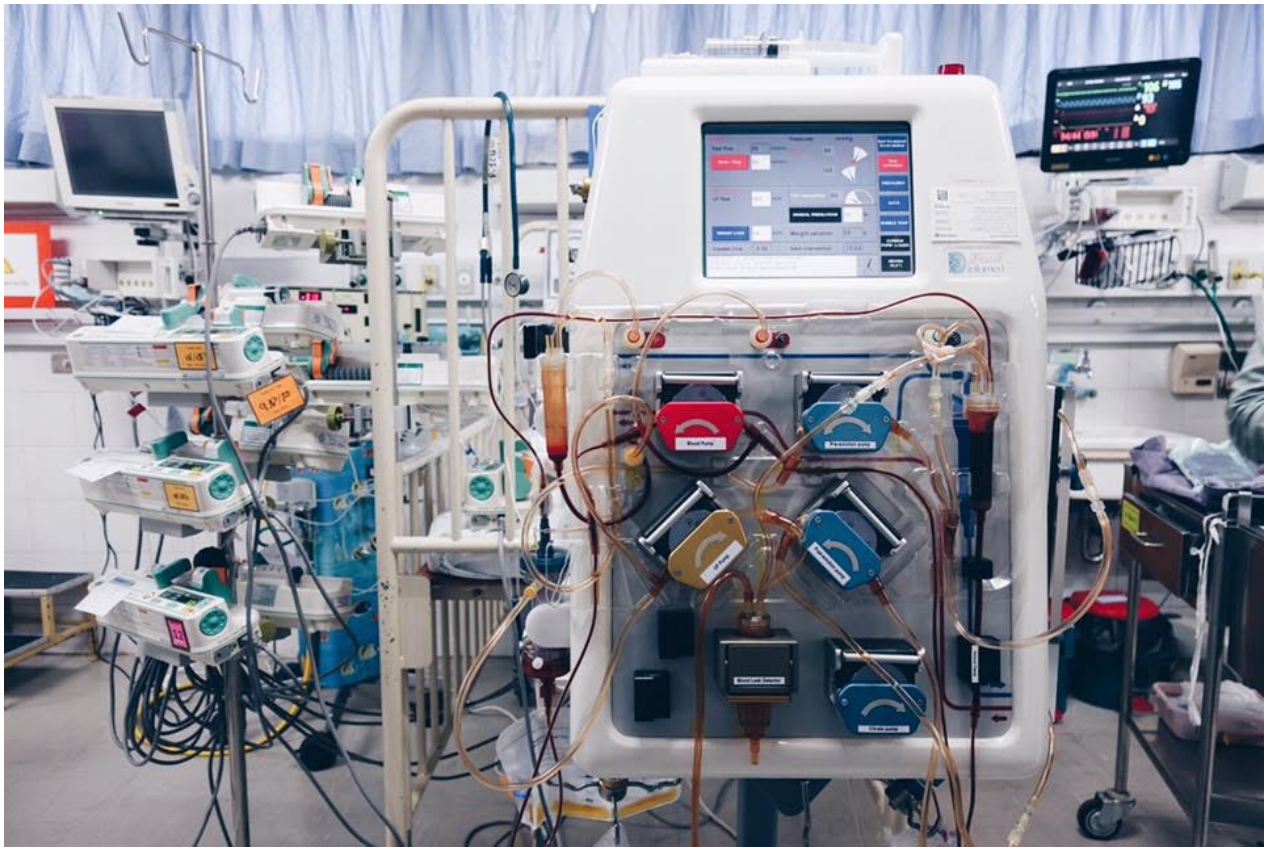
Essential in Renal Replacement Therapy
“ Pediatrics CRRT ”



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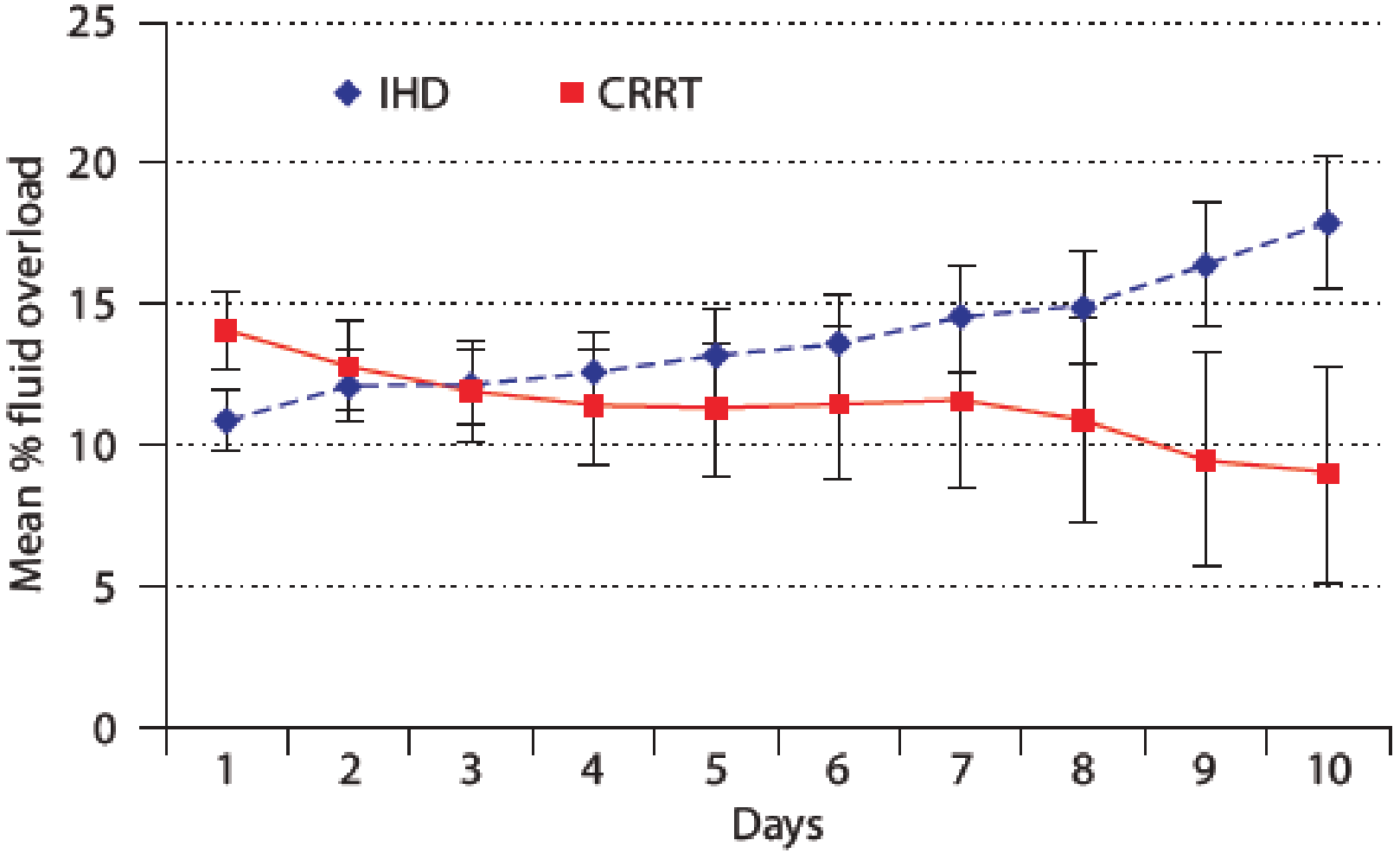
Department of Pediatrics, Phramongkutklao Hospital

Correction of fluid overload in patients with AKI by IHD and CRRT



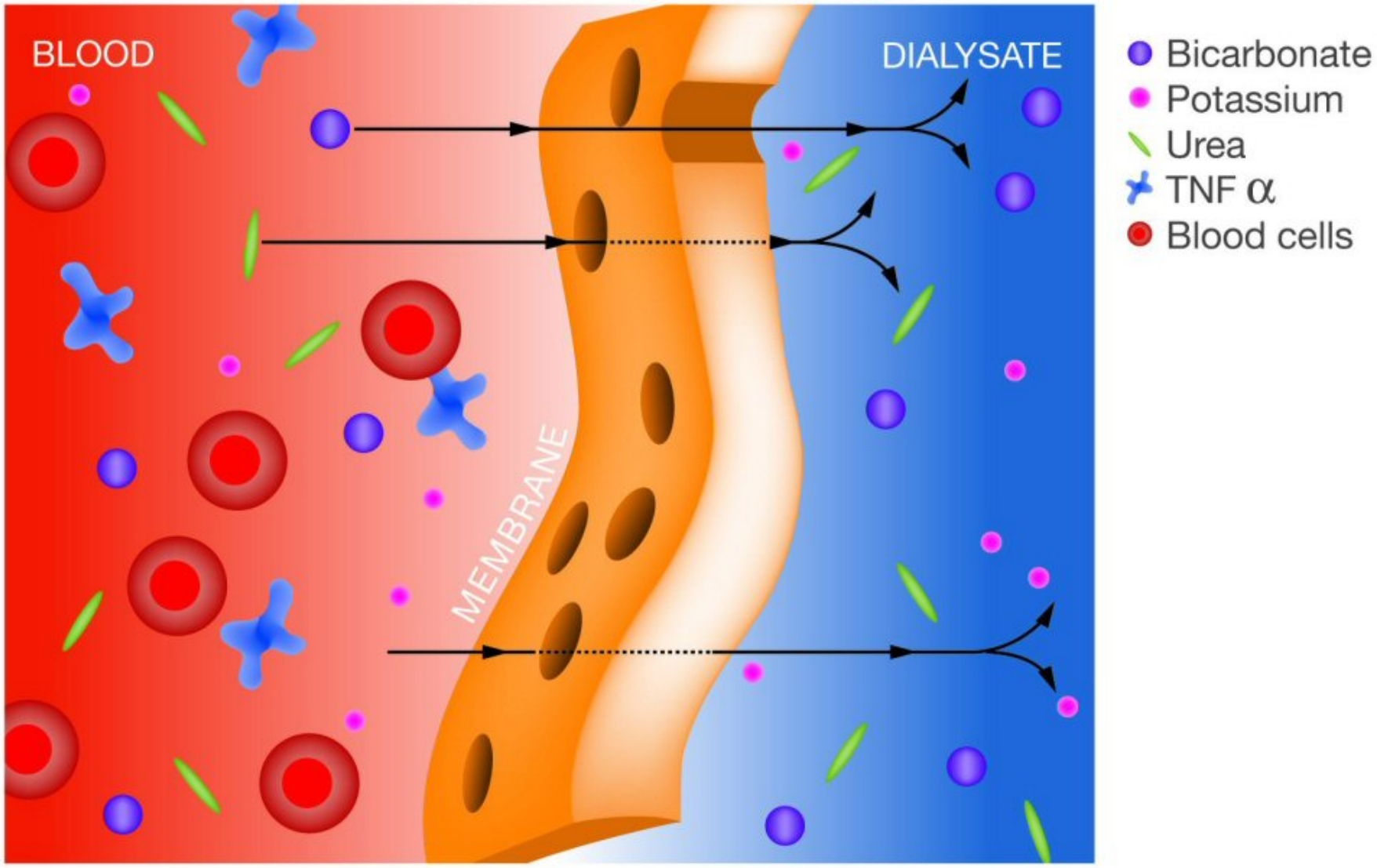
Bouchard J, Kidney Int 2009

Question to ask about a solute to determine if it can be removed by dialysis?

