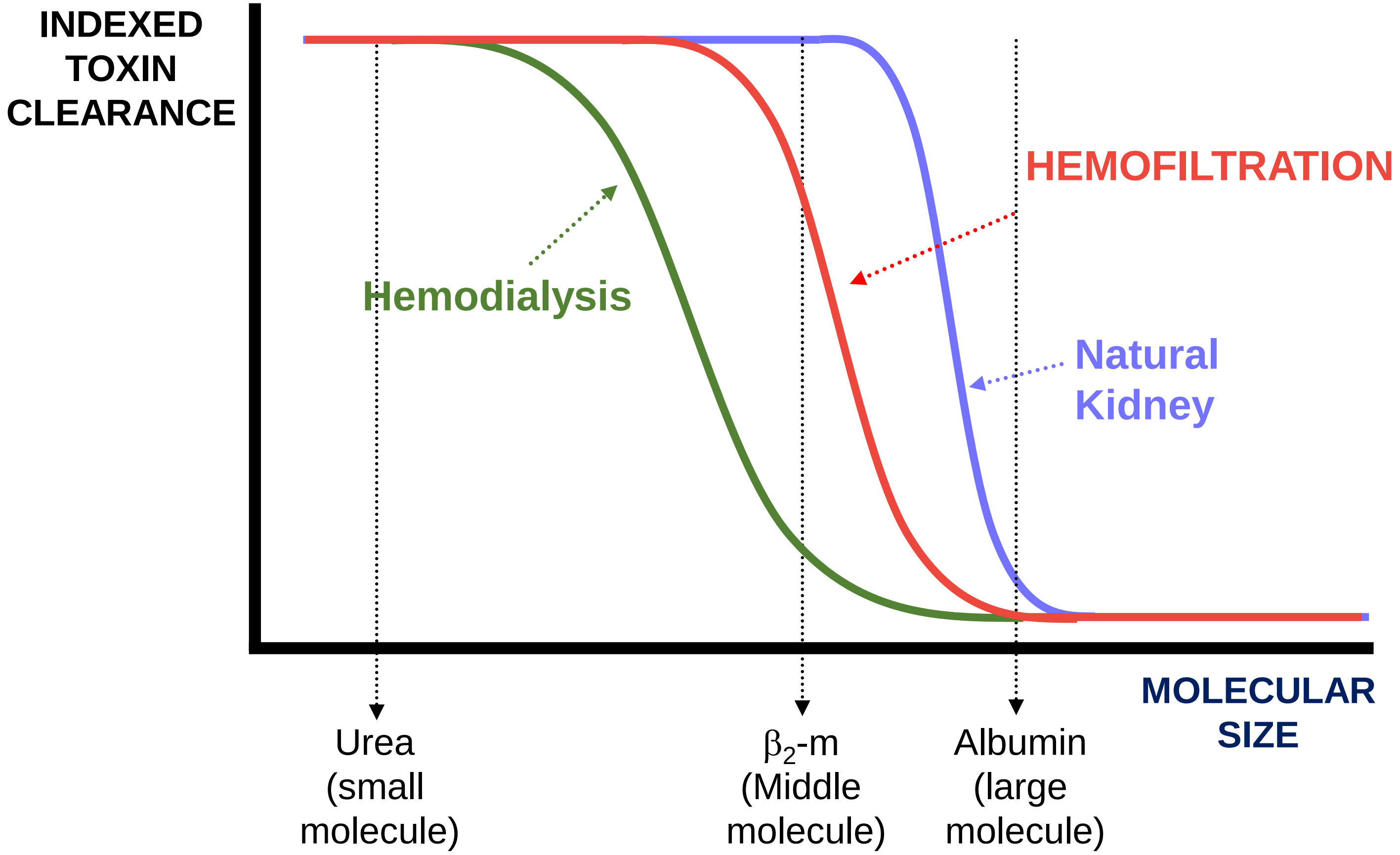
The interaction membrane-molecule is driven by individual molecule and membrane characteristics

- Molecular adherence to the surface or interior of the membrane.

