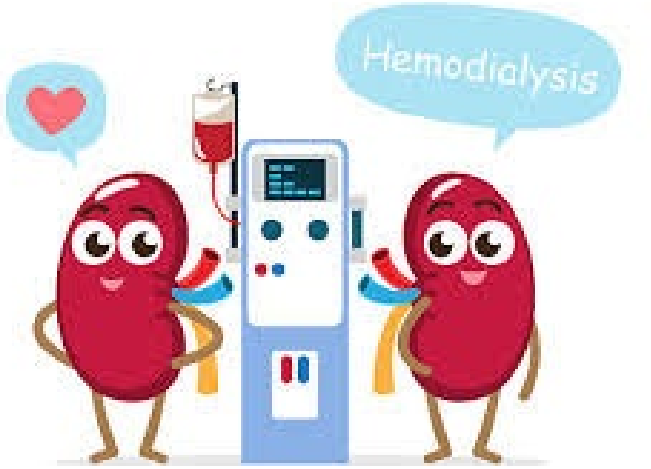
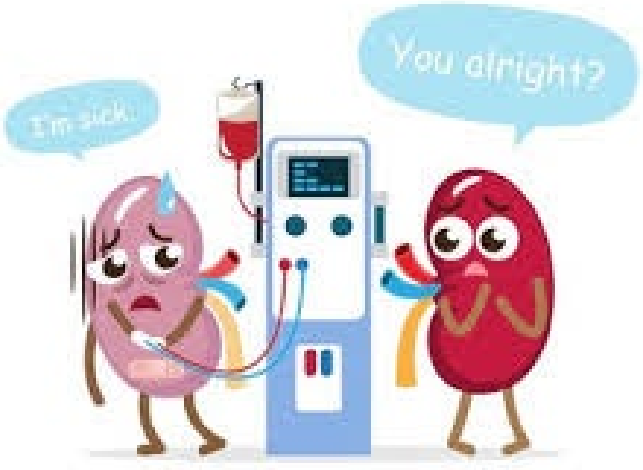


CRRT Basics

Terms and Technology



John Daniel, IV, MD, MS

Director, Neonatal ECLS Program

Associate Professor of Pediatrics

Children's Mercy Hospital, Division of Neonatology

Children's Mercy

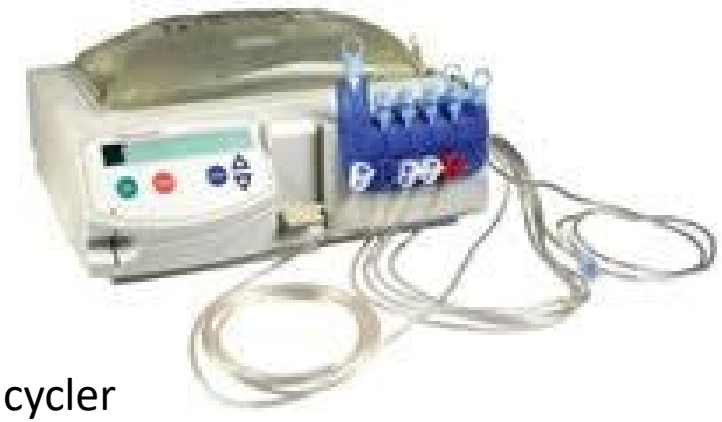
Outline

- Indications
  - Fluid overload, acute kidney injury, sepsis, CAKUT, metabolic
- What is clearance
  - Ultrafiltration, convection, diffusion, molecular size factors
- Modes of CRRT
  - SCUF, CVVH, CVVHD, CVVHDF
- Equipment
  - Hemofilter, PrismaFlex, Prismax, CARPEDIEM

What is CRRT?

- Kidney Support Therapy (global term)
  - Peritoneal Dialysis (PD)
  - Hemodialysis (HD)
    - Intermittent Hemodialysis (IHD)
    - Continuous Renal Replacement Therapy (CRRT)

- *CRRT is used over intermittent hemodialysis (HD) for critically ill, hemodynamically unstable patients because its **slow**, continuous fluid and solute removal **maintains better hemodynamic stability**, reduces hypotension and arrhythmias, and is less disruptive to the body.*



PD cycler

PrismaFlex

Prismax

Newcastle System

CARPEDIEM

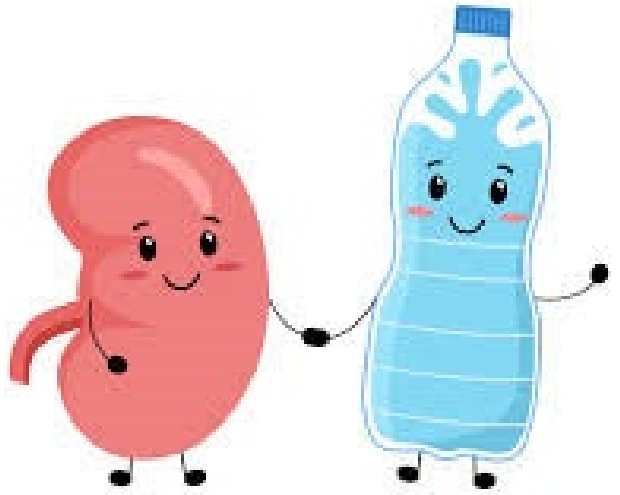
AQUADEX

Outline

- Indications
- What is clearance
- Modes of CRRT
- Equipment

Indication: Fluid Overload

- In critically ill infants' fluid intake can often be greater than the neonate’s ability to excrete fluid, especially in preterm infants due to their immature kidneys.



- Fluids needs come from:
  - Meds (antibiotics, drips, TPN)
  - Capillary leak/third spacing

- DIRECT association with degree of fluid overload and mortality
  - For every 1% increase in fluid overload, there is a 6% increase in mortality

Indication: Fluid Overload

>5% overload

>10% overload

Study or Subgroup	FA Events	FA Total	No FA Events	No FA Total	Weight	Odds Ratio M-H, Random, 95% CI
%FA>5% within 24h						
Selewski et al. 2023	82	1753	70	2843	1.5%	1.94 [1.41, 2.69]
Li et al. 2016	10	64	8	306	1.2%	6.90 [2.60, 18.27]
Rauf et al. 2021	11	21	10	80	1.2%	7.70 [2.61, 22.74]
Wang et al. 2020	2	33	0	55	0.4%	8.81 [0.41, 189.33]
Chen et al. 2016	30	41	31	161	1.3%	11.44 [5.17, 25.31]
Márquez-González et al. 2019	78	156	2	84	1.0%	41.00 [9.74, 172.60]
Subtotal (95% CI)		**2068**		**3529**	**6.7%**	**7.93 [2.81, 22.39]**
Total events	213		121			
Heterogeneity: Tau² = 1.28; Chi² = 37.40, df = 5 (P < 0.00001); I² = 87%						
Test for overall effect: Z = 3.91 (P < 0.0001)						
%FA>10% within 24h						
Selewski et al. 2023	43	537	109	4059	1.5%	3.15 [2.19, 4.54]
Kaiser et al. 2023	3	9	6	47	0.9%	3.42 [0.67, 17.43]
Huang et al. 2020	8	11	19	55	1.0%	5.05 [1.20, 21.30]
Sachdev et al. 2021	16	38	4	40	1.1%	6.55 [1.94, 22.11]
Armenda et al. 2021	8	63	0	83	0.5%	25.58 [1.45, 452.13]
Márquez-González et al. 2019	64	72	16	154	1.3%	69.00 [28.08, 169.54]
Subtotal (95% CI)		**730**		**4438**	**6.2%**	**8.77 [2.42, 31.77]**
Total events	142		154			
Heterogeneity: Tau² = 2.05; Chi² = 42.50, df = 5 (P < 0.00001); I² = 88%						
Test for overall effect: Z = 3.31 (P = 0.0009)						

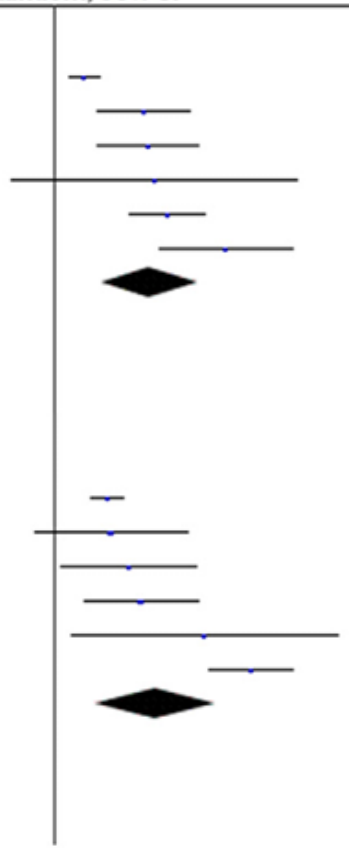


Fig. 2: Association between mortality and the percentages of fluid accumulation (%FA) higher than 5% and 10% within 24 h.