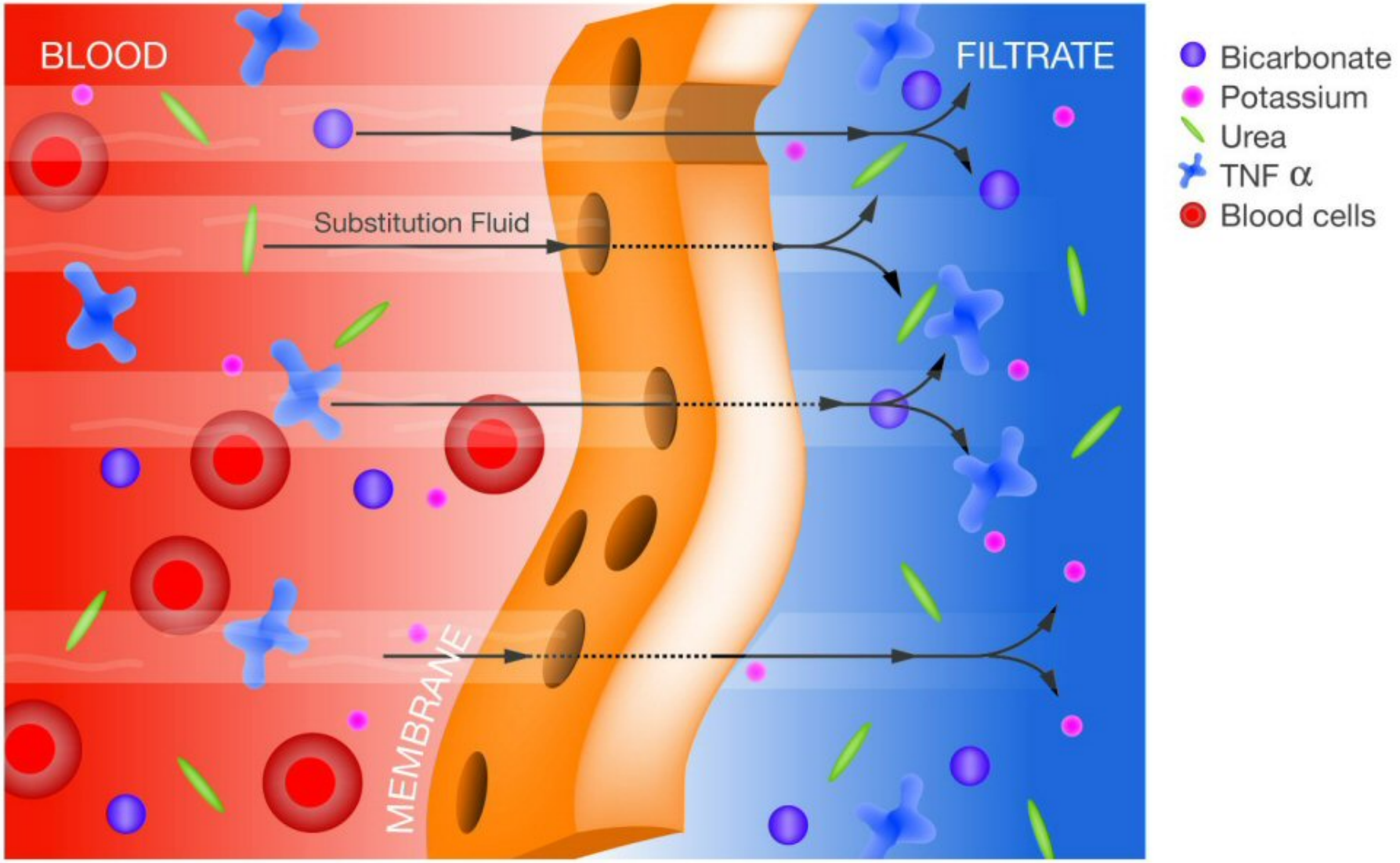
- ❑Molecular weight
- ❑Protein binding
- ❑Volume of distribution
- ❑Water solubility
- ❑charge

MW (daltons)	Representative	method
Small < 500	urea, Cr, amino acid	Diffusion convection
Middle 500-5,000	B12, vancomycin inulin	Convection diffusion
LMW protein 5,000-50,000	B2 microglobulin myoglobin, heparin, IgG	Convection adsorption
Large protein > 50,000	Albumin, TNF, Hb	Convection adsorption

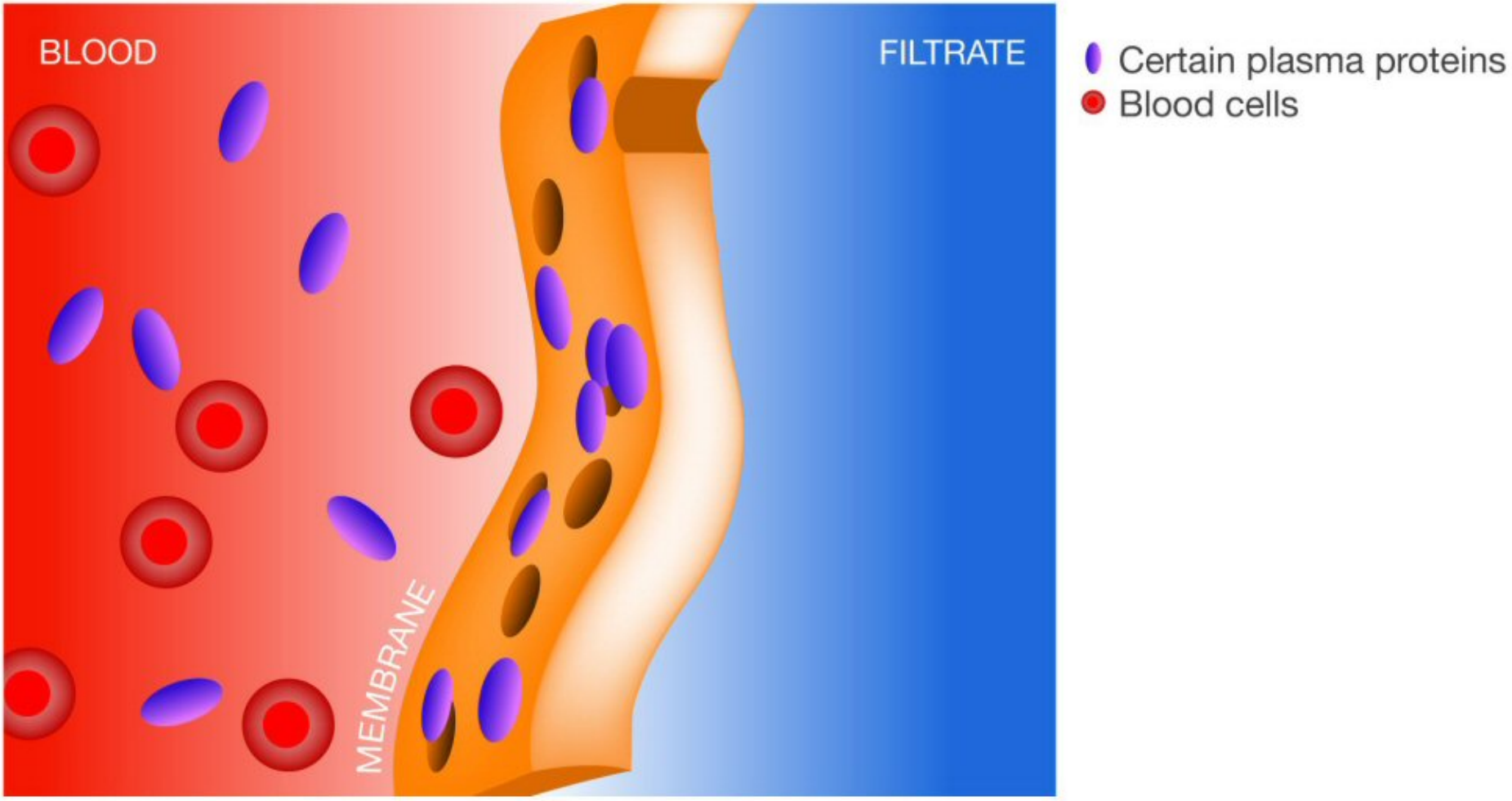
Principle of CRRT
“ Diffusion ”



Principle of CRRT
“ Convection ”



Principle of CRRT
“ Adsorption ”