Solute Classes by Molecular Weight

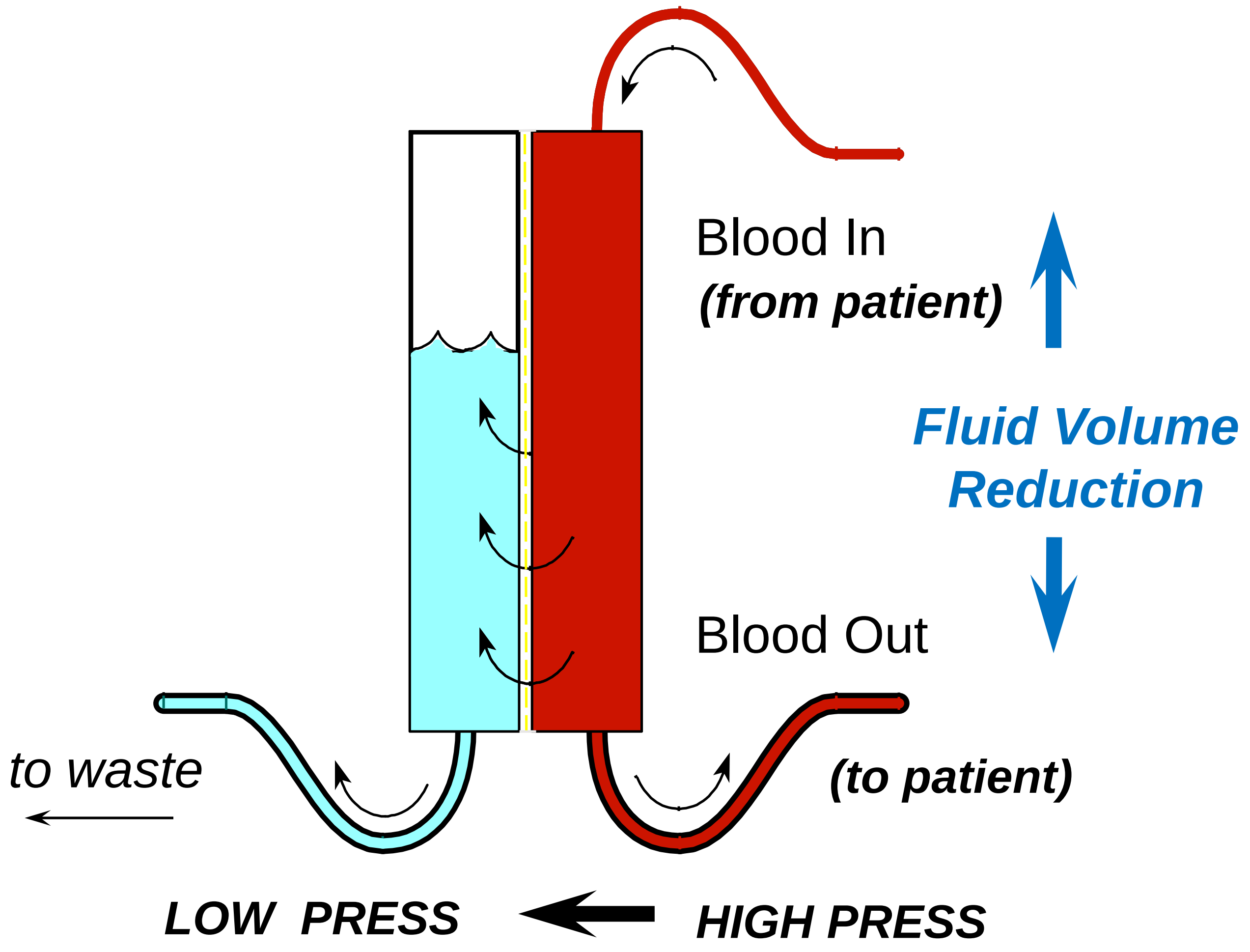


Clearance Profiles by Modality



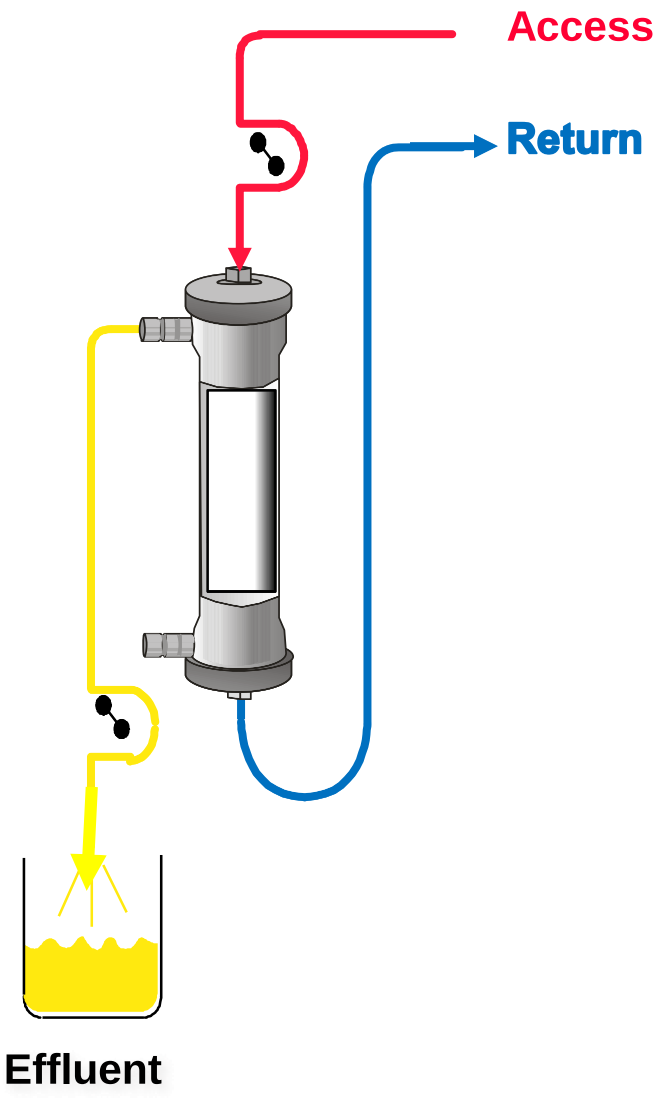
CUTOFF POINT:
The MW of the smallest solute retained by the membrane:
The MW of a solute with a sieving coefficient of 0.1

Ultrafiltration



SCUF: Slow Continuous Ultrafiltration

- Primary therapeutic goal:
  - Safe management of fluid removal
- Fluid removal rate dictated by patient tolerance
- Blood Flow: variable (not critical)
- Dialysate: Not required
- Replacement: Not required



Membrane Performance Characteristics

- Membrane Ultrafiltration Coefficient K_{UF} (ml/h/mmHg/m2)

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

DEFINES MEMBRANES:

LOW FLUX $K_{UF}<10$
HIGH FLUX $K_{UF}>25$

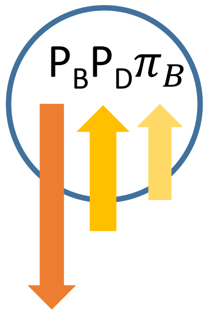
- Filter Ultrafiltration Coefficient (DK_{UF}) (ml/h/mmHg)