Lintz VC, Vieira RA, Carioca FL, Ferraz IS, Silva HM, Ventura AMC, de Souza DC, Brandão MB, Nogueira RJN, de Souza TH. Fluid accumulation in critically ill children: a systematic review and meta-analysis. EClinicalMedicine. 2024 Jul 3;74:102714. doi: 10.1016/j.eclinm.2024.102714. PMID: 39070177; PMCID: PMC11278930.

Indications: Acute Kidney Injury

- AKI (Acute Kidney Injury) is the sudden, short-term loss of kidney function, defined by specific increases in serum creatinine (LATE) or decreased urine output (EARLY), or both, within a short period
- Monitoring
  - UOP
  - Serum CR
  - Urinary NGAL

Indications: Acute Kidney Injury

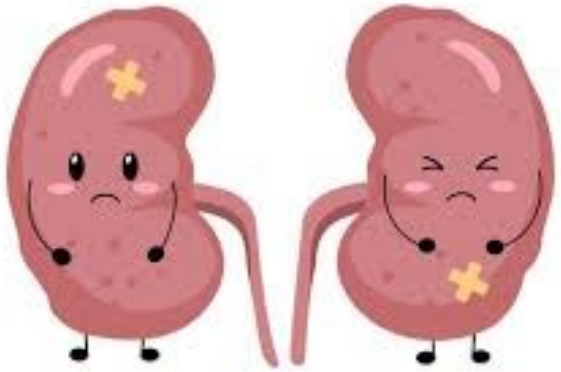
- KDIGO (Kidney Disease: Improving Global Outcomes) criteria

Table 2 | Staging of AKI

Stage	Serum creatinine	Urine output
1	1.5–1.9 times baseline OR ⩾0.3 mg/dl (⩾26.5 μmol/l) increase	<0.5 ml/kg/h for 6–12 hours
2	2.0–2.9 times baseline	<0.5 ml/kg/h for ⩾12 hours
3	3.0 times baseline OR Increase in serum creatinine to ⩾4.0 mg/dl (⩾353.6 μmol/l) OR Initiation of renal replacement therapy OR, In patients <18 years, decrease in eGFR to <35 ml/min per 1.73 m^2	<0.3 ml/kg/h for ⩾24 hours OR Anuria for ⩾12 hours

Indications: CAKUT

- Congenital anomalies of the kidney and urinary tract (CAKUT)
  - Commonly identified parentally, between 1:500 live births.
  - Often managed with fetal procedures to help survival
    - No improvement in kidney function long term.
- HD/CRRT will often be needed to bridge kids to PD.
  - Transplant occurs around 2-3 years of age.
- Outcomes vary by diagnosis
  - LUTO (PUV)
  - Renal Agenesis
  - Cystic Renal dysplasia



Indications: Metabolic/Liver Failure

- Toxic effects of accumulating metabolites in the CNS
- Neurological prognosis related to *DURATION* of coma and peak NH3 level
- Affect 1 in 30,000 to 40,000 live births
- Treatment is stopping toxin production and removal of organic intermediates/ammonia

Outline

- Indications
- What is clearance
- Modes of CRRT
- Equipment

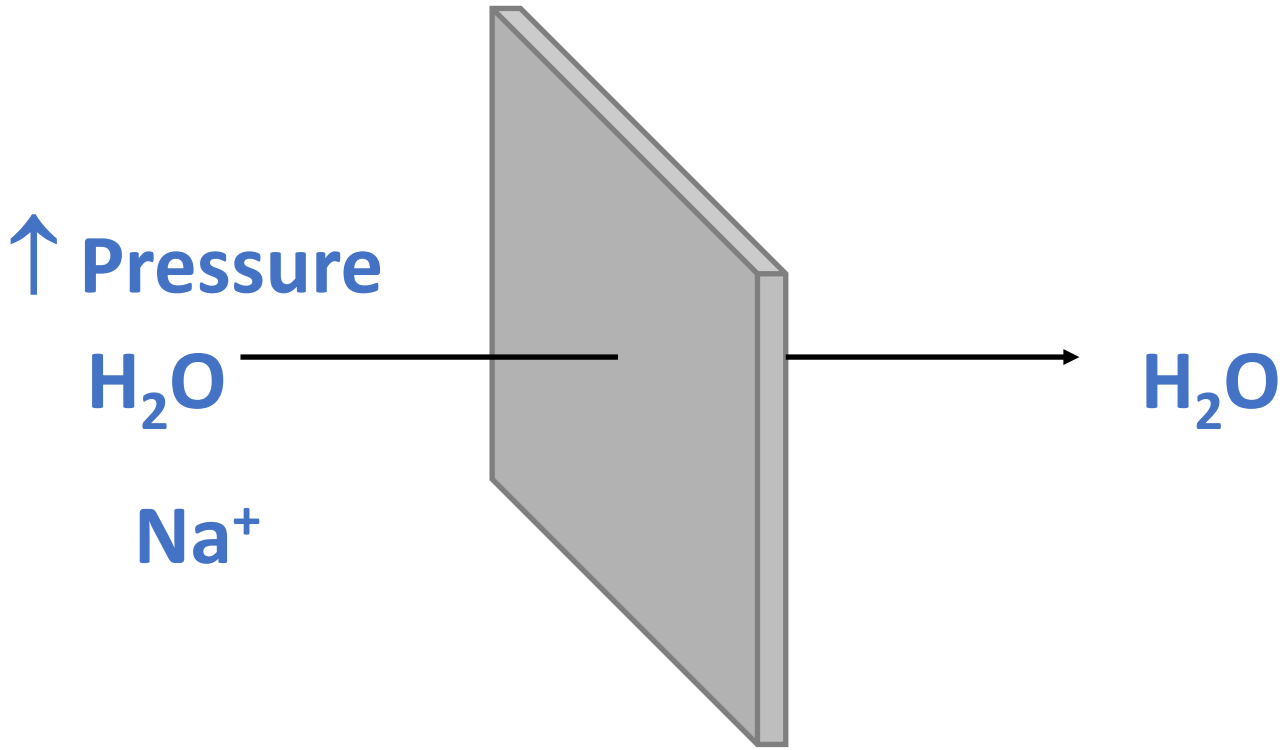
Clearance

- The amount of a substance cleared from the plasma per unit time.
- Multifactorial
  - Mechanism of actions
    - Ultrafiltration
    - Convection
    - Diffusion
  - Molecular size and charge
  - Protein bound or free
  - Blood flow rate

Clearance: Ultrafiltration

- Movement of FLUID through a membrane caused by a pressure gradient, either hydrostatic or osmotic
  - Hydrostatic pressure is the pushing force, pushing the fluid through a membrane.
  - Osmotic pressure is the pull force, pulling the fluid through a membrane.
    - Difference in solute concentrations.