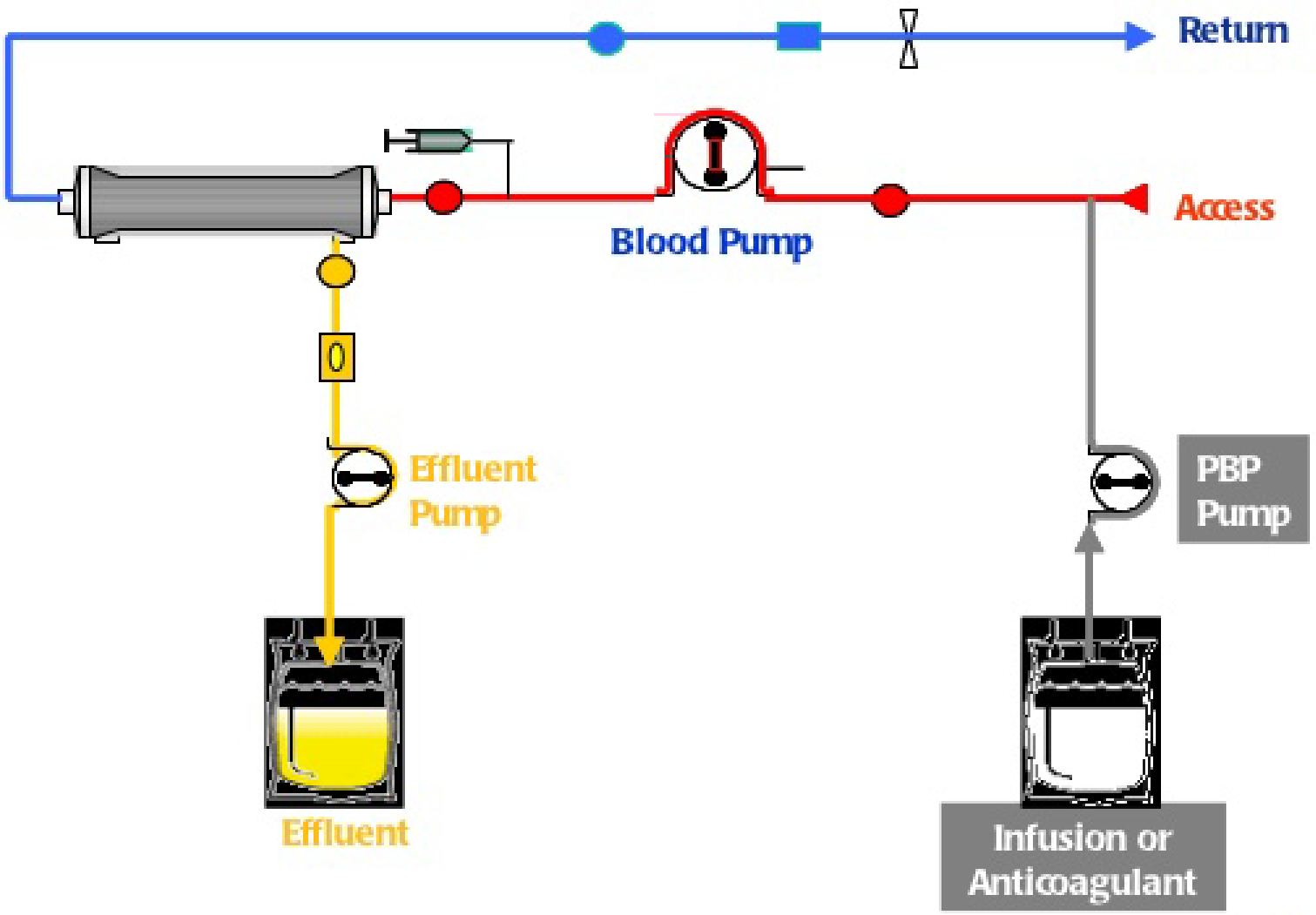


Mode of CRRT

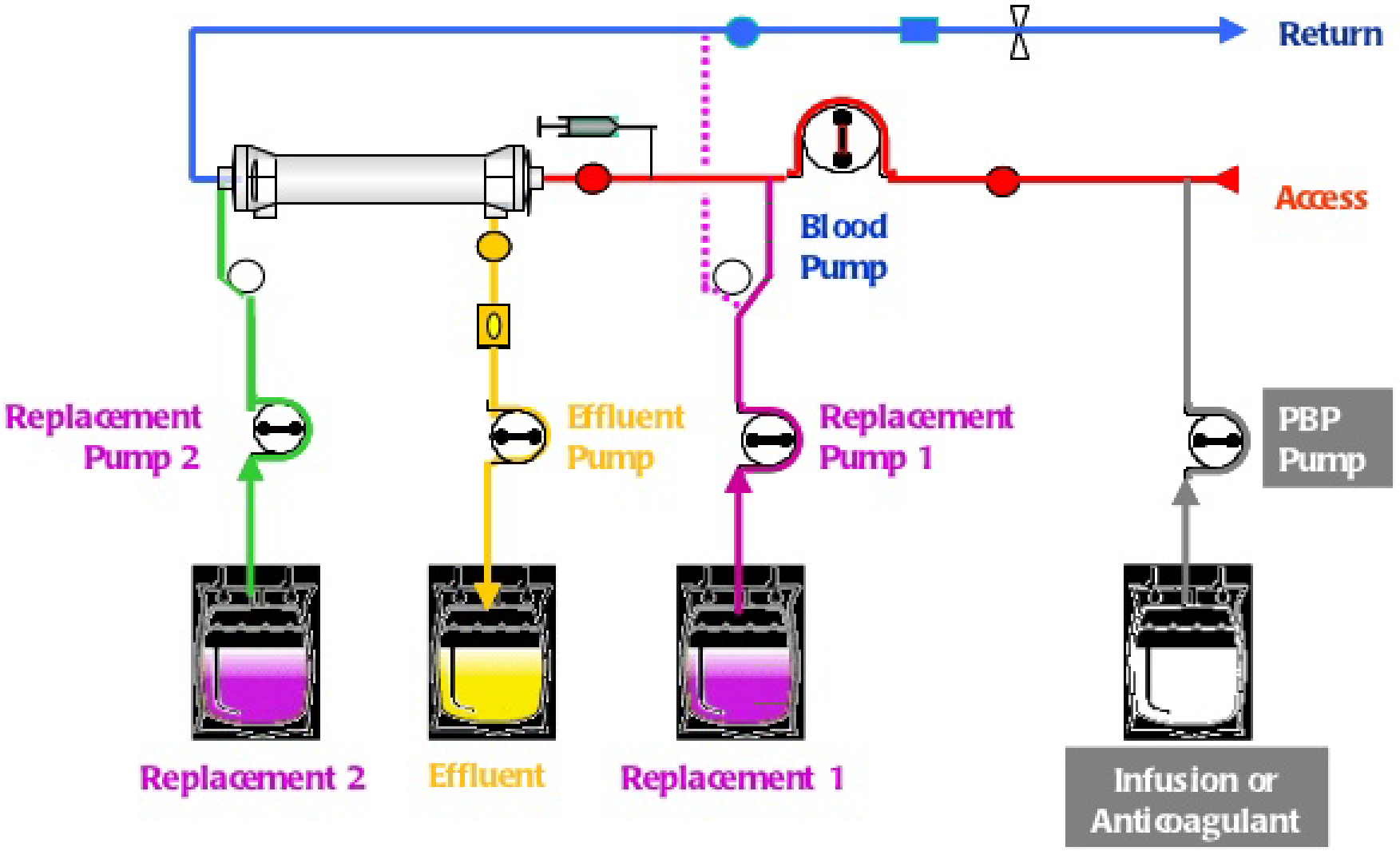
- Slow continuous ultrafiltration (SCUF)
- Continuous veno-venous hemofiltration (CVVH)
- Continuous veno-venous hemodialysis (CVVHD)
- Continuous veno-venous hemodiafiltration (CVVHDF)
- Others: single pass albumin dialysis, MARS, ECMO, TPE/DFPP, blood purification etc.