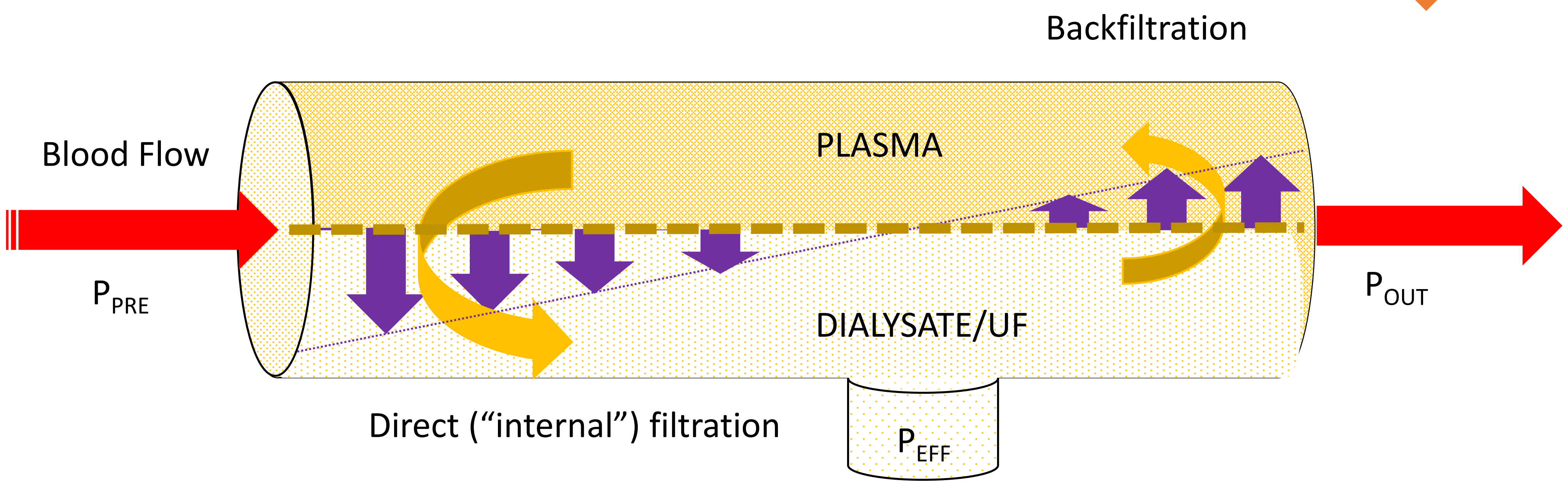
$$DK_{UF} = K_{UF} \cdot A$$

- Ultrafiltration Rate

$$Q_{UF} = DK_{UF} \cdot TMP$$

Transmembrane Pressure (TMP)



