Pediatric CRRT 2020

Online Web Symposium

일 자 | 2020. 9. 12. (토) 09:20 – 12:30

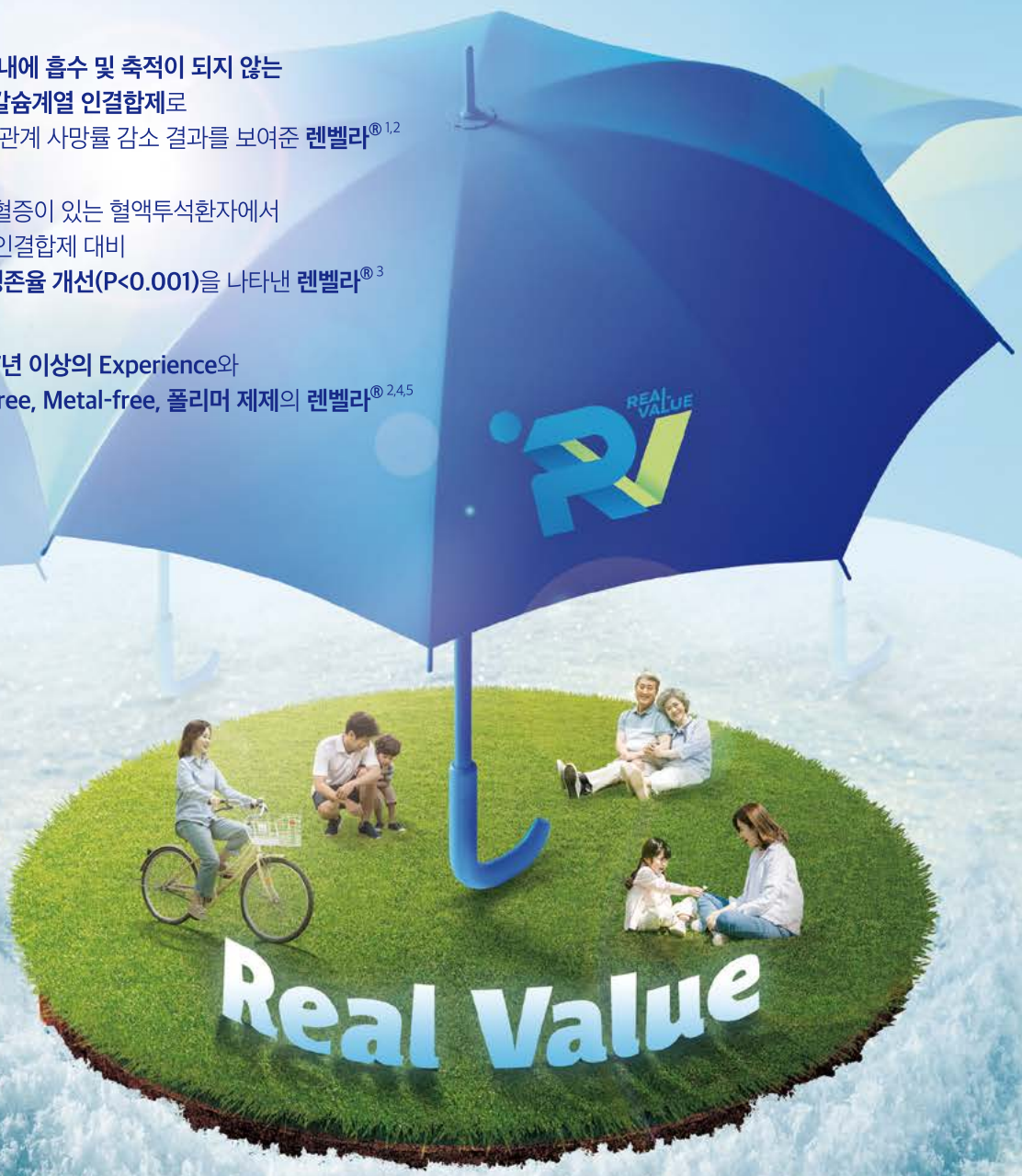
진 행 | Online Web Symposium

대한소아신장학회

SANOFI

Real Value Renvela®

- **체내에 흡수 및 축적이 되지 않는 비칼슘계열 인결합제**로 심혈관계 사망률 감소 결과를 보여준 **렌벨라®** [1,2]
- 고인산혈증이 있는 혈액투석환자에서 칼슘계 인결합제 대비 **유의한 생존율 개선(P<0.001)**을 나타낸 **렌벨라®** [3]
- **국내에서 7년 이상의 Experience**와 **Calcium-free, Metal-free, 폴리머 제제**의 **렌벨라®** [2,4,5]