Clearance: Ultrafiltration



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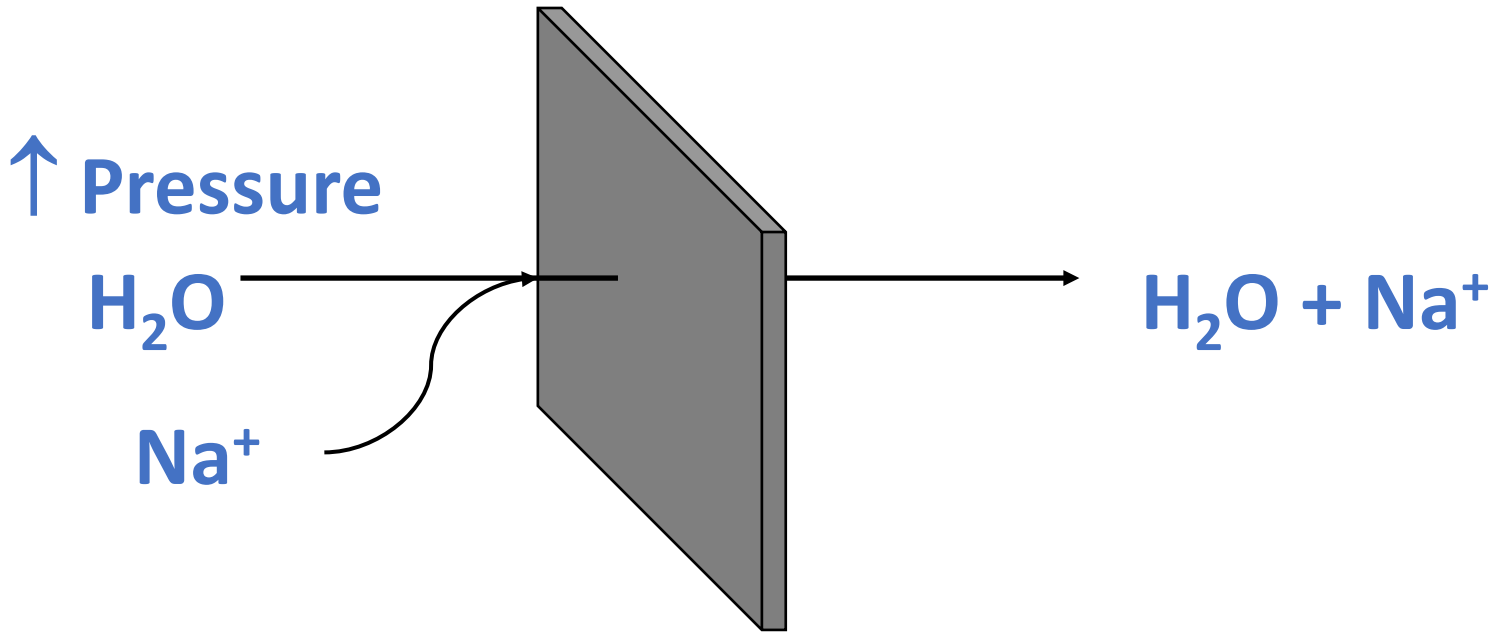
Clearance: Convection

- Movement of SOLUTES with a water flow “solvent drag”.
- PUSHING water through a filter and the water then dragging SOLUTE
- Biggest determinant of convection is ultrafiltration rate.
  - The higher the rate, the more convection.
- Other factors:
  - High plasma oncotic pressure (higher pressure, lower convection)
  - Membrane permeability (more permeable, more convection)

Clearance: Convection



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Clearance: Convection

- More effective at clearing middle molecules
  - Some small molecules will tag along.
- Limit is cut-off size of membrane
- Increasing the ultrafiltration rate yields higher convective clearance *but* increases the risk of hypotension

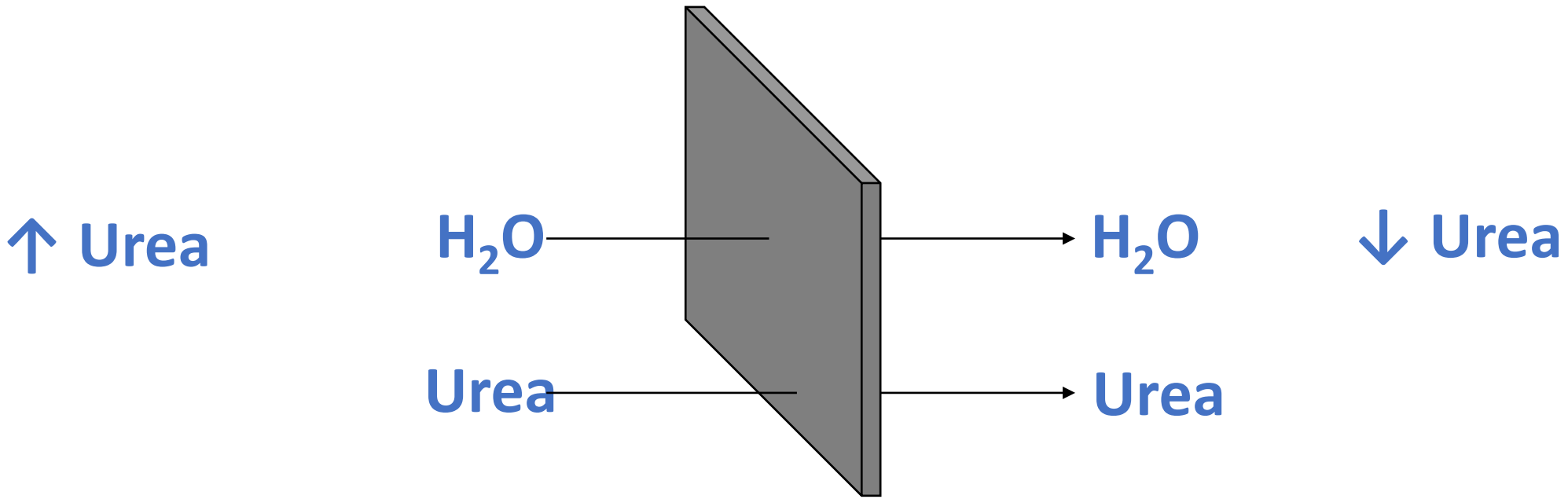
Clearance: Diffusion

- Movement of solutes from higher to lower concentration areas.
- Affected by:
  - Concentration gradient
  - Membrane characteristics
    - Surface area of the membrane
    - Membrane thickness
    - Membrane permeability
  - Solute characteristics.
    - Different solutes have different clearance rates with diffusion.

Clearance: Diffusion

- Solvent (water) moves up a concentration gradient
- Solute (urea) diffuses down a concentration gradient
  - The larger the concentration gradient the more drive for movement
  - Therefore, smaller molecules with greater concentration gradients move more quickly across membrane

Clearance: Diffusion



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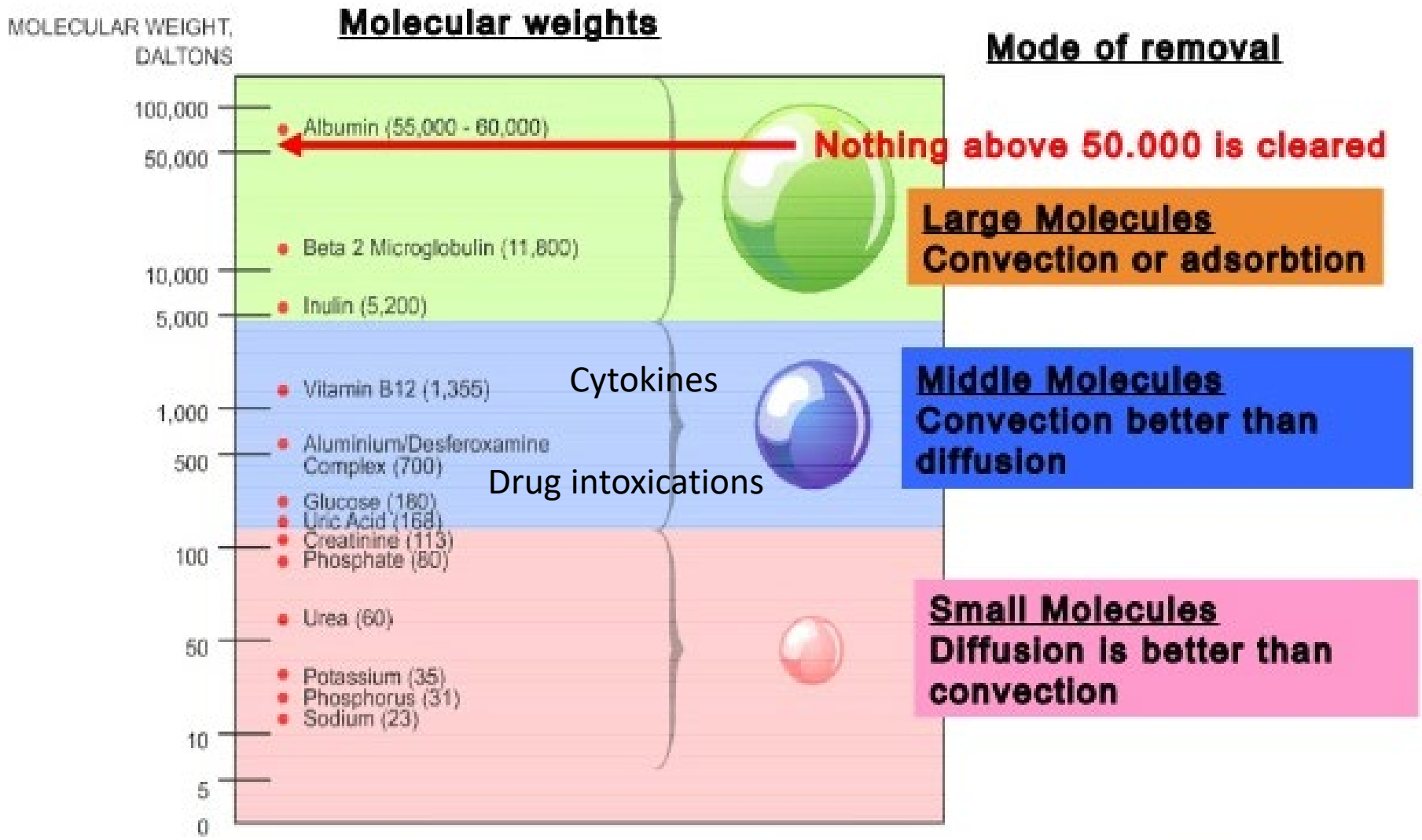
Clearance: Diffusion