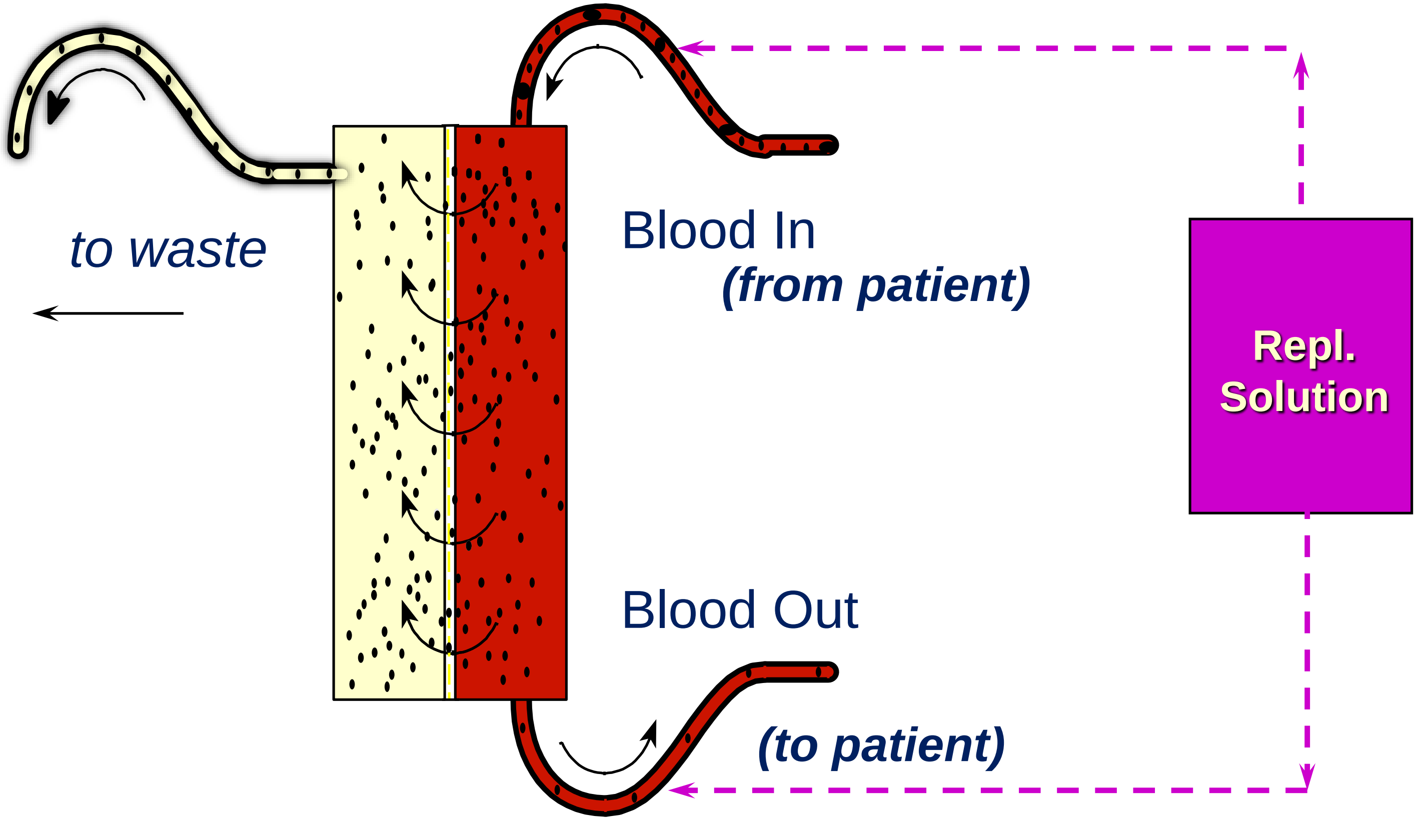


$$TMP(l) = P_B(l) - P_D(l) - \pi_B(l)$$

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

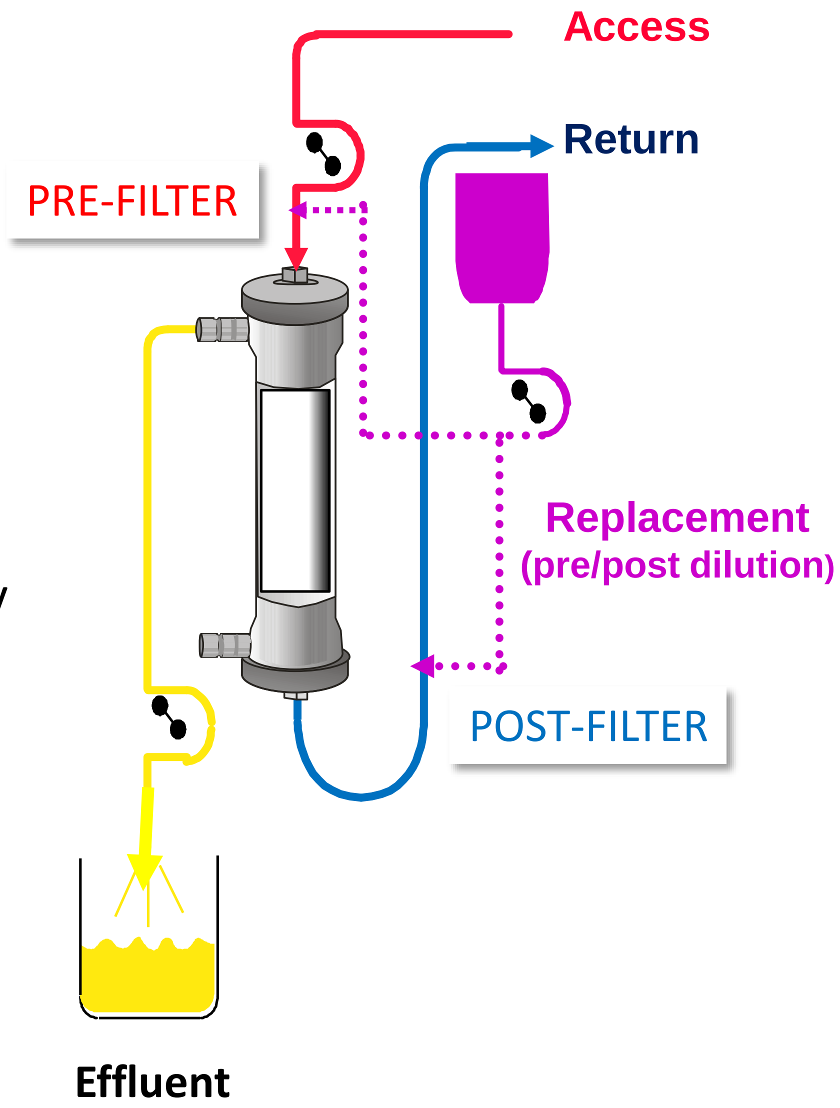
$$TMP^* = \frac{P_{PRE} + P_{OUT}}{2} - P_{EFF}$$

Hemofiltration



CVVH: Continuous Venovenous Hemofiltration

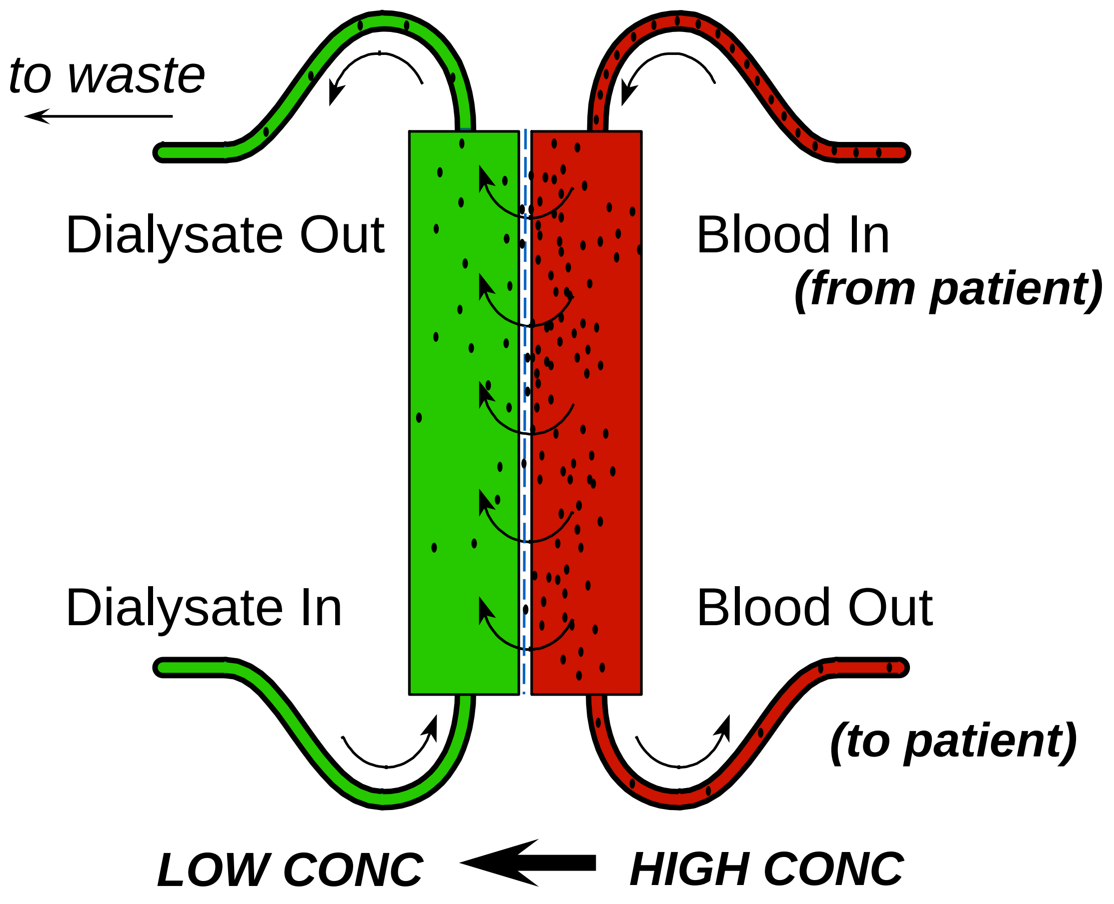
- Primary therapeutic goal:
  - **Convective** solute removal
- Blood Flow: variable
- Replacement (for convection): ~35 - 70 mL/min (~2 – 4 L/hr)
  - Solute clearance determined primarily by replacement fluid rate and dilution mode
- Dialysate: Not required