SCUF

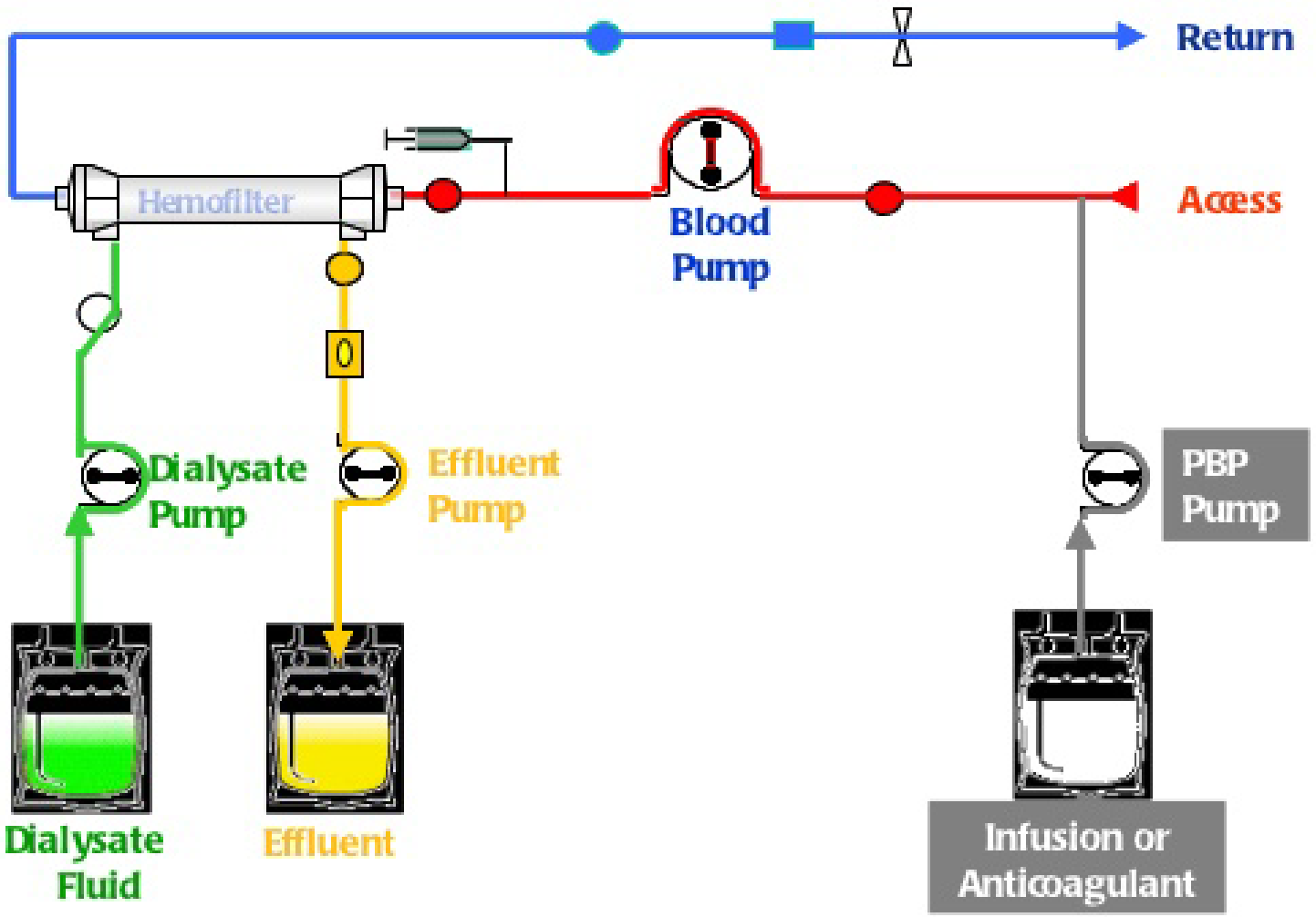
Slow Continuous UltraFiltration



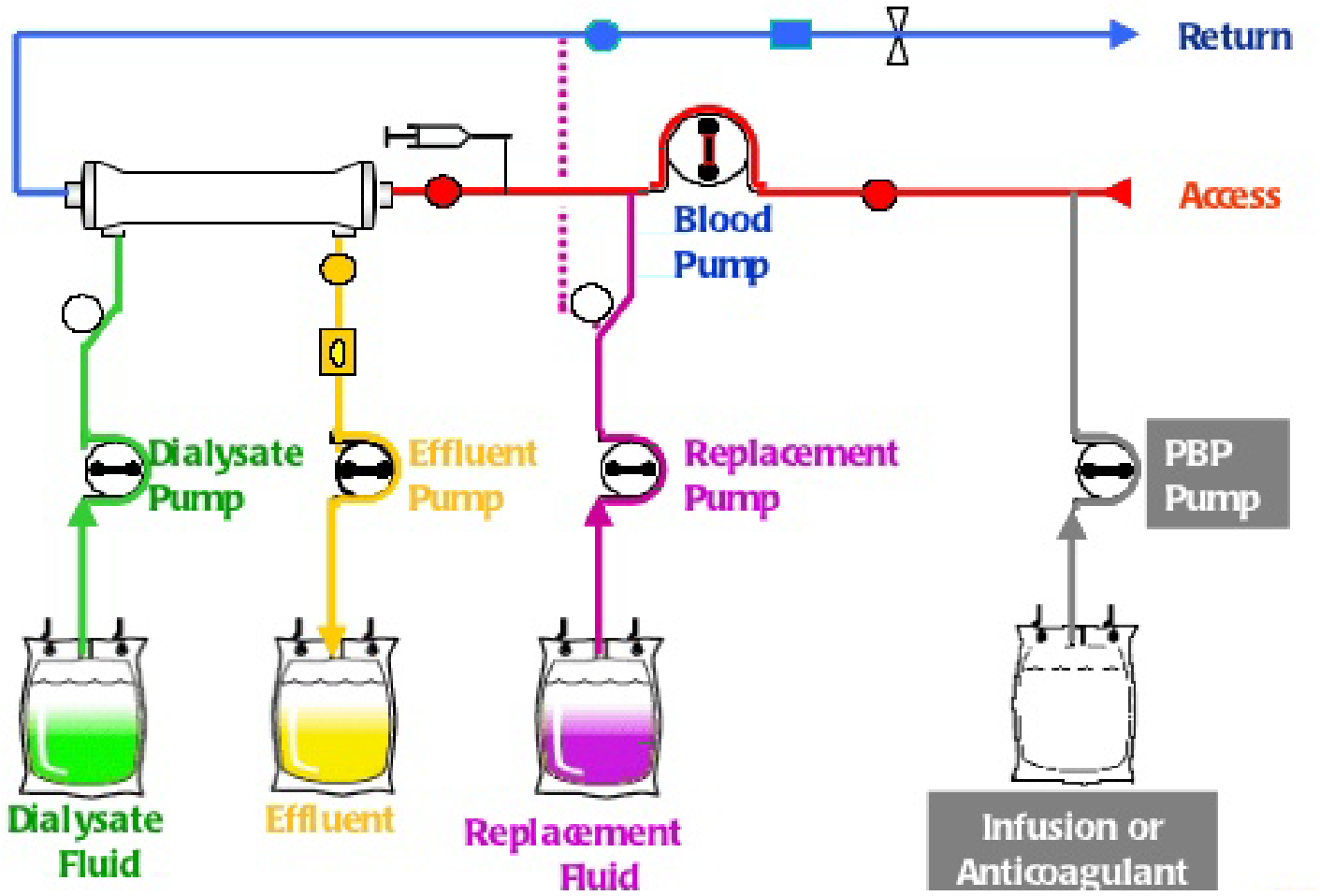
CVVH
Continuous VV Hemofiltration



CVVHD
Continuous VV HemoDialysis



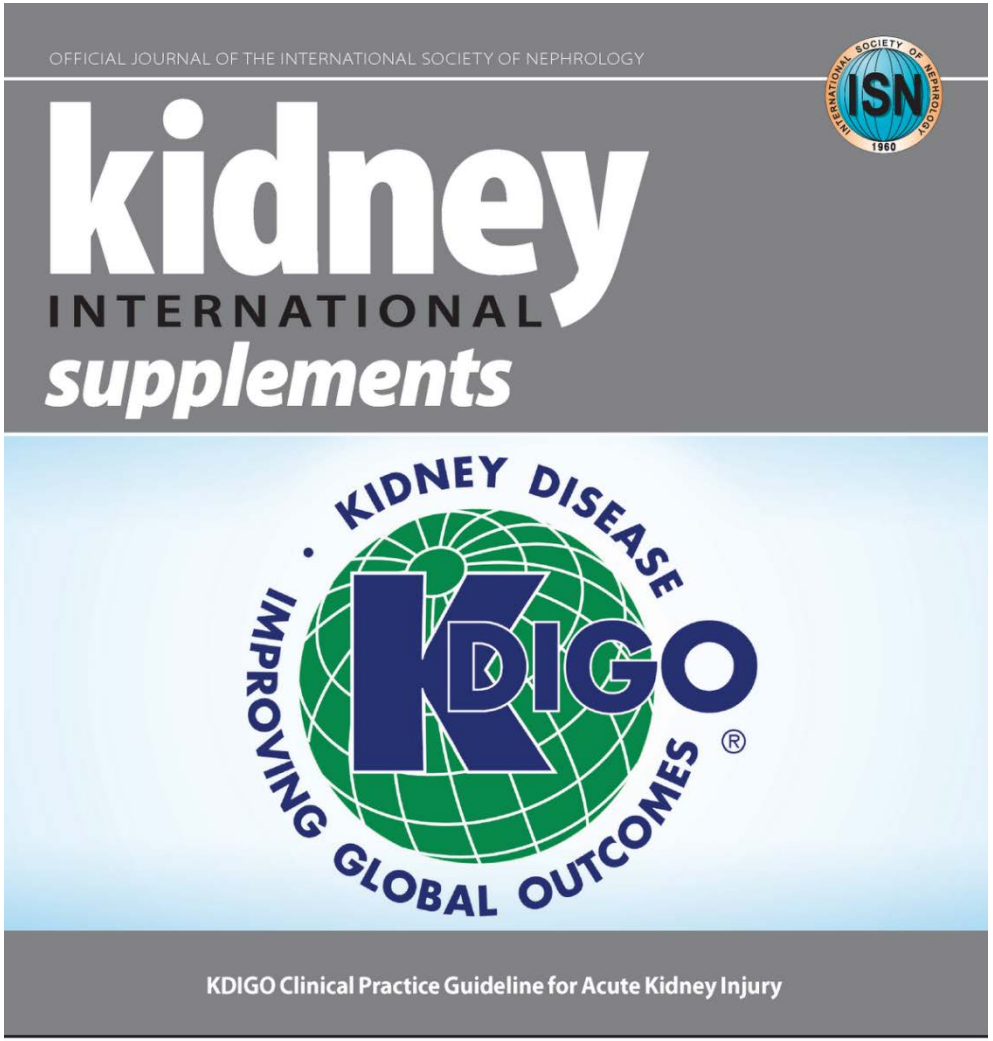
CVVHDF
Continuous VV HemoDiaFiltration



CRRT goal

- Volume control
- Solute control
- Metabolic control
- Good clinical tolerance and avoid complication
- Safe and effective anticoagulation
- Improve mortality rate
- Improve renal survival

Timing and indication of RRT



ERBP

KDIGO 2012, ERBP 2013

Life-threatening indications

- Hyperkalemia
- Acidemia
- Pulmonary edema
- Uremic complications
  (bleeding, pericarditis, etc.)

Drugs overdose, intoxication and
inborn errors of metabolism (hyperammonemia/ urea cycle defect)
Post cardiac surgery

KDIGO 2012

Renal support

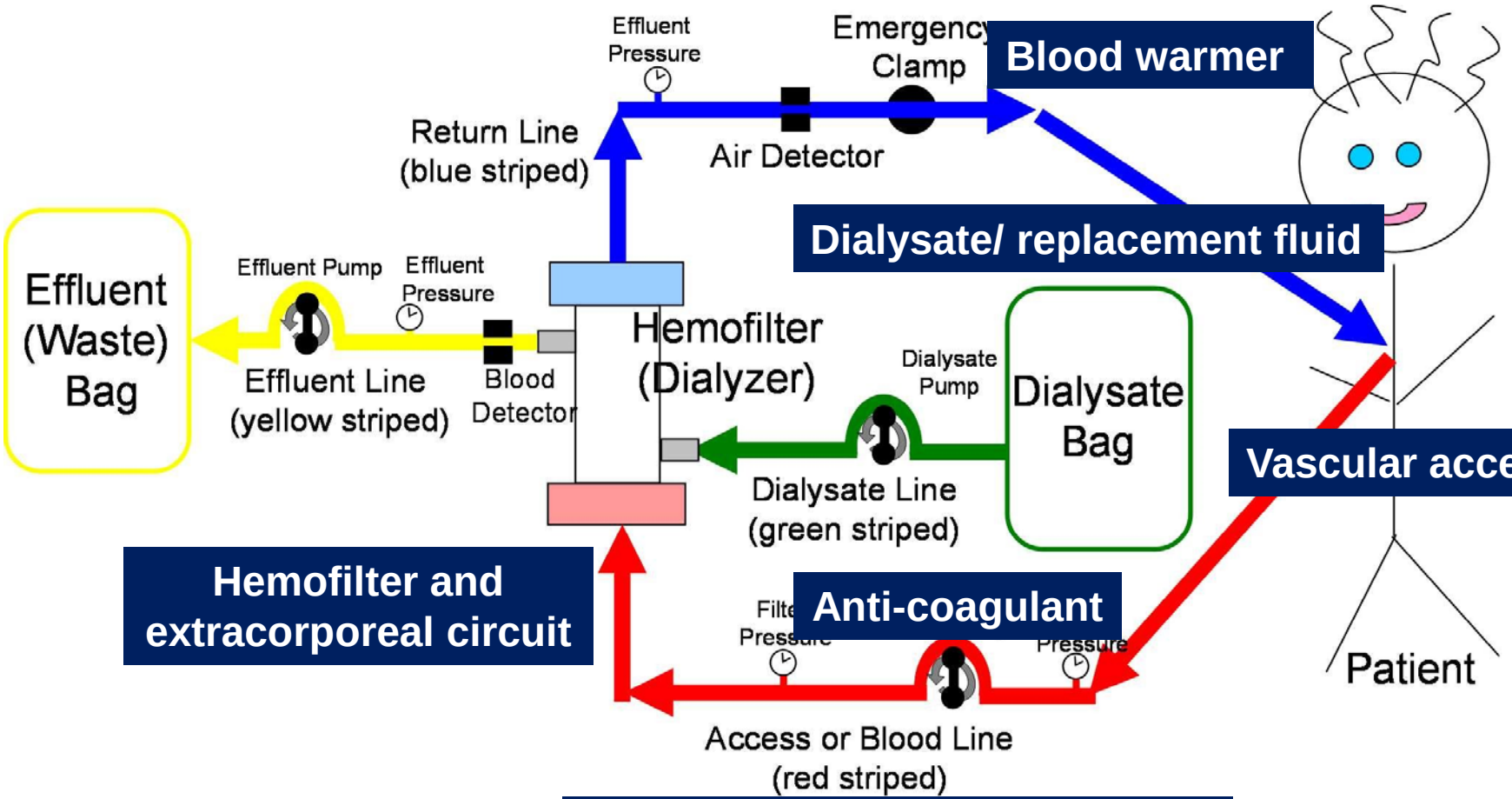
- Volume control
- Nutrition
- Drugs and blood products delivery
- Regulation of acid-base and electrolyte status
- Blood purification (cytokine and endotoxin manipulation in sepsis)

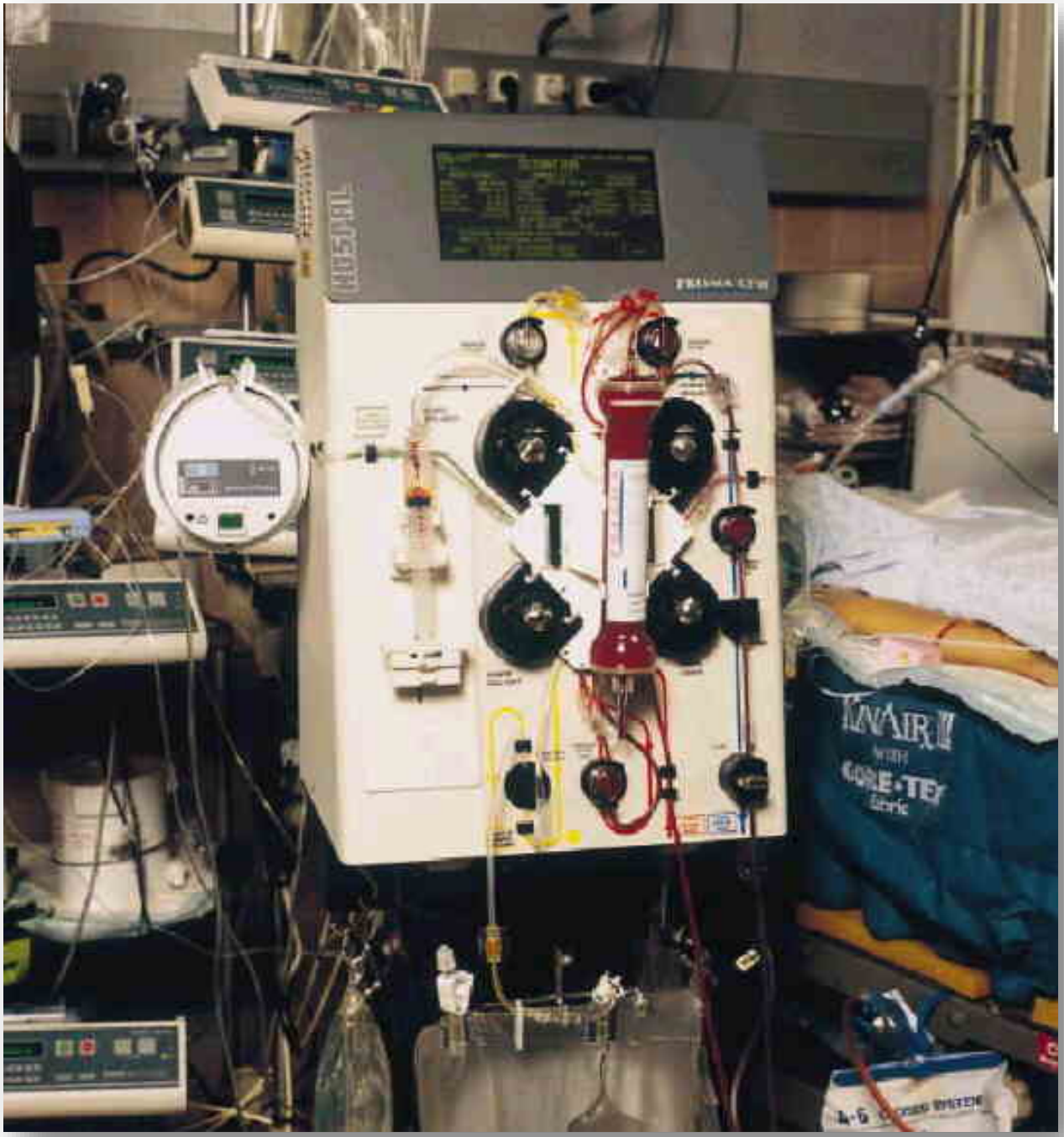
KDIGO 2012

Fluid overload and outcome in critically ill children with AKI

Author	Cohort (n)	Outcome	P
Goldstein 2001	Single-center (22)	Survivors 16%FO,Non survivors 34%FO	0.03
Gillespie 2004	Single-center (77)	%FO>10% with OR death 3.02	0.002
Foland 2004	Single-center (113)	3 organs MODS Survivors 9%FO,Non survivors 16% FO 1.78 OR death for each 10%FO increase	0.001
Goldstein 2005	Multicenter (116)	2+ organs MODS Survivors 14%FO,Non survivors 25% FO <20%FO:58% survival >20%FO:40% survival	0.002
Hayes 2009	Single-center (76)	Survivors 7%FO, non survivors 22%FO OR death 6.1 for >20%FO	0.001
Sutherland 2010	Multicenter (297)	<10%FO:70% survival 10-20%FO:57% survival >20%FO:34% survival OR 1.03 (1.01-1.05) per %FO	0.001

CRRT system & circuit





PRISMA

Specs.