- Small molecules diffuse easily
- Larger molecules diffuse slowly
- ***Dialysate*** required
  - Concentration gradient
  - Faster dialysate flow increases mass transfer

Clearance: Sieving Coefficient

- A known value for how well a solute (electrolyte/drugs) crosses a membrane.
  - It is a value between 0-1
    - 0 = does not pass through membrane
    - 1 = freely passes through membrane
  - Can changed based on CRRT mode.
    - Example:
      - Vancomycin SC 0.86 in CVVH
      - Vancomycin SC 0.76 in CVVHD

Molecular size and clearance



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Outline

- Indications
- What is clearance
- Modes of CRRT
- Equipment

CRRT Modes

- All CRRT modes function using the principles of mass for clearance.

- Each mode has its strengths and weaknesses.

CRRT Modes

- Slow Continuous Ultrafiltration (SCUF)
  - Ultrafiltration
- Continuous VenoVenous Hemofiltration (CVVH)
  - Convection
- Continuous VenoVenous HemoDialysis (CVVHD)
  - Diffusion
- Continuous VenoVenous HemoDiaFiltration (CVVHDF)
  - Ultrafiltration, Convection, Diffusion

Slide modified from original by Marita Thompson, MD

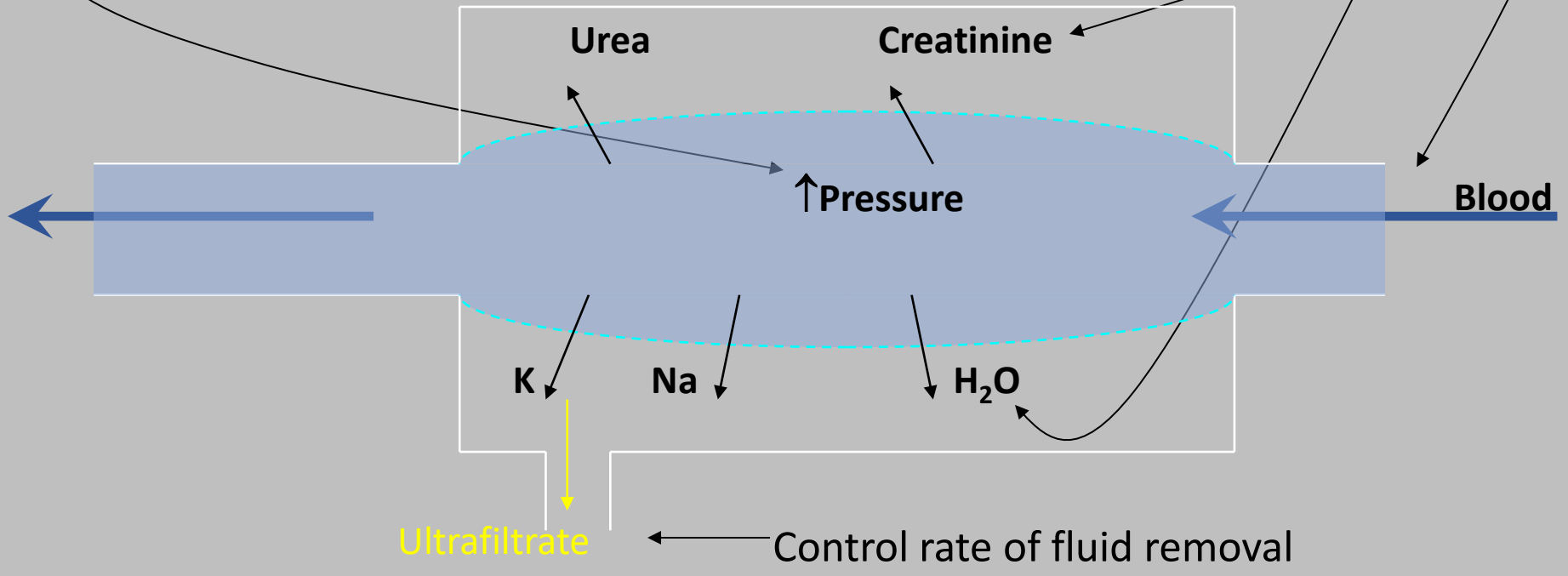
CRRT Modes: SCUF

- Ultrafiltration (H2O)
- Convection (medium size molecules)

Blood is pushed through a hemofilter

Pressure generated within filter pushes solvent (serum) through semi-permeable membrane (convection)

Some solutes are carried through membrane by a process known as “solvent drag”