References 1. Renvela [package insert]. Cambridge, MA: Genzyme Corp. 2016 **2.** Rodriguez-Osorio L, et al. Nefrologia. 2015;35(2):207-217. **3.** Di Iorio B, et al. Am J Kidney Dis 2013;62:771-778. **4.** 식품의약품안전처. 렌벨라 허가정보. nedrug.mfds.go.kr Accessed 16 Mar 2020 **5.** Connor et al J Polym. Sci. Part A: Polym. Chem. 2017; 55. 3146-3157

렌벨라®정(세벨라머탄산염) 렌벨라®산0.8그램(세벨라머탄산염) [원료약품 및 그 분량] 렌벨라정 1정 중 세벨라머탄산염(별규) 800.0mg, 렌벨라산 1포 중 세벨라머탄산염 (별규) 800mg **[효능·효과]** 투석을 받고 있는 만성 신장질환 환자의 혈청인 조절 **[용법·용량]** 1일 3회 식사와 함께 복용. 산제 복용시 이 약 1포는 최소 30mL의 물로 완전히 혼합하여 30분 이내에 복용하고, 복용 전에 재현탁한다; 1) 인산결합제를 복용하고 있지 않는 환자에 투여: 이 약의 권장초기용량은 0.8g 내지 1.6g 이며, 이 약 1~2정(포)을 다음과 같이 혈청 인 수치에 따라 매 식사와 함께 복용한다. 혈청 인 5.5 - 7.5 ㎎/dL의 경우 1회 1정(포), 1일 3회, 7.5 ㎎/dL이상의 경우 1회 2정(포), 1일 3회, 2) 세벨라머 염산염 정제를 복용하고 있는 환자에서 이 약을 대체 투여: 동일 용량을 투여한다. 투석을 받는 만성신장질환 환자에서 연구된 세벨라머 탄산염의 최대 1일 용량은 14g이었다. 3) 세벨라머 탄산염의 정제에서 산제로 또는 산제에서 정제로 대체투여: 동일 용량을 투여한다. 4) 초산칼슘제제를 복용하고 있는 환자에게 이 약을 대체 투여하는 경우 초산칼슘제제 (1정당 초산칼슘 667mg) 1회 1정, 1일 3회 시 이 약 1회 1정(포) 1일 3회, 초산칼슘제제 1회 2정,1일 3회 시 이 약 2정(포) 1회, 1일 3회, 초산칼슘제제 1회3정, 1일 3회 시 이 약 1회 3정(포), 1일 3회 5) 이 약을 복용하고 있는 모든 환자에서의 용량 조절 목표 혈청 인 수치에 도달하기 위해 적절한 용량 조절이 필요할 수 있다. 필요 시 2주 간격을 두고 1일 3회 이 약의 용량을 0.8g씩 증량 또는 감량한다. **[사용상의 주의사항] [금기]** 이 약의 주성분 및 부형제에 과민한 환자, 저인산혈증 환자, 장폐색 환자 (이 약은 장관내에서 팽윤하여 장관천공을 일으킬 우려가 있다.) **[신중투여]** 장관협착 또는 변비가 있는 환자 **[이상반응]** - 혈액투석환자 대상으로 한 연구에서 세벨라머 탄산염 정제의 이상반응과 세벨라머 염산염에서 보고된 이상반응이 유사하였다. 혈액투석환자를 대상으로 한 또 다른 교차연구에서 세벨라머 탄산염 산제의 이상반응과 세벨라머 염산염에서 보고된 이상반응이 유사하였다. - 세벨라머 염산염 연구에서, 세벨라머 염산염으로 치료받은 환자 (n=99)의 5% 이상에서 발생한 이상반응 : 구토(22%), 구역(20%), 설사(19%), 소화불량(16%), 복통(9%), 고창(8%), 변비(8%) - 복막투석환자 대상으로 한 세벨라머 염산염 연구에서 대부분의 이상반응은 혈액투석 환자에서 관찰된 이상반응과 유사하였다. - 세벨라머 탄산염 및 세벨라머 염산염의 시판 후 확인된 이상반응 : 과민반응, 가려움증, 발진, 복통, 대변 막힘, 흔하지 않은 케이스로 장폐색증과 장폐쇄증, 장관천공. 변비증상이 나타나거나 기존의 변비증상이 심해진 환자는 중증의 합병증을 피하기 위해 적절한 의료처치가 필요하다.
※ 보다 자세한 내용은 홈페이지나 제품설명서를 참고하시기 바랍니다. [문안개정연월일] 2019.06.03.