Qb 10-180 ml/min

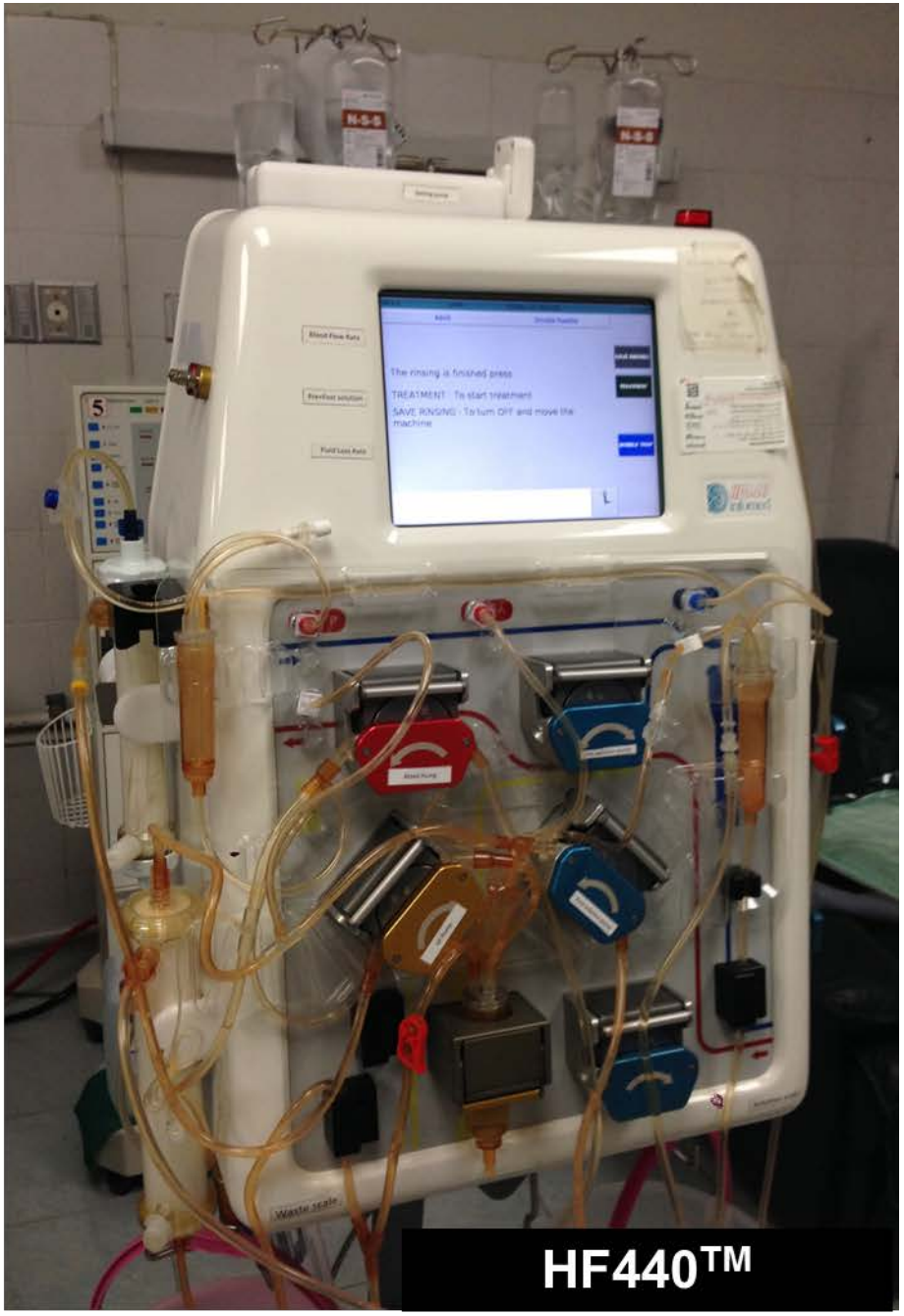
Qr 100-2000 ml/hr

(100-4500 CVVH)

Qd 100-2500 ml/kr

net UF 10-1000 ml/hr


AQUARIUS™


HF440™

Max. Qb 450 ml/min, Max Qd 8000 ml/hr predilution
8000 ml/hr postdilution, Max. net UF 2000 ml/hr

The CARPEDIEM

Cardio Renal Dialysis Emergency Machine

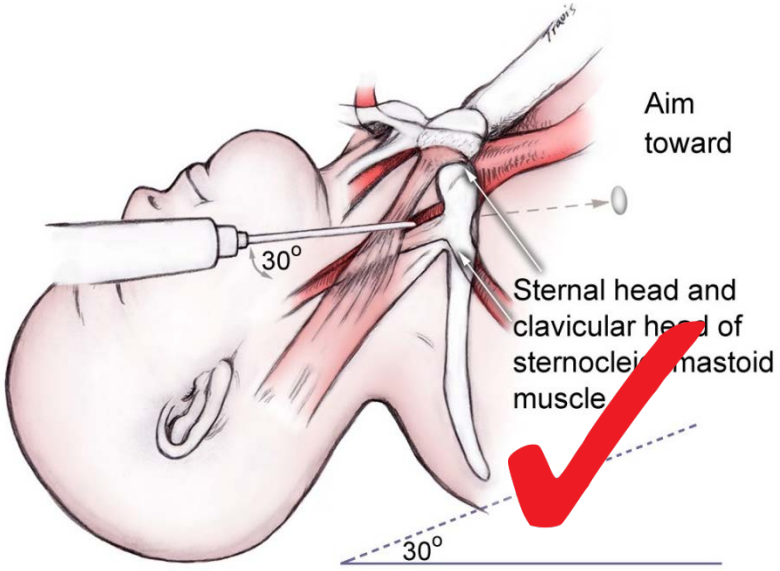
ECV 27 ml
Miniature roller pump
Qb 5-50 ml/min
Qd/Qr 0-10 ml/min
Precision scales accurate to 1 g
Filters size of 0.075, 0.15, 0.25 m^2

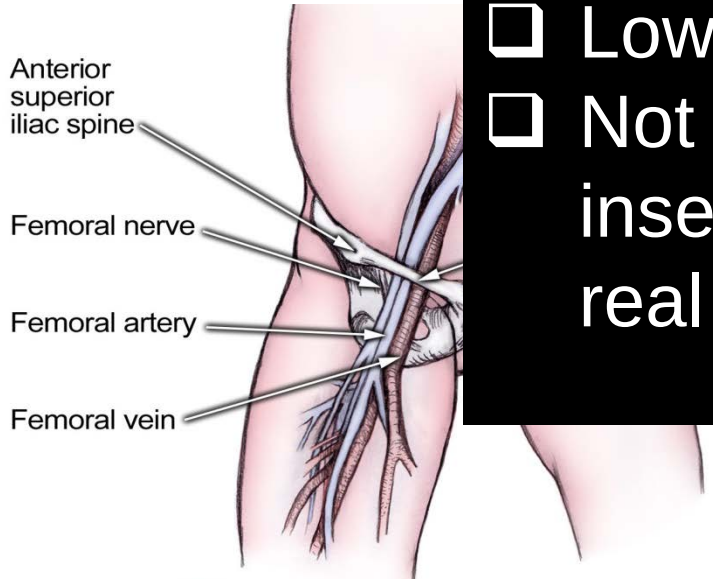
Ronco C. Lancet 2014

CRRT prescription

- ✓ Select vascular access
- ✓ Select machine/modality
- ✓ Select filter/blood line
- ✓ Prime?
- ✓ Set blood flow
- ✓ Effluent/dialysate/replacement fluid
- ✓ Pre/post-dilution
- ✓ Fluid balance plan/net UF
- ✓ Anticoagulant
- ✓ Monitoring plan

Vascular access





Rt. Internal Jugular

- ❑ Good blood flow rate
- ❑ Suitable for larger and shorter catheter
- ❑ Low rate of cathether dysfunction
- ❑ Low risk of infection
- ❑ Not too difficult to insert, and safe under real time US guided

Vascular access

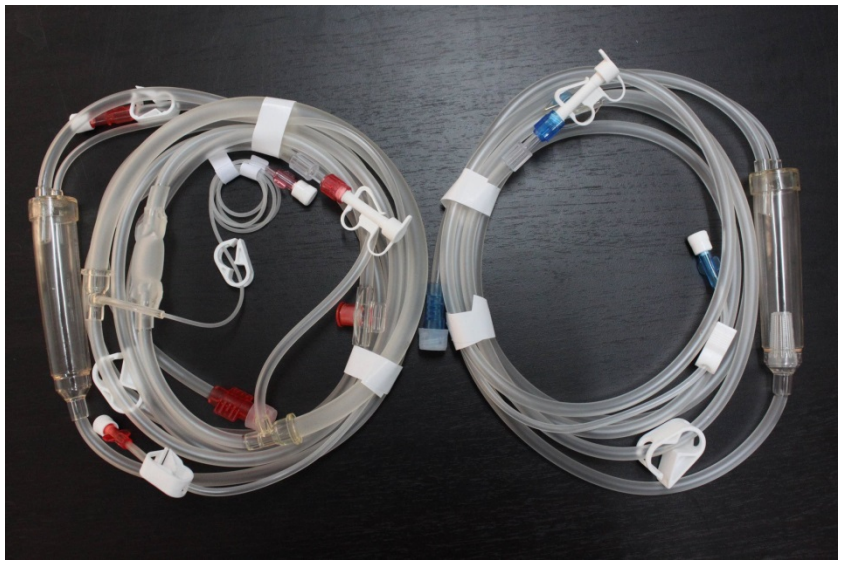
Patient size	Double lumen (Fr)
Newborn	5-7
3-6 kg	7
6-15 kg	8
15-30 kg	9-10
> 30 kg	11.5-12.5

ppCRRT registry: lower circuit survival rate

- ✓ **Small catheter (5-7 Fr)**
- ✓ **Femoral vein insertion**

Bloodline
Manual: Blood line (Kawasumi™)

Patient size	Type	Internal volume (ml)	Internal diameter (mm)
< 30 kg	pediatric	48	6
> 30 kg	adult	88	8



Bloodline

Patient size	Type	Internal volume (ml)	Internal diameter (mm)
≤ 40 kg	Aqualine S	64	6
> 40 kg	Aqualine	105	8

Filter type

- High flux
- Optimal surface area/ priming volume
- Biocompatibility
    - complement pathway
    - coagulation cascade
    - platelet, neutrophil, monocyte
- Adsorption property

Type of membrane

- Cellulose: cuprophane, cuprammoniumryon
- Modified cellulose: cellulose triacetate
- **Synthetic**: **PMMA, polysulfone, AN69, polyamide**