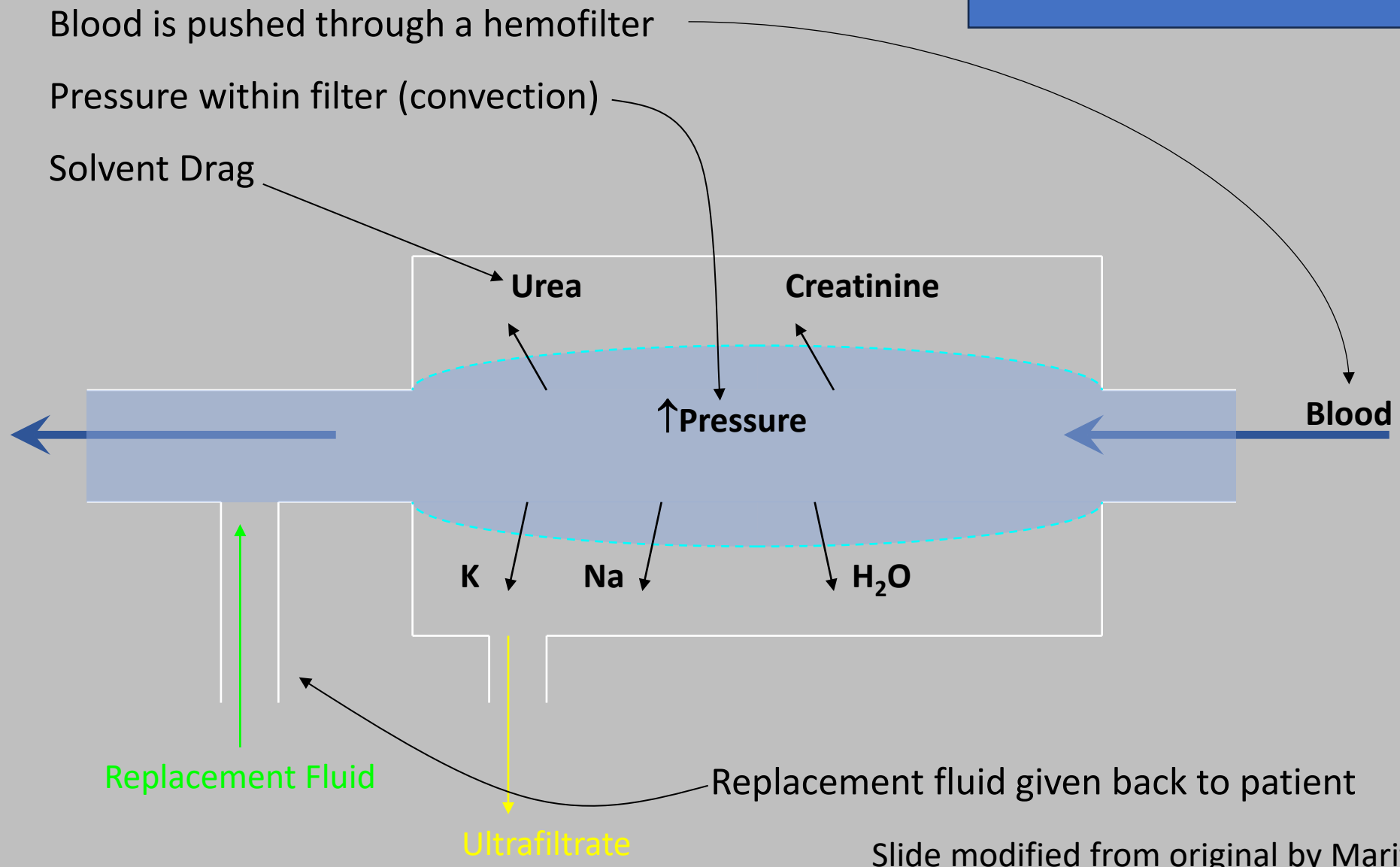


CRRT Modes: SCUF

- Multiple benefits for our ECMO patients
  - Hemofilter built into ECMO circuit
  - Easy to pull off volume
    - Cannot control what you pull.
    - Some Electrolytes come with water
- Just ultrafiltration, essential just plasma
- Max fluid removal weight is 5mL/kg/hr
- Better UF removal with SLOWER rates.

CRRT Modes: CVVH

- Ultrafiltration (H2O)
- Convection (Medium size molecules)



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CRRT Modes: CVVH

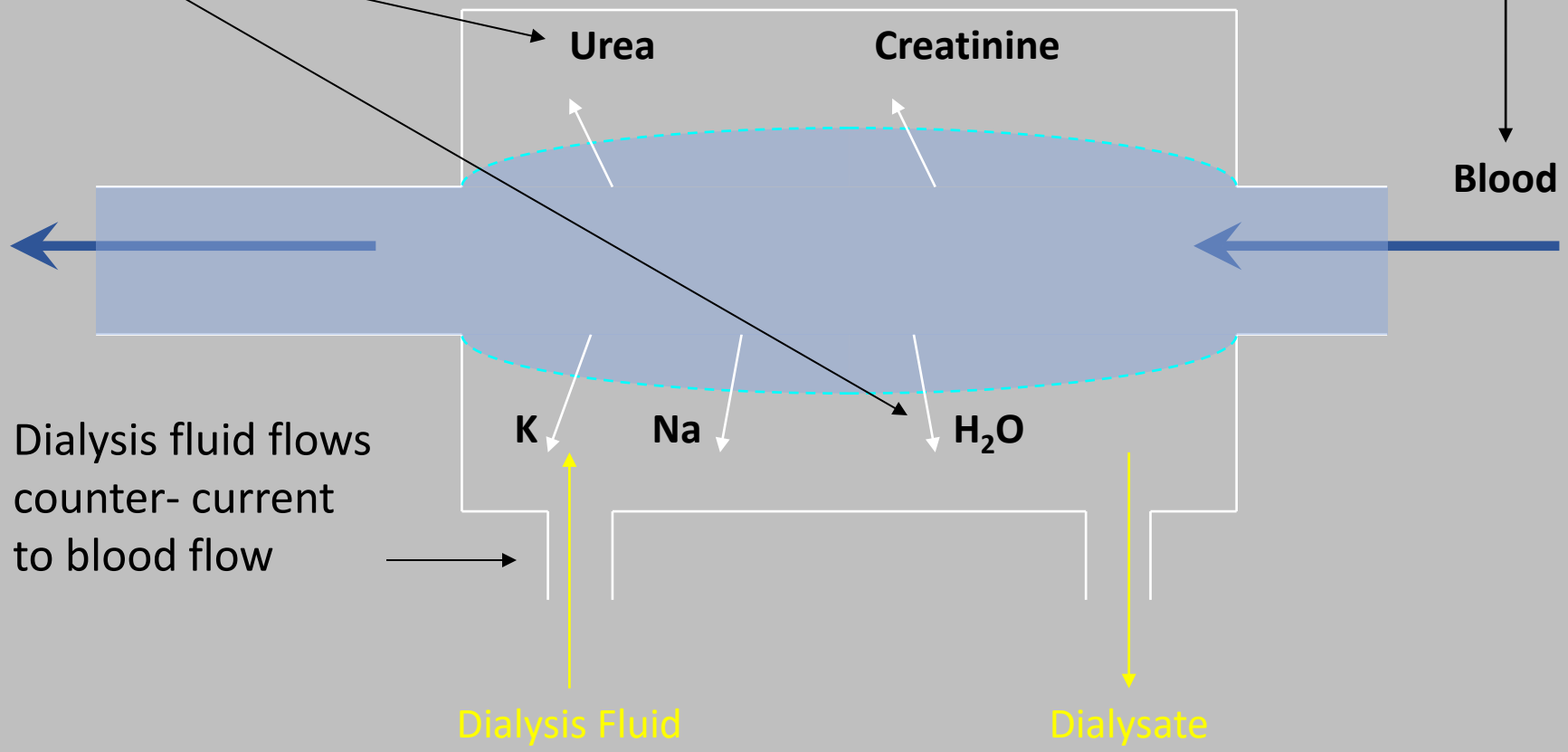
- Higher blood flow rate
  - Ultrafiltration AND convection
    - Recall: convective clearance is dependent on blood flow rate (i.e. ultrafiltration rate).
- Ultrafiltrate is replaced by a sterile solution (replacement solution)
  - Usually, nephrology will select this fluid.
  - Patient fluid loss (or gain) results from the difference between ultrafiltration and replacement rates

CRRT Modes: CVVHD

- Diffusion (small molecules)

Blood is pushed through a hemofilter

Water and Solutes move across concentration gradients (diffusion)



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CRRT Modes: CVVHD

- Diffusion (main effect)
  - Some convection (very minor) occurs due to transmembrane pressure created by roller-head pump
- Solute removal is directly proportional to DIALYSYS FLUID flow rate
  - Increased dialysate rate, increased removal.
  - Dialysate flow rate is slower than BFR and is the limiting factor to solute removal