Hemodialysis

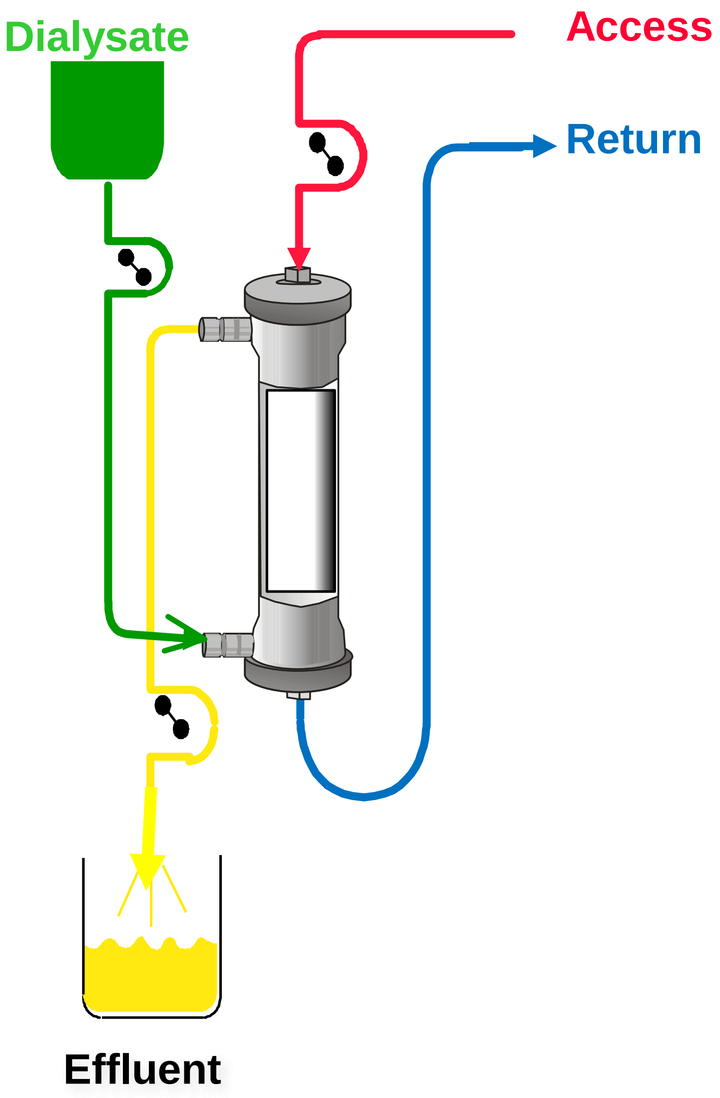
INTERMITTENT HEMODIALYSIS: DIALYSATE FLOW **500-800 ml/min**