Hemofilter

Hemofilter (Aquamax)	Surface area (m^2)	Priming volume (ml)
HF03 (0-15 kg)	0.3	32
HF07 (>15-40 kg)	0.7	54
HF12 (>40-80 kg)	1.2	73
HF19 (>80 kg)	1.9	109

$$\sqrt{\frac{BW(kg) \times HT(cm)}{3600}}$$

Prismaflex dispossible set

Hemofilter (Prismaflex)	Surface area (m^2)
HF20 (5 -15 kg)	0.2
M60 (> 11 kg)	0.6
M100 (>30 kg)	1.0

Prismaflex™
HF20 set
Extracoporeal volume 60 ml

If extracorporeal circuit volume > 10% total blood volume, should be primed

Whole blood
PRC/NSS (1:1)
5% albumin

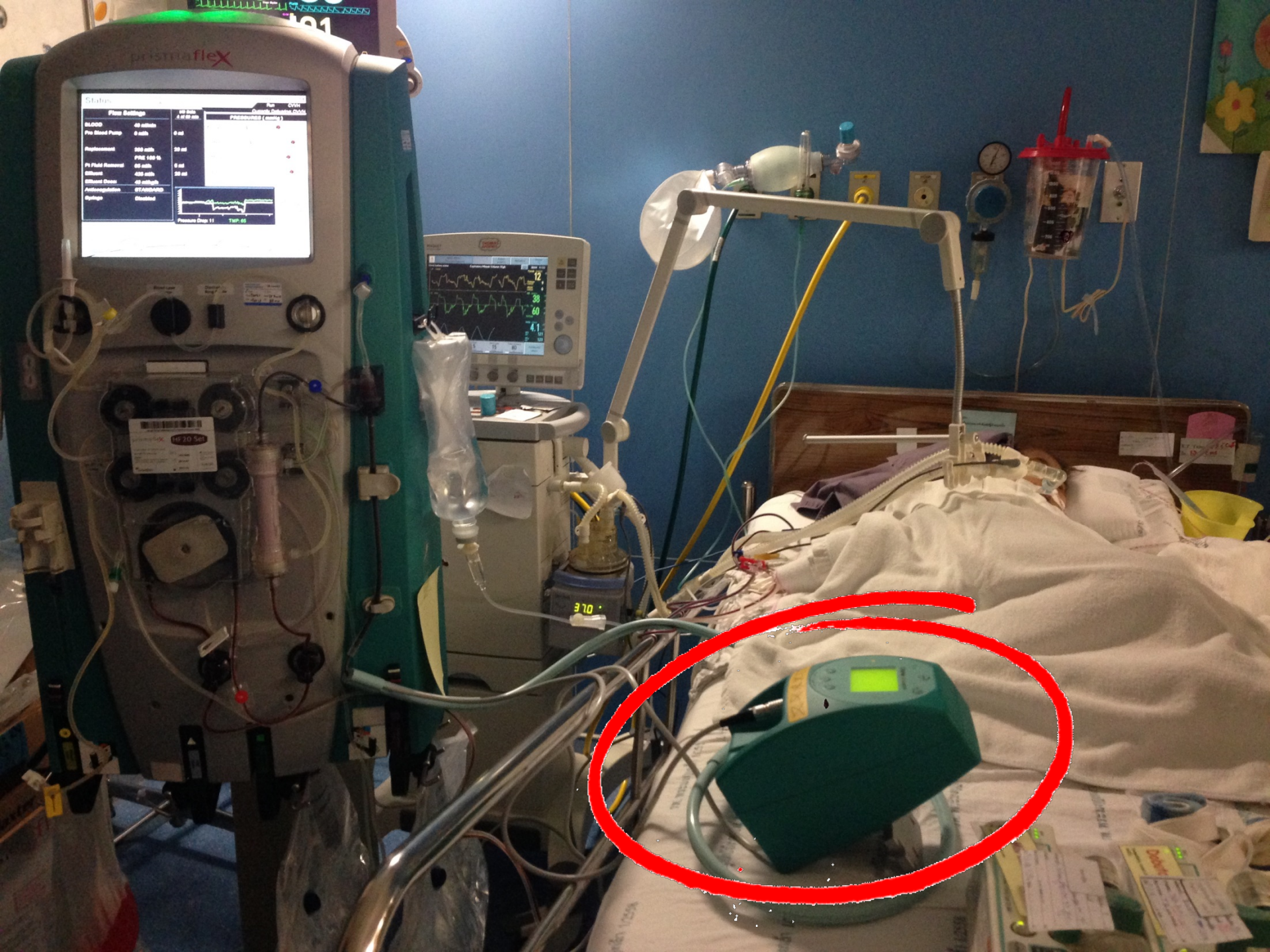
Total Blood Volume

- ✓ 100 ml/kg 0-1 mo.
- ✓ 80 ml/kg < 16 yrs
- ✓ 70 ml/kg > 16 yrs

< 15 kg : circuit prime

Downside of blood prime

- ✓ High K (5-20 mmol/l)
- ✓ Contain citrate
- ✓ May contribute to CV instability
- ✓ Bradykinin reaction


prismaflex

Blood warmer
Prismatherm II & Prismacomfort

- ✓ Pediatric warmer
- ✓ No extracorporeal volume
- ✓ Warming sleeve on return line

CRRT prescription

- ✓ QB : 2-12 ml/kg/min (4-5)
- ✓ Replacement fluid : 2 L/1.73m^2/hr
  (35 ml/1.73m^2/min)
- ✓ Dialysate : 2 L/1.73m^2/hr
- ✓ Net UF rate : 1-2 ml/kg/hr or higher

Actual fluid removal rate; AFR (ml/hr)

- ✓ A = desired net fluid hourly removal
- ✓ B = All total fluid intake
- ✓ C = All output

AFR = A + B - C

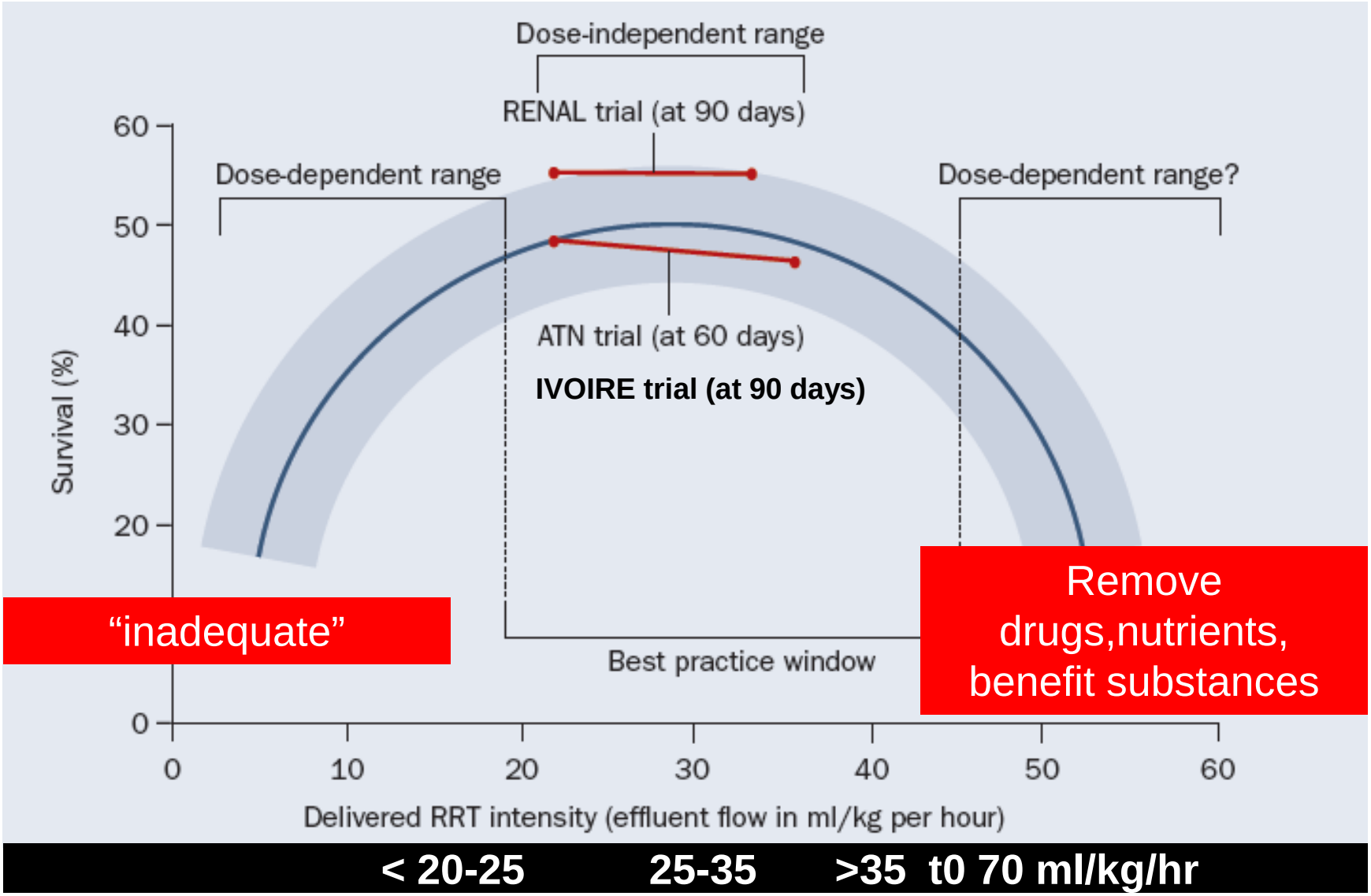
Blood flow rate

Patient size	Blood flow rate (ml/kg/min)
3-6 kg	8 - 12
6-15 kg	5 - 8
15-30 kg	4 - 6
> 30 kg	2 - 4

Blood flow dose not determine clearance in CRRT

Intensive Care Med 2009

Relationship between delivered RRT intensity and survival in critically ill patients with AKI



Kellum JA, Nat Rev Nephrol 2010

Replacement fluid/dialysate

- Glucose
- Electrolyte

  Na, Cl, K, Ca, P, Mg
- Buffer

  - lactate
  - acetate
  - bicarbonate
  - citrate

Replacement fluid/dialysate

	RL	RA	1.5%PD	Accusol 35	Costume made
Na	130	130	132-134	140	123.7
K	4	4	-	0/2/4	3.8
Cl	109	109	96-102	109-116	101.6
HCO_3	-	-	-	30-35	25.9
Lactate	28	-	40	-	-
Acetate	-	28	-	-	-
Ca	3	3	2.5-3.5	2.8-3.5	-
P	-	-	-	-	-
Mg	-	-	0.5-1.5	1-1.5	1.5
Dextrose (mg/dl)	-	-	1500	0-110	144

Replacement fluid/dialysate

	Hemosol BO	Prismasol 4	Prism0cal	Normocarb 25/35
Na	140	140	140	140/140
K	0	4	0	0
Cl	109.5	113.5	106	106.5/116.5
Ca	1.75	1.75	0	0
Mg	0.5	0.5	0.5	0.75/0.75
Lactate	3	3	3	0
Glucose	0	6.1	0	0
HCO_3	32	32	32	25/35

Additions

- Potassium chloride up to 4 mEq/L
- Calcium chloride up to 1.25 mMol/L (2.5 mEq/L)
- Potassium **phosphate** up to 1.2 mMol/L (2.4 mEq/L) or **monosodium phosphate** 0.8 ml:dialysate 1L (1 mMol/ml)