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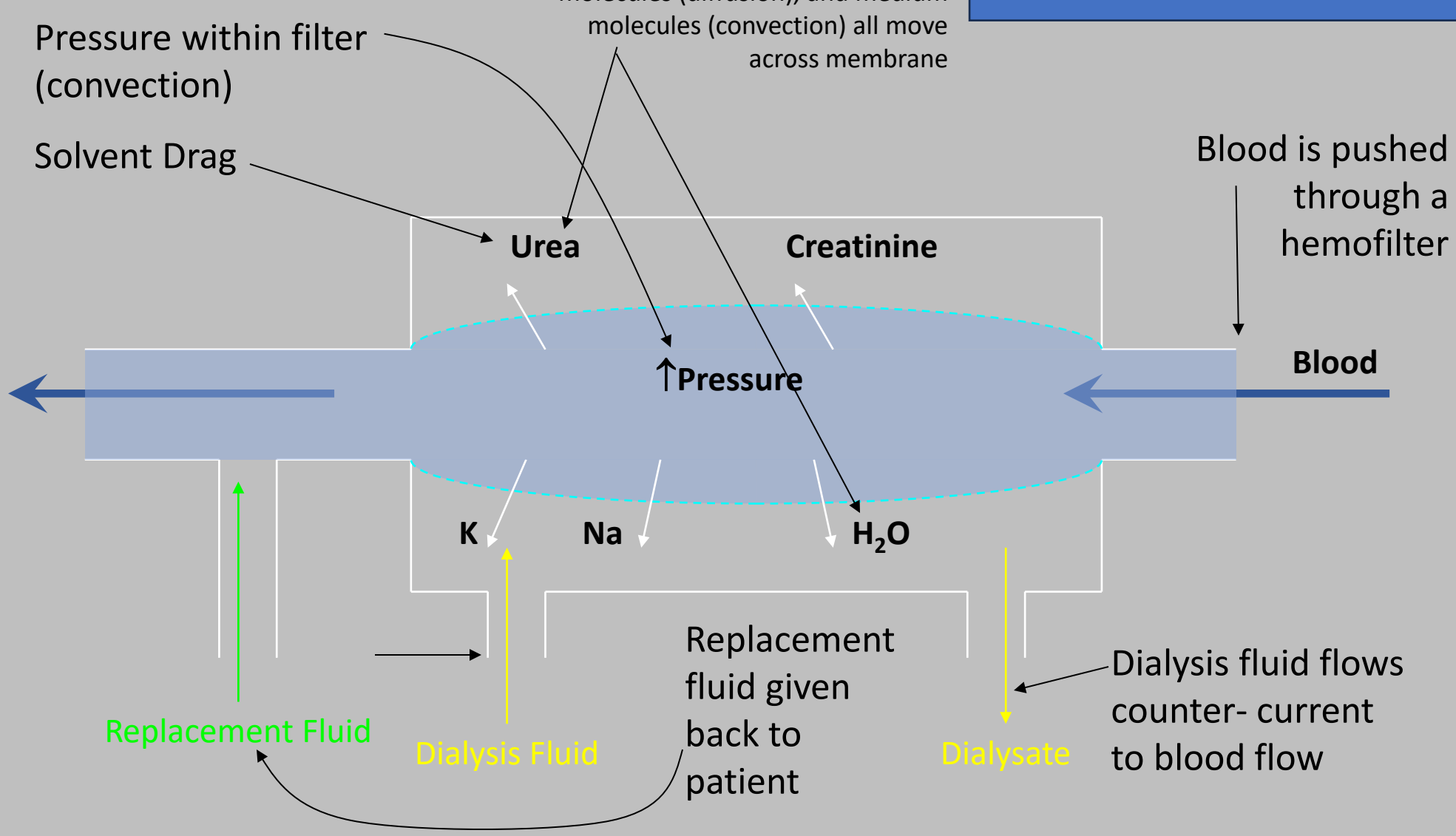
CRRT Modes: CVVHDF

- Ultrafiltration (H2O)
- Convection (Medium size molecules)
- Diffusion (Small molecules)



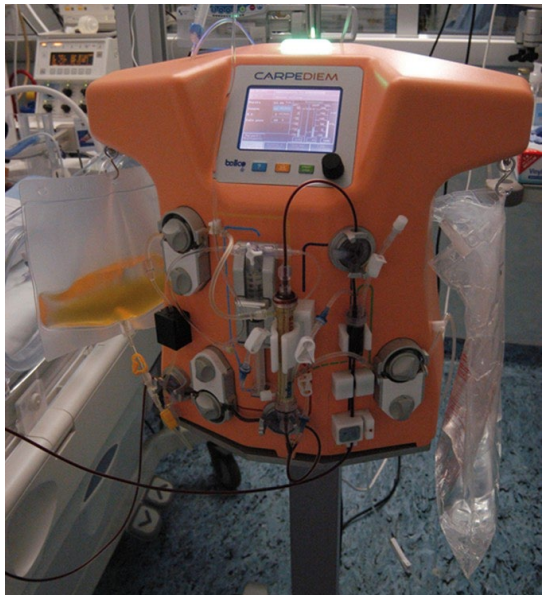
CRRT Modes: CVVHDF

- Can provide ultrafiltration, convection, and diffusion.
  - Large, medium, and small molecules.
- Complex to set up.

- ***CARPEDIEM does not support this mode****

CRRT Modes: CRRT Bags

- Dialysis bags will have certain concentrations of electrolytes in them.
- This will help drive the concentration gradient across which electrolytes will flow.
- Two standard bags at CMH
  - Prismasol BGK 2/0
  - Prismasol B22GK 4/0



CRRT Modes: CRRT Bags

		Calcium Formulas			Calcium-Free Formulas			Dextrose-Free
	Plasma*	PRISMASOL BGK 4/2.5	PRISMASOL BGK 2/3.5	PRISMASOL BGK 0/2.5	PRISMASOL BGK 4/0/1.2	PRISMASOL BGK 2/0	PRISMASOL B22GK 4/0	PRISMASOL BK 0/0/1.2
Potassium K^+ (mEq/L)	3.5-5.0	4	2	0	4	2	4	0
Calcium Ca^{2+} (mEq/L)	2.3-2.6†	2.5	3.5	2.5	0	0	0	0
Magnesium Mg^{2+} (mEq/L)	1.4-2.0	1.5	1	1.5	1.2	1	1.5	1.2
Sodium Na^+ (mEq/L)	135-145	140	140	140	140	140	140	140
Chloride Cl^- (mEq/L)	100-108	113	111.5	109	110.2	108	120.5	106.2
Bicarbonate HCO_3^- (mEq/L)	22-26	32	32	32	32	32	22	32
Lactate (mEq/L)	0.5-2.2	3	3	3	3	3	3	3
Dextrose (mg/dL)	70-110	100	100	100	100	100	100	0
Osmolarity (mOsm/L)	280-296	300	296	292	295	291	296	282
NDC Number		24571-105-06	24571-103-06	24571-108-06	24571-114-06	24571-102-06	24571-111-06	24571-113-06
Catalog Number		110242	110243	110240	110241	110244	115001	110239

CRRT Modes: CRRT Bags

- Electrolytes to watch!!!
  - Calcium
    - We use calcium free bags, so there is a massive gradient to remove calcium.
    - Need to watch iCal and serum calcium closely.
  - Phosphorous
    - Hypophosphatemia is also extremely common.
- MUST have daily calcium and phosphorous levels as a MINIMUM.