CONTINUOUS V-V HEMODIALYSIS: DIALYSATE FLOW **17 TO 33 ml/min**



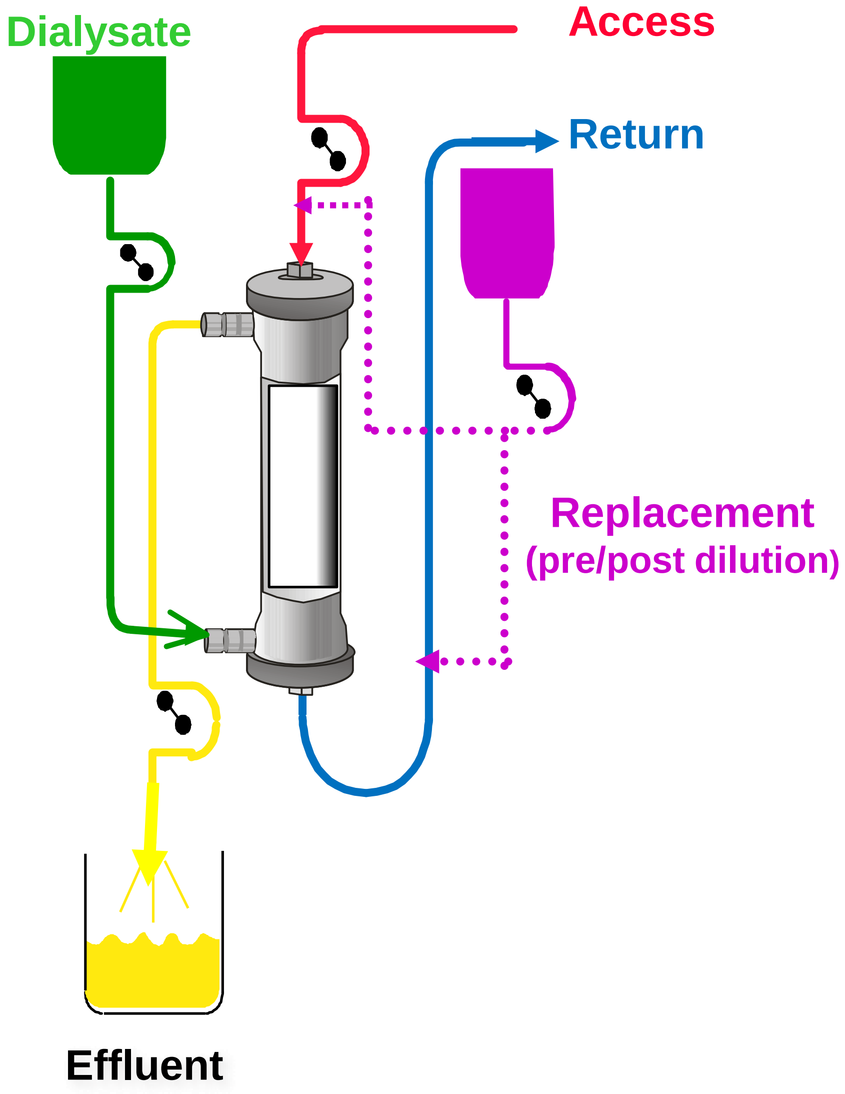
CVVHD: Continuous Venovenous Hemodialysis

- Primary therapeutic goal:
  - Solute removal by **diffusion**
- Blood Flow rate: variable
- Dialysate (for diffusion): ~35-70 ml/min (~2- 4 L/hr)
  - Solute removal determined primarily by dialysate flow rate
- Replacement: Not required



CVVHDF: Continuous Venovenous Hemodiafiltration

- Primary therapeutic goal:
  - Solute removal by **diffusion and convection**
  - Combines CVVH and CVVHD therapies
- Blood Flow: variable
- Dialysate: typically ~15 – 50 mL/min (~1 – 3 L/hr)
- Replacement: typically ~15 – 50 mL/min (~1 – 3 L/hr)
- Total (dialysate + replacement): typically ~2 – 4 L/hr



Blood Flow Rate (Q_b)

- 200 ml/min is the usual blood flow rate
  - When using heparin, a low flow rate promotes coagulation of the system
  - When using citrate, a low flow rate is convenient
  - It allows to keep a low ionized calcium (bound to citrate) within the filter

Ultrafiltration (UFR)

- Rate of fluid removal from the patient (ml/hr)
- UF orders can mean different things in different protocols:

  – Net 24 hour net fluid balance + desired patient fluid removal
    – Patients are too variable to predict 24 hour goals

  – Hourly desired patient fluid management
    – The nurse measures patient I and O every hour, and sets the difference as the fluid to be removed during the next hour PLUS the ordered NET fluid removal rate.

How is UF ordered in different protocols?

- Total input: 5.2 L/day (pressors, TPN, antibiotics, etc)
- Urine output: 200 ml/day
- Desired negative balance in the next 24 hrs: Negative 1 L

- **24 hour protocols**
  - (5.2-0.2+1)/24= 250 ml/hour
  - (1000/24)= ~ 50 ml/hr
- **Hourly protocol: CRRT as a continuous volume regulation device**
  - Input during last hour 216 ml
  - Output during last hour 8 ml
  - Desired hourly loss: -100 ml/hour
  - Calculated necessary NET fluid removal *next hour*: (216+100)-8= 308 ml

Filtration Fraction (FF)

- Measures how much the plasma entering the filter is concentrated by ultrafiltration
- $$FF= \frac{1-Prot_{IN}}{Prot_{OUT}}$$
- Estimated as
- $$FF= \frac{Q_{UF}}{Q_P} = \frac{Q_{UF}}{Q_B(1-HCT)+ Q_R^{PRE}}$$
- Practically,
-
- $$CR= \frac{Q_R^{POST}+ Q_{UF}^{NET}}{Q_B}$$

SHOULD BE KEPT
BELOW 25%
TO REDUCE HEMOCONCENTRATION AND PROTEIN-MEMBRANE INTERACTION

Let’s use what we just learned…

- 44 yr. old male baseline Cr 1.2 mg/dl, with a history of B-cell lymphoma is started on chemotherapy and develops tumor-lysis syndrome, septic shock and AKI. Admission weight: 100 Kg

TIME	Sodium (mEq/L)	Potassium (mEq/L)	Chloride (mEq/L)	Bicarbonate (mEq/L)	Blood Urea N (mg/dl)	Creatinine (mg/dl)	Glucose (mg/dl)	Htc (%)
23:00	132	6.4	98	14	54	5.6	122	30

- Liver function normal
- Last night, the fellow on call started the patient on CRRT.

Components of the prescription

COMPONENT	23:00 pm	07:00 am
MODALITY	CVVH	
BLOOD FLOW RATE Q_B	200 ml/min	
ULTRAFILTRATION RATE Q_{UF}	Zero	
REPLACEMENT FLUID Q_{RF}	BGK 4/0 2200 ml/hour	
TYPE OF DILUTION	2000 pre- and 200 post-filter	
ANTICOAGULATION	Citrate	

Is this a good prescription?

- Strengths:
  - Used a protocol
  - Anticoagulation to prevent clotting

Next morning

- The patient has been on CRRT for the last 12 hrs. You see the patient in the morning.