Costume made

0.45% NaCl 1000 ml +

7.5% $NaCO_3$ 30 ml

15% KCl 2 ml

20% NaCl 7.5 ml

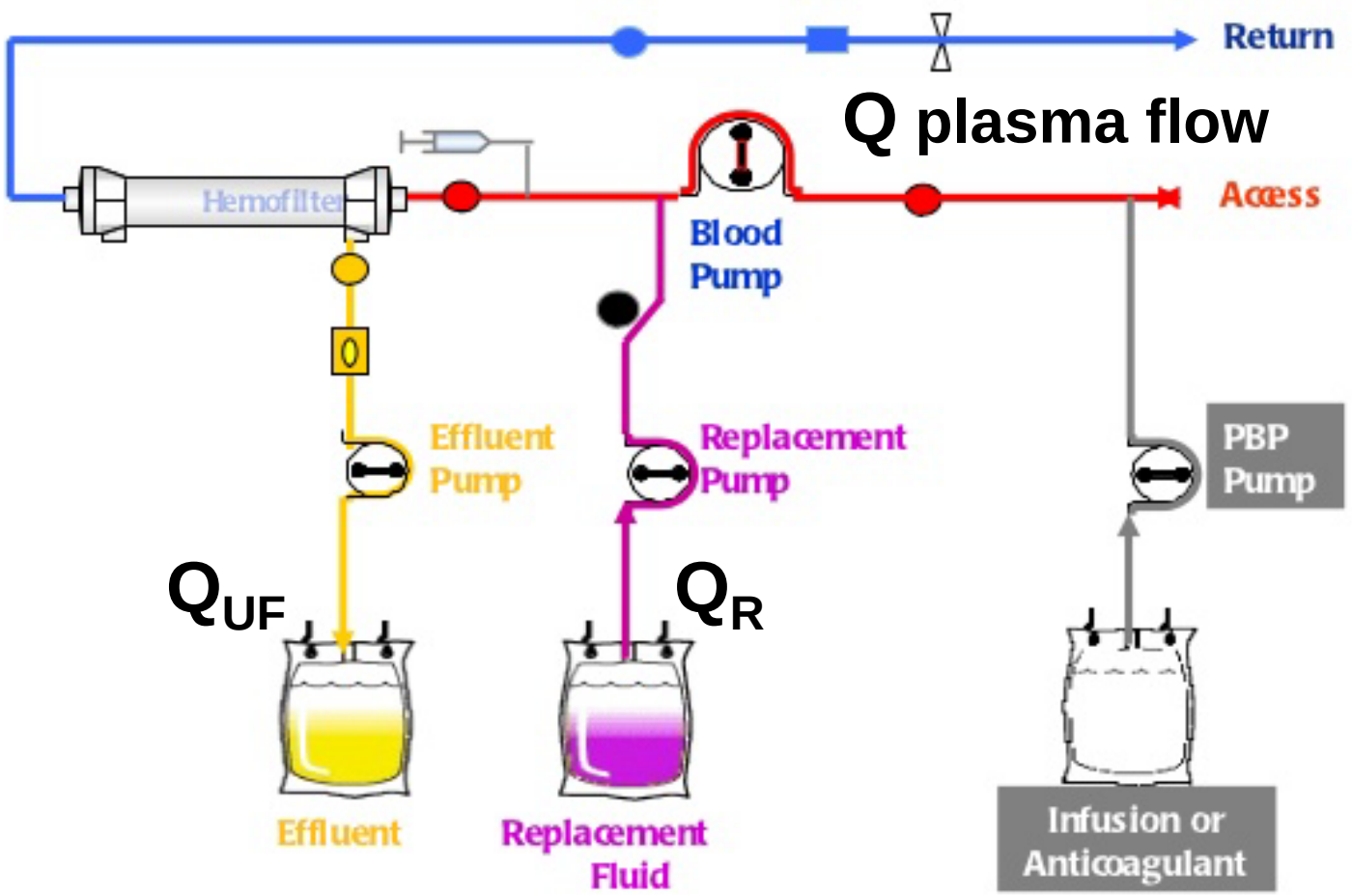
50% $MgSO_4$ 0.4 ml

50% glucose 3 ml

Preferred modality for pediatric CRRT

Pre-Dilution Replacement Solution

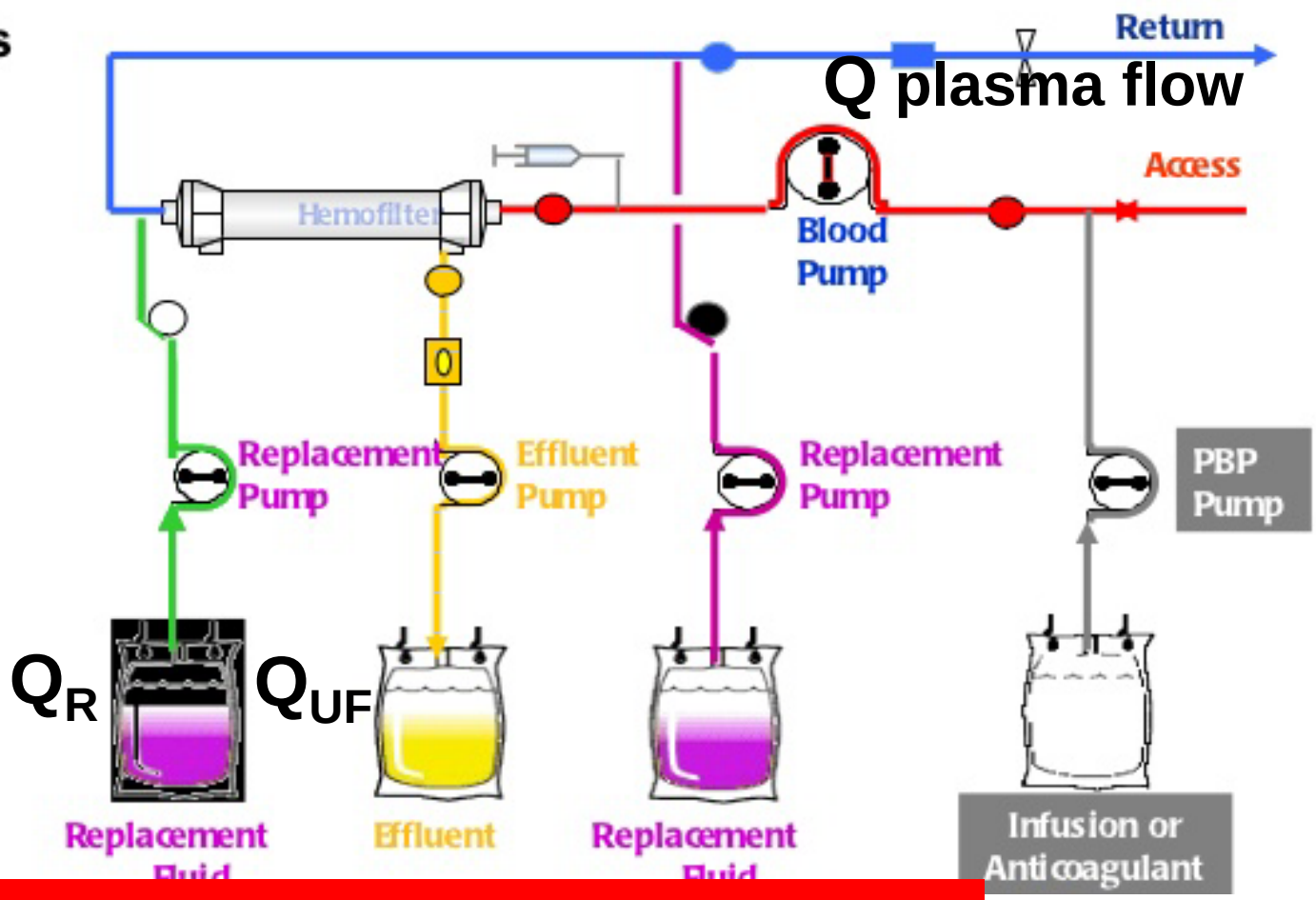
- Decreases risk of clotting
- Higher UF capabilities
- Decreases Hct. In filter



Filtration fraction = Q_{UF} / Q plasma flow + Q_R (<25%)

Post-Dilution Replacement Solution

- Consider lowering replacement rates (filtration %)
- Higher BFR (filtration %)
- Higher anticoagulation
- More efficient clearance (>15%)



Filtration fraction = Q_{UF} / Q plasma flow

Pre and Post-Dilution Replacement Solution

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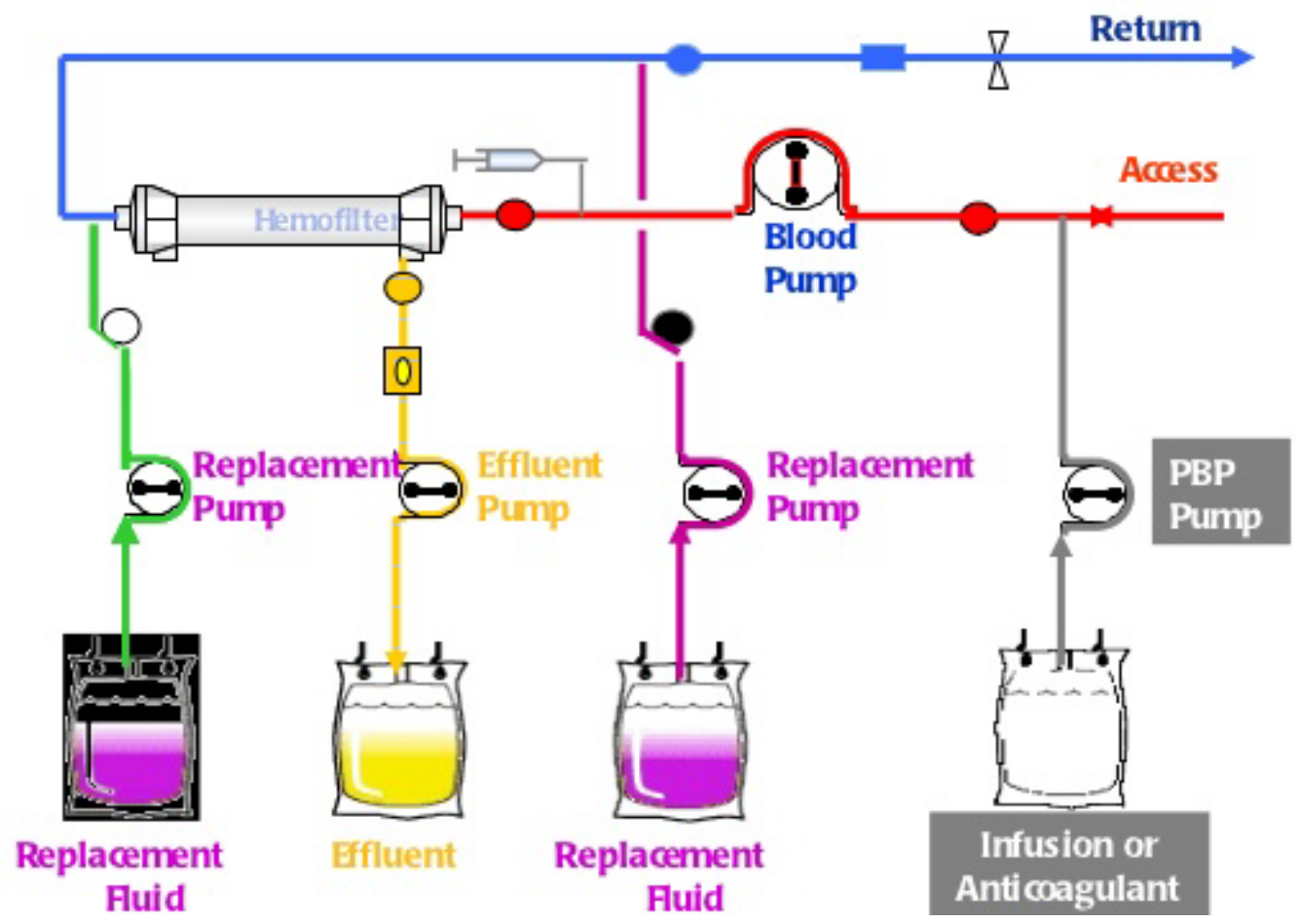