Outline

- Indications
- What is clearance
- Modes of CRRT
- Equipment

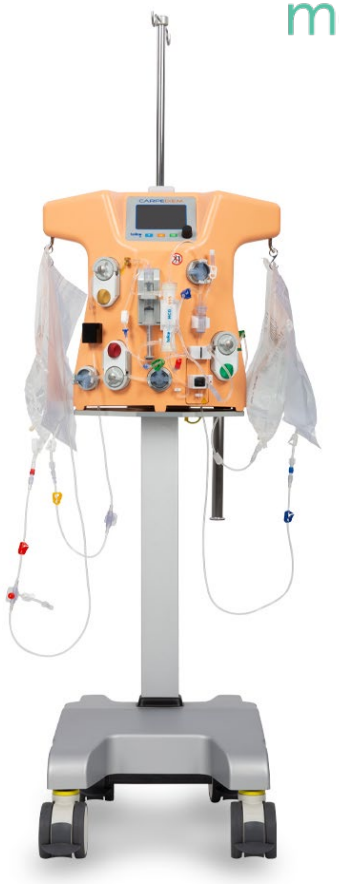
Our systems

Baxter

PrismaFlex

PrisMax

Mozarc medical

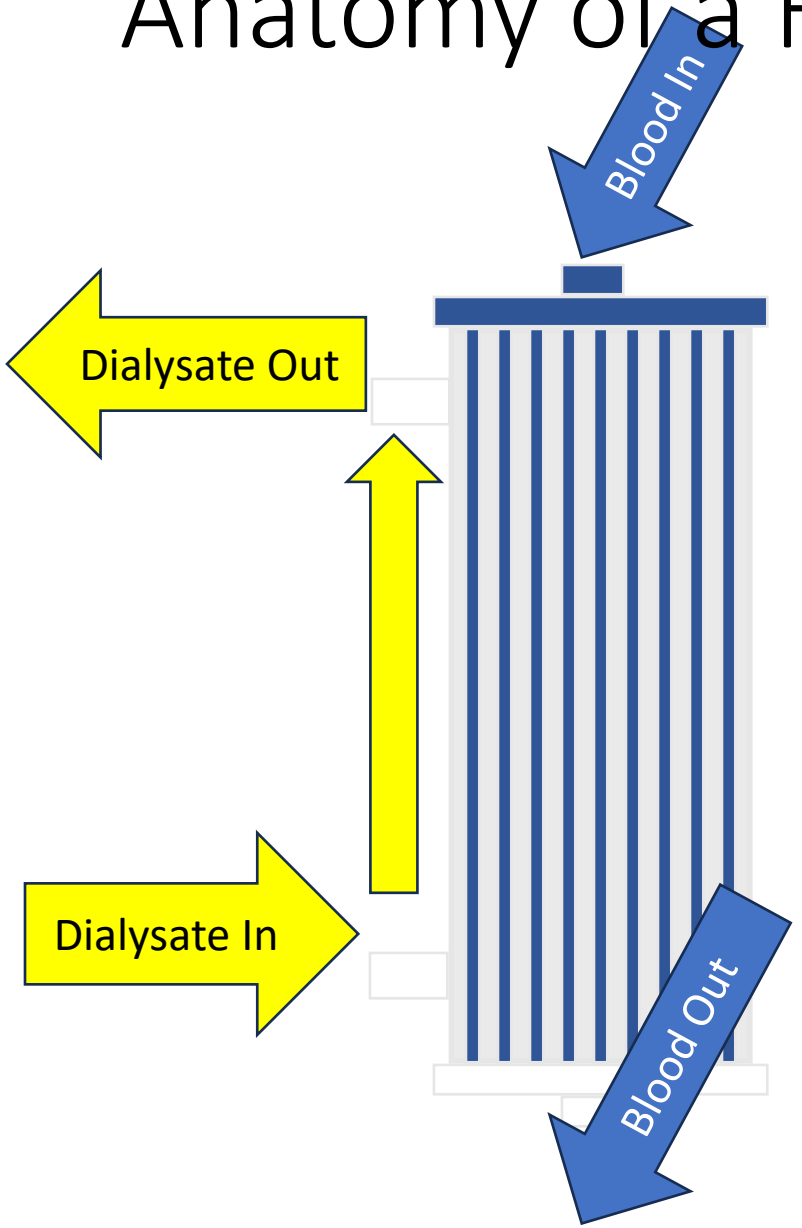


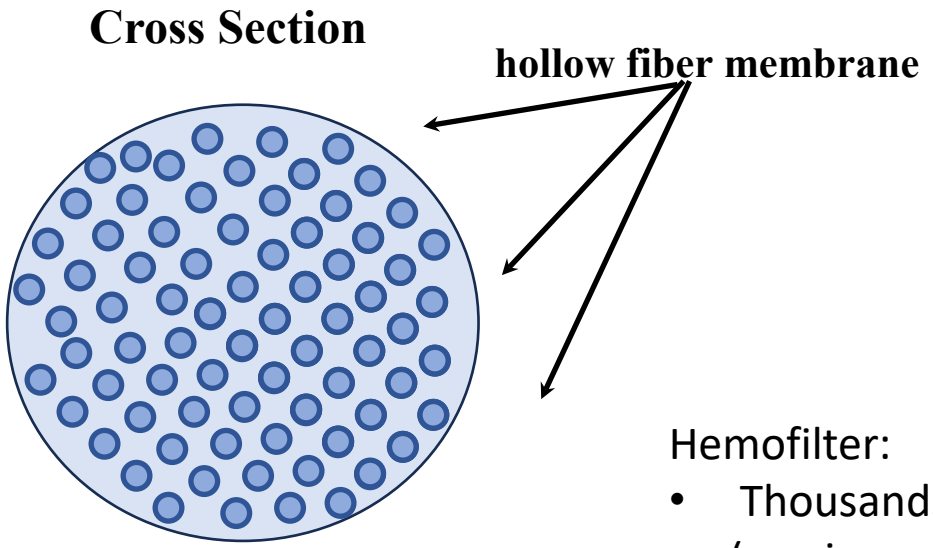
CARPEDIEM

Equipment: Hemofilter

- The essential piece of the dialysis circuit.
- Each has varying size, thickness, priming volume, blood flow rates, sieving coefficients, etc.

Anatomy of a Hemofilter





Outside the Fiber (effluent)
Inside the Fiber (blood)

Hemofilter:

- Thousands of hollow fibers (semipermeable membrane) Blood passes through fibers
- Dialysate circulates around the fibers
- Diffusive gradient produced for solute removal

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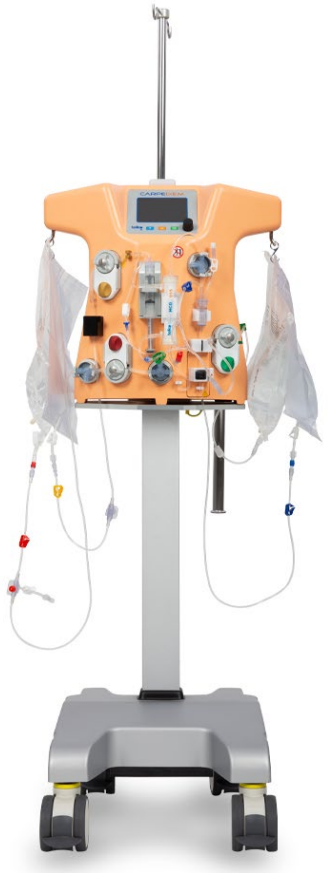
Our Systems: Prisma (Baxter)

- **Not Licensed for Small Infants**
  - Not licensed for use in children weighing < 20 kg in the US (< 8 kg in Europe).
  - However, it is frequently used off licence for smaller babies.
- Large circuit volume
- Can generate higher clearance flow rates than CARPEDIEM
  - Dialyslate flow rates 0 to 8000mL/1.73m^2/hr
- Used in the NICU for tandem ECMO therapy.
- Can support ALL CRRT modes:
  - CVVH, CVVHD, CVVHDF
- Multiple filter sizes: HF20 (stand alone in babies), HF1000 (tandem)

Our Systems: CARPEDIEM

- **CA**dio **R**enal **PED**iatric **DI**alysis **E**mergency **M**achine
- Timeline
  - 2010 – CARPDEIEM conceived by Dr. Claudio Ronco in Italy.
  - 2014 – First use in a patient, 2.9 kg infant.
  - 2020 – FDA approval given for use in infants 2.5 – 10kgs.
  - 2023 – CMH acquires the CARPEDIEM system.
  - 2024 – PICU goes lives with CARPDIEM system.
  - 2026 – NICU going live with CARPEDIEM system.