TIME	Sodium (mEq/L)	Potassium (mEq/L)	Chloride (mEq/L)	Bicarbonate (mEq/L)	Blood Urea N (mg/dl)	Creatinine (mg/dl)	Glucose (mg/dl)	Htc (%)
23:00	132	6.4	98	14	54	5.6	122	30
07:00	132	6.8	98	16	56	4.8	96	29

- What is happening with the patient?
- **Make the needed adjustments to the treatment.**

Learning Points

- Was there treatment downtime?
- What is the prescribed dose?
- What is the delivered dose?
- What is the composition of the replacement and dialysate fluid?

- What changes would you like to make?

Dose of therapy

- **Prescribed dose** : Approximates the effluent rate normalized to the patient's weight

- Prescribed dose =
  - CVVH:
  - Effluent flow rate = Qrf + Ultrafiltration

  - CVVHDF:
  - Effluent flow rate + Dialysis flow rate + Ultrafiltration

  (Q_{rf} + Q_d + patient fluid removed) in ml/h/Kg BW

KDIGO Guidelines

- Recommended dose: 20-25 ml/Kg/h

- To achieve this delivered dose, it is generally necessary to prescribe in the range of 25–30 ml/kg/h, and to minimize interruptions in CRRT.

Dose Calculations

CVVH

POST-DILUTION

Dose = Q_e * SC

Where SC = C_e/C_b =1 and $Q_e = Q_{rf}$ + UF

DILUTION FACTOR

PRE-DILUTION

Dose = $Q_e * \boxed{(Q_{bw} / Q_{bw} + Q_{preRF})}$

CVVHD

Dose = Q_d * SC

DILUTION FACTOR

CVVHDF

POST-DILUTION

Dose = Q_e * SC

Where $Q_e = Q_d + Q_{rf}$ + UF

PRE-DILUTION

Dose = $(Q_d + [(Q_{rf} + UF) * \boxed{(Q_{bw} / Q_{bw} + Q_{preRF})]}$

Estimated delivered dose:
Predilution systems are a bit more complicated

- Prescribed dose * dilution factor.
- Dilution factor = $Q_{bw}/(Q_{bw} + Q_{preRF})$
  - Q_{bw}: Rate of blood water flow. Q_b(1-Hct)
  - Q_{preRF}: Rate of prefilter replacement fluid
- Dilution factor = $$\frac{[Q_b(1\text{-}Htc)]}{[Q_b(1\text{-}Htc)] + Q_{preRF}}$$

Back to our patient

- Was there treatment downtime?
  - Ask the nurse or look at the run sheet; TOUCH THE SCREEN!!!
- What is the prescribed dose?
  - Calculate: 2200/100= 22 ml/kg/hr
  - Where can you find in on the machine?
- What is the *delivered* dose?
  - 22 * (0.8)= 17.6ml/kg/h
- What is the composition of the replacement and dialysate fluid?
  - K concentration: 4 meq/l

You change the prescription from this one…

COMPONENT	23:00 pm	07:00 am
MODALITY	CVVH	CVVH
BLOOD FLOW RATE Q_B	200 ml/min	200 ml/min
ULTRAFILTRATION RATE Q_{UF}	Zero	Zero
REPLACEMENT FLUID Q_{RF}	BGK 4/0 2200 ml/hour	BGK 4/0 2700 ml/hour
TYPE OF DILUTION	2000 ml/h pre-filter 200 ml/h post-filter	200 ml/h pre-filter 2500 ml/h post-filter
ANTICOAGULATION	Citrate	Citrate
Prescribed Dose	22 ml/Kg/h	
Delivered Dose	17 ml/Kg/h	

Components of the new prescription

- Type of anticoagulation: Citrate
- Treatment Modality: CVVH
- Blood flow rate: 200ml/min
- Ultrafiltration rate: 0 ml/hr
- Replacement fluid: BGK 4/0, 2700 ml/hr
- Type of dilution: 200 ml pre-filter, 2500 ml post-filter
- Labs: BMP, systemic and post cell ionized calcium

To this new prescription…

COMPONENT	23:00 pm	07:00 am
MODALITY	CVVH	CVVH
BLOOD FLOW RATE Q_B	200 ml/min	200 ml/min
ULTRAFILTRATION RATE Q_{UF}	Zero	Zero
REPLACEMENT FLUID Q_{RF}	BGK 4/0 2200 ml/hour	BGK 4/0 2700 ml/hour
TYPE OF DILUTION	2000 ml/h pre-filter 200 ml/h post-filter	200 ml/h pre-filter 2500 ml/h post-filter
ANTICOAGULATION	Citrate	Citrate
Prescribed Dose	22 ml/Kg/h	27 ml/Kg/h
Delivered Dose	17 ml/Kg/h	26.9 ml/Kg/h

Is this a good CRRT order?