50/70%

50/30%

Clot/Thrombosis

- **Predisposing factors**

  vascular access, blood flow, hemofilter, coagulation pathway activation, convective mass transfer (filtration fraction)

- **Site of clotting**

  Hemofilter, blood line, bubble trap, catheter, area of turbulence resistance

Ideal anticoagulant

- No effect on systemic hemostasis
- No increase in bleeding risk
- Effect limited to the extracorporeal circuit
- Optimal filter performance and survival of circuit
- Short half life
- Easy to monitor and reverse the effect
- Less metabolic and electrolyte complications
- Cheap/ cost-effectiveness

Type of anticoagulant in CRRT

- No anticoagulation ✓
- Unfractionated heparin ✓
- Low molecular weight heparin
- Direct thrombin inhibitors
- Citrate ✓
- Prostaglandins

No anticoagulant

- Risk of bleeding: recent major surgery, coagulopathy, thrombocytopenia, hepatic failure
- **Technical aspects**

✓ Prime circuit with saline/heparin

✓ Blood flow rate

✓ Pre-dilution

✓ Low filtration fraction

✓ Saline flush (50-200 ml q 30-60 mins)

✓ Variable results

Heparin

- Bolus 10-30 units/kg, MT 5-20 units/kg/hr

A	B (infant)	ACTION
Qb ≥ 50	Qb < 50	
ACT <140	<170	Bolus 5 u/kg increase rate 10%
ACT140-170	170-225	No change
ACT>170	>225	Repeat in 1 hr, if still elevated, decrease rate by 10%

Keep aPTT 1.5 – 2X (35-45 sec)

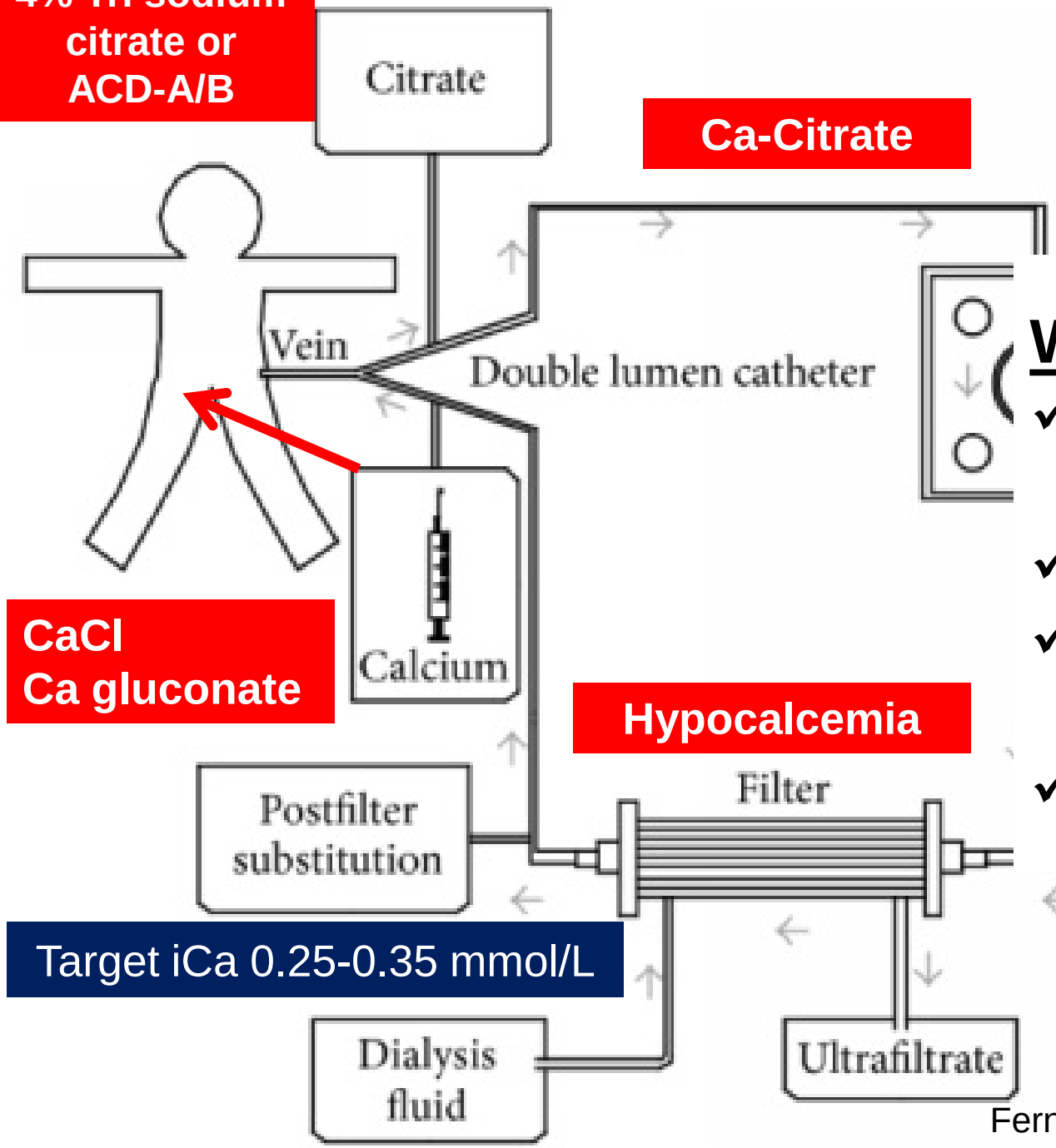
Low molecular weight heparin

- Fixed dose vs dose based on anti-Xa
- Target anti-Xa : 0.25-0.35 u/ml
- Enoxaparin
    - loading dose 0.15 mg/kg
    - MT dose 0.05 mg/kg/hr
- Nadroparin, dalteparin

Alternative anticoagulants for heparin induced thrombocytopenia (HIT)

- Danaparoid (heparinoid)
- Fondaparinux (pentasacharide)
- Direct thrombin inhibitor
  - 1st generation: hirudin, bivalirudin
  - 2nd generation: argatroban
  - 3rd generation: ximelagatran

4% Tri sodium citrate or ACD-A/B



Ca-Citrate

CaCl
Ca gluconate

Hypocalcemia

Target iCa 0.25-0.35 mmol/L

Why is citrate?

- ✓ Regional anticoagulation
- ✓ Less bleeding
- ✓ Longer circuit survival
- ✓ Buffer

ppCRRT 2014
Fernandez SN. Biomed Res Int 2014

Citrate order

- STEP 1 : Qb 3-4 ml/kg/min (50-150)
- STEP 2 : Citrate @ 1.5 X Qb (ml/hr))
- STEP 3 : $CaCl_2$ 8000 mg/0.9% NSS 1000 ml
  Start @ 0.4 x Citrate rate (ml/hr)
- Monitor circuit and patient iCa q 30 min after any change in Ca/Citrate infusion then q 2-4 hr if stable, monitor tCa q 12 hr

Citrate order

- Titration of citrate infusion depend on circuit iCa
- Titration of CaCl infusion depend on patient iCa
- Notify CCU MD and Nephrology MD if
  HCO_3 > 30 mmol/l
  Patient iCa < 0.75 mmol/l
  Na > 150
- Circuit iCa 0.25-0.39 mmol/L
- Patient iCa 1.1-1.3 mmol/L

Citrate lock

- Rising patient total Ca (>2.8 mmol/l)
- Dropping patient iCa
- Decreasing pH (wide gap metabolic acidosis)
- Decreasing HCO_3
- Risk : liver failure
- RX : Citrate and Ca infusions were stopped for 2-4 hrs. to allow tCa to drop, then restart at 70% of the previous dose

	Cause	Treatment
Metabolic acidosis	Citrate accumulation	Give more buffer, D/C or decrease citrate, increase citrate removal
Metabolic alkalosis	Too much citrate, low effluent flow, inadequate replacement solution/dialysate	D/C or decrease citrate, increase citrate removal, change to CVVHDF
Hypocalcemia	Ca^{2+} loss, citrate accumulation	Increase Ca^{2+} replacement, D/C or decrease citrate, increase citrate removal
Hypercalcemia	Over Ca^{2+}replacement	Decrease Ca^{2+}replacement

Monitoring

- Clinical: V/S, I/O
- Laboratories

- ABG, Na, K, Cl, HCO3, Ca, P, Mg, BS q 4-12 hr
- BUN, Cr, CBC, PT,PTT q 12-24 hr
- ACT/ PTT depend on heparin protocol (q 4 hr)
- iCa, Ca, total Ca/iCa depend on citrate protocol

- Venous pressure: keep < 150-200 mmHg

Complications

- **<u>Vascular access</u>**
- Bleeding/ hematoma
- Thrombosis
- Hemothorax, pneumothorax
- Arrhythmia
- Air embolism
- Infection

Santiago MJ Crit Care 2009

Complications

- **<u>Extracorporeal circuit</u>**
- Air embolism
- Clotting
- Hypothermia
- Bioincompatibility
- Anaphylaxis
- **Bradykinin release phenomenon**

Bradykinin reaction

- AN 69 , blood prime, acidosis
- Severe hemodynamic instability at start of circuit (5-10 min)
- **Prevention**

  Avoid AN69 membrane or use AN69 ST (surface treated)

  Correction of acidosis in patient/circuit

  Bicarb 2 mmol/kg with blood prime

  Avoid blood prime

Complications

- **<u>Hematologic complication</u>**
- Bleeding
- Hemolysis
- Thrombocytopenia
- Heparin induced thrombocytopenia
- Citrate: hypocalcemia, hypernatremia, metabolic alkalosis, metabolic acidosis, **citrate intoxication (citrate-locked)**

Complications

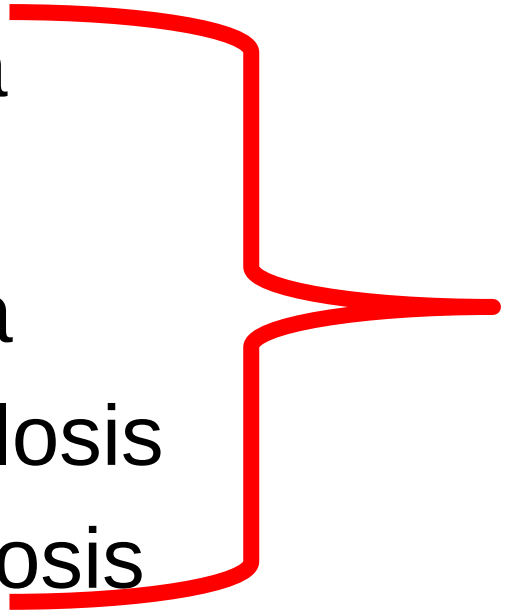
- **Associated with CRRT**
- **Hemodynamic instability** ✓
- Fluid balance error
- **Electrolyte and acid-base disturbance** ✓
- Nutrient losses (need protein 2.5-3 g/kg/day)
- Drugs removal*
- Delayed renal recovery

Santiago MJ.Crit Care 2009

***Veltri MA. Pediatr Drugs 2004**

Electrolytes disturbance in CRRT

- Hypophosphatemia
- Hypokalemia
- Hypernatremia
- Hypocalcemia
- Hypercalcemia
- Metabolic alkalosis
- Metabolic acidosis



Citrate*

Summary

- CRRT is preferred modality for critically ill with AKI/fluid overload especially in unstable patients
- CRRT is a complex therapy requiring substantial technical expertise
- There are advantages and disadvantage to each RRT which need to be clearly understood in order to best deliver care

WE BELIEVE

PMK KIDNEYKIDS CARE

Pediatric Nephrology PMK