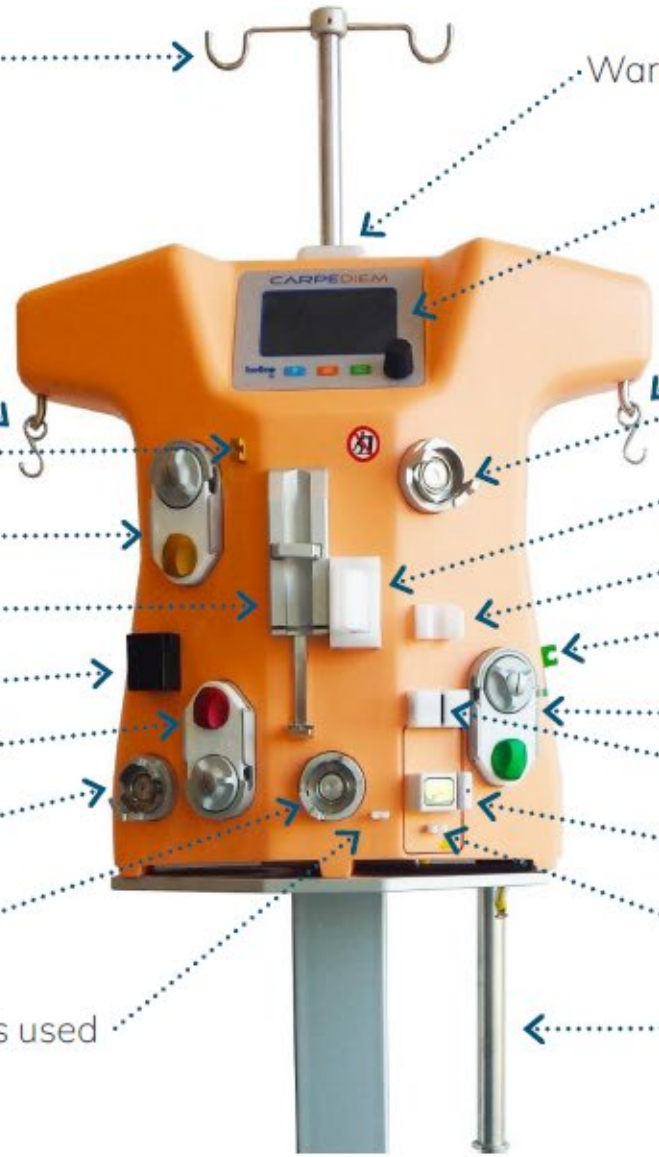


Our Systems: CARPEDIEM

- Designed for infants weighing between 2.5 and 10 kg.
- Maximum dialysate flow 4000mL/1.73m2/hr
- Cannot change fluid removal rate, set it for the day, not per hour.
- Supports CVVH and CVVHD
  - Does not support CVVHDF
- Multiple Filter types:
  - HCD 015 model – 0.16 m2 filter surface area with 32 mL total priming volume
  - HCD 025 model – 0.29 m2 filter surface area with 41 mL total priming volume

Carpediem™ System Components

Front View



IV pole holder

Warning light

Control panel

Effluent (EFF) scale

Infusion/dialysis (INF/DIA) scale

Venous pressure transducer (Dome)

Clip for effluent (EFF) pump segment

Filter holder

Effluent (EFF) pump

Venous drip chamber holder

Heparin pump

Clip for infusion/dialysis (INF/DIA) pump segment

Blood leakage detector (BLD)

Infusion/dialysis (INF/DIA) pump

Blood pump

Air sensor

Arterial pressure transducer (Dome)

Venous electroclamp

Pre-filter pressure transducer (Dome)

Clip for venous line

Clip for infusion/dialysis (INF/DIA) line if a warmer is used

Warmer holder

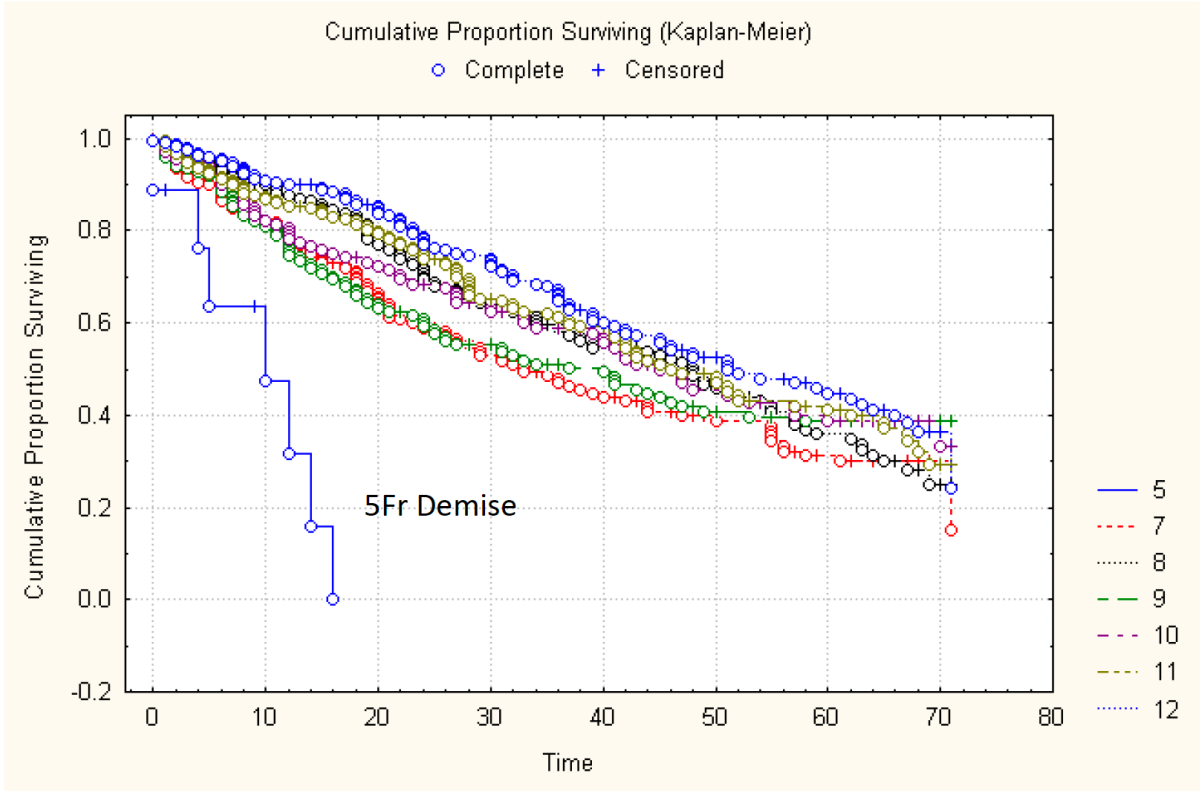
Mozarc medical

Our Systems: Prisma vs CARPEDIEM

- Prisma
  - CVVH, CVVHD, CVVHDF
  - Larger circuit volume (60mLs)
  - Max flow 8L/1.73m^2/hr
  - Can change hours removal
  - Good system for:
    - Hyperammonemia
    - Severe electrolyte derangements
    - Severe MODS
    - Liver disease
- CARPEDIEM
  - SCUF, CVVH, CVVHD
  - Smaller circuit volume (32-41mLs)
  - Max flow 4L/1.73m^2/hr
  - Cannot change hourly removal
    - Set for 24 hours
  - Good system for:
    - Small/inactive ESKD child who is too small to tolerate HD
    - AKI with minimal pressor support
    - Descent lungs, minimal to moderate lung disease

Vascular Access

- Recall flow dynamics in catheters
  - $Resistance = \frac{8nL}{2r^4}$
  - Two most important factors are radius and length.
  - We want short, wide catheters
- SVC is better than femoral vessels
- 7ft is the minimum size for dual lumen cannulas



Hackbarth R et al: *IJAIO* December 2007

Vascular Access

- Subclavian/SVC
  - Very accessible
  - Large caliber
  - Great flows
  - Low recirculation rate
  - Risk for Pneumothorax

- Femoral/IVC
  - Usually accessible
  - Smaller than SVC
  - Flows may be diminished
    - Abdominal Pressures
    - Patient movement
  - Risk for retroperitoneal hemorrhage

  Higher recirculation rate

Vascular Access

Patient Size	Catheter Size
Neonates	7 Fr
3 – 6 Kg	7 Fr
6 – 12 Kg	8 Fr
12 – 20 Kg	9 Fr
20 – 30 Kg	10 Fr
> 30 Kg	10 – 12 Fr

Adapted from Cincinnati Children's Hospital Center for Acute Care Nephrology Acute Dialysis/CRRT/Pheresis Access Guideline

Our Systems: CRRT Prescription

- Things to think about when considering CRRT and the CRRT prescription.
  - Why are we doing CRRT?
    - Fluid overload, AKI, Sepsis, etc. → can help us determine which mode to use.
  - What does out vascular access look like?
    - Catheter size and location
  - What do we want out fluid goal to be?
    - Is there any native renal function to consider?

Our Systems: CRRT Prescription

- CRRT Mode: SCUF, CVVH, CVVHD
- Blood flow (Q_b) ~ 3-5mL/kg/hr
- Dialysate flow (Q_d) ~ 2000-3000mL/1.73m^2/hr
- Prefilter replacement flow (Q_{pre})
- Postfilter replacement flow (Q_{post})

Summary

- DIFFUSION and CONVECTION are the main modes of clearance for neonatal CRRT patients.
- Mode of CRRT is dependent on goals of what we are trying to clear/remove.
  - CARPEDIEM does not offer CVVHDF
- CARPEDIEM has less clearance ability and Prisma and should not be used for metabolic conditions.
- Vascular access is a critical component of achieving adequate flow and clearance.