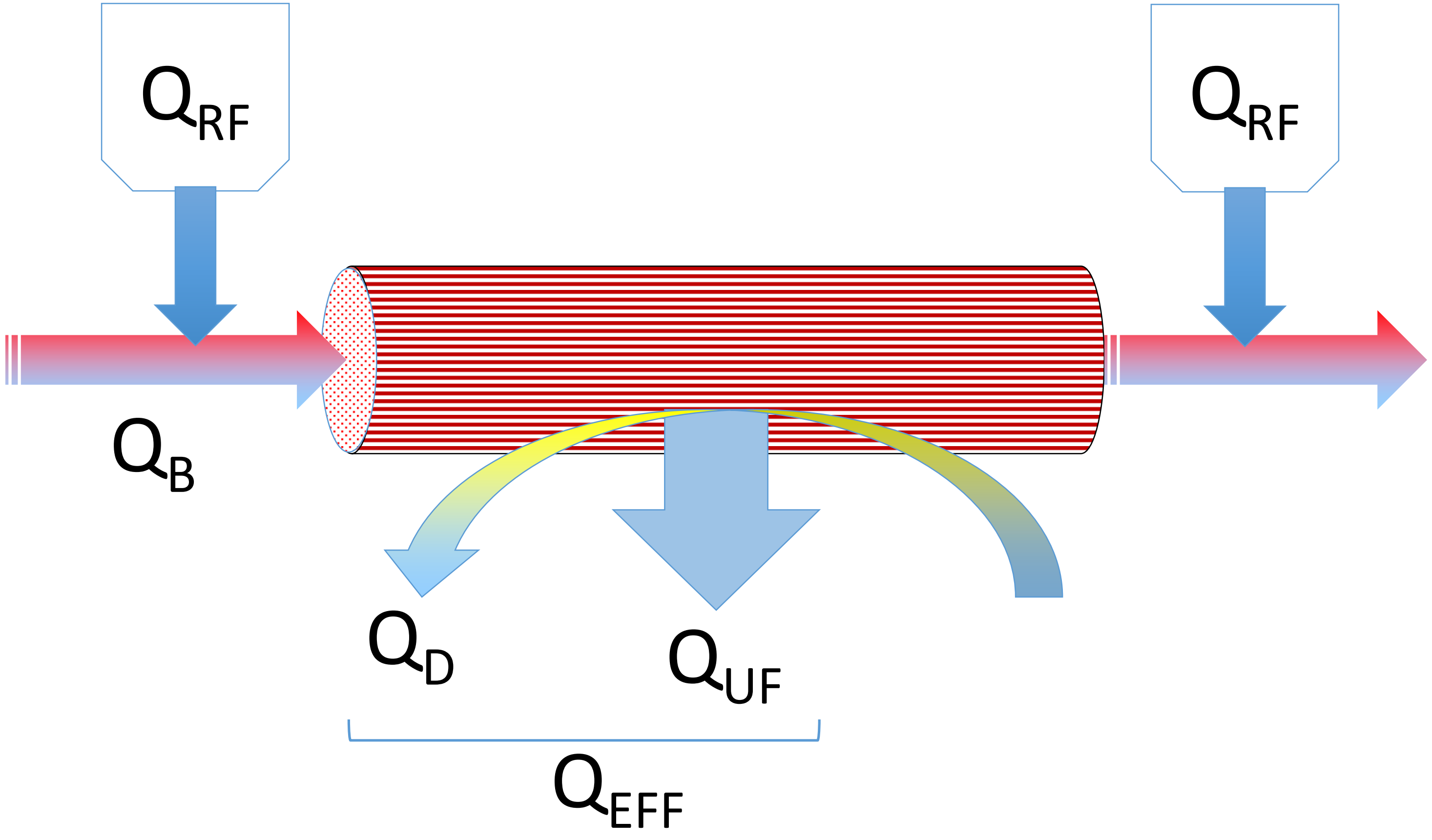
- Anticoagulation: uses regional citrate anticoagulation
- Modality: CVVH post filter
- Prescribed Dose: 2700/100= 27 ml/kg/h
- Delivered Dose: 26.9 ml/Kg/h

- Appears to be good CRRT prescription!

- But the nurse is upset: she tells you that the filter clotted 6 hrs. after starting the treatment, and has clotted for the second time in the last 12 hrs.

Filtration Fraction

That mysterious, scary, silly math formula…



WHAT FRACTION OF THE FLUID THAT ENTERS THE FILTER (PLASMA + REPLACEMENT FLUID) IS LOST BY FILTRATION? → HOW CONCENTRATED DOES PLASMA BECOME?

Filtration Fraction

- FF= $(Q_{eff} – Q_d) /(Q_{bw} + Q_{rf(pre)})*100$
  - Q_{eff} : Effluent flow rate
  - Q_d: Dialysate flow rate
  - Q_{bw}: Q_b (1-Hct)
    - Q_b: Blood flow per hour
  - $Q_{rf(pre)}$: Pre-filter replacement fluid

CVVH	CVVHD	CVVHDF
FF = $Q_e/Q_b(1\text{-}Htc)+Q_{RFpre}$	FF = $Q_e\text{-}Q_d/Q_b(1\text{-}Htc)$	FF = $Qe\text{-}Qd/Q_b(1\text{-}Htc)+Q_{RFpre}$

Can I find this on the machine?

- You can find it on the screen on good machines
- Make sure the nurse has entered the Hct for that day

Filtration Fraction

- FF= Q_{eff} /(Q_{bw}+ $Q_{rf(pre)}$)*100
- Q_{eff}: 2700 ml/h
- Q_{bw}: 12000 (0.70) = 8400 ml

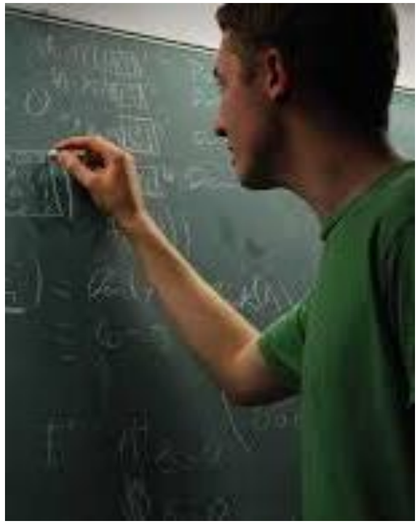
- FF= 2700/(8400+ 200)*100
- FF= 31% !!!
- What are your options?
  - Redistribute the pre and post RF
  - Increase blood flow
- GOAL: FF <25%

Filtration Fraction

- Keep FF below 25%.

- How do I decrease filtration fraction?
  - Increase blood flow rate.
  - Change replacement to pre-filter fluid.

CONCLUSIONS



- Know the basics
- Review the prescription: Do your own calculations
- **Touch** the machine; know where goes what
- Adjust the treatment to the moment-to-moment patient needs
- Be part of the team