(주)사노피-아벤티스 코리아 서울특별시 서초구 반포대로 235 (반포동) Tel .02)2136-9000 Fax. 02)2136-9099

Renvela sevelamer carbonate

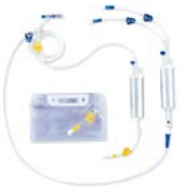
SAKRSSC.20.03.0320(20.03)

Paediatric Dialysis

Special solutions for special people

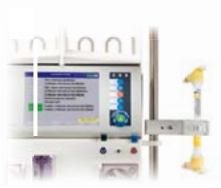
sleep•safe

Cycler for automated peritoneal dialysis



PD-Paed Plus

For acute and chronic PD in premature babies, neonates and infants



multiFiltrate CRRT

Treatment of acute renal failure in paediatric intensive care

5008

First HD machine validated for treatment of chronic patients > 10 kg

BCM - Body Composition Monitor

Assessment of hydration and nutritional status

"The right fit for paediatric patients"

㈜프레제니우스메디칼케어코리아는 콩팥병과 관련된
우수한 제품과 차별화된 서비스를 제공하는 콩팥치료 전문기업입니다.

FRESENIUS
MEDICAL CARE

Baxter

모든 CRRT 환자들에게 사용할 수 있는 쉽고, 안전한 Baxter의 Premium Solution으로 시작해 주십시오 !

Making possible personal.

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초대의 글

안녕하십니까?

COVID-19 감염증이 지속되는 의료 현장에서 어린이들의 건강을 위해 최선을 다하시는 선생님들께 감사 드립니다.

Critical care가 필요한 소아청소년 환자에서 급성신손상은 환자의 예후를 악화시키는 중요한 합병증입니다. 대한소아신장학회는 소아청소년 환자의 신손상을 연구하고 효과적으로 치료하기 위해 2018년부터 Pediatric CRRT Workshop을 개최하였습니다.

지속적 신대체요법 (Continuous renal replacement therapy, CRRT)은 혈역학적으로 불안정한 환자들에서 안전하고 효과적으로 수분과 노폐물을 제거할 수 있는 치료법으로, 선천성 대사이상, 패혈증에 동반되는 대사성 산증의 치료에도 활용되고 있습니다. 따라서 PICU와 NICU, 응급환자와 중환자의 치료에서 반드시 필요한 치료방법입니다.

“Pediatric CRRT 2020”에서는 모든 소아청소년과 의사와 중환자실 의료진, 소아CRRT를 활용하고자 하는 모든 분들께서 소아CRRT를 쉽게 시작하고 정확하게 적용하실 수 있도록 강의를 마련하였습니다.

올해는 COVID-19로 인하여 온라인 학술대회로 진행하기로 하였습니다.

여러 질환과 환경에서의 CRRT의 적용에 대한 강의와 질의 응답 시간으로 준비하였으니 관심 있는 선생님들의 많은 참여와 토론을 부탁 드립니다.

소아신대체요법연구회

대한소아신장학회 이사장 **김기혁**

회장 **배기수**

Pediatric CRRT 2020

일시 : 2020년 9월 12일(토) 09:20 - 12:30
진행 : Online Web Symposium

I. How to Conduct Pediatric CRRT

좌장: 조희연(성균관의대)

CRRT in pediatric patients

Joo Hoon Lee

Asan Medical Center Children's Hospital
Departementof Pediatrics, Division of Nephrology

Choice of Filter

Fluid balance

Plasma volume: 4% of body weight = 1000 ml X 0.04/kg
= 40 ml/kg

Extracorporeal volume: < 10-20% of plasma
< 40 X 0.1~0.2 ml/kg
< 8 mL/kg

Bwt	3 kg	10 kg	60 kg
TBW(mL)	2,100 (70%)	6,000 (60%)	36,000 (60%)
Plasma(mL)	120	400	2,400
ECV(mL)	24	80	480

Prisma/prismaflex Kits

( )은 prismaflex

contents	**Prisma M10**	**Prismaflex HF20**	**ST60**	**ST100**
Application	10Kg 미만	8Kg이상	10Kg이상	30Kg이상
SA (m²)	**0.042**	**0.2**	**0.6**	**1.0**
M. material surface	AN69 Negative	PAES Neutral	AN69ST Neutral	AN69ST Neutral
Priming vol (ml)	50	60	86 (93)	107 (152)
UF coefficient (ml/h/mmHg)	0.87 QB=15ml/min	-	15 TMP 25-100	25 TMP 25-100
Sieving co. 조건(ml/min) urea/creatinine Vit B12 Inulin Myoglobin Albumin	Qb=10,Quf=2 1/1 1 1 0.42 < 0.01	Qb=50, Quf=10 1/1 1 0.92 - < 0.01	Qb=100, Quf=20 1/1 1 0.96 0.58 < 0.01	Qb=100, Quf=20 1/1 1 0.96 0.58 < 0.01
Sterilization	ETO	ETO	ETO	ETO

Problems associated with blood priming

1. Bradykinin release syndrome with AN69 circuits
   Blood with a low pH (pH 6.1-6.4)
   → Contact with electronegative membranes
   → Elicits (pH dependent) bradykinin response
   → Cause tachycardia, vasodilatation, hypotension
   cf) Polyarylethersulfone filter, such as HF20
2. Hypocalcemia
   Low iCa (~ 0.10 mmol/L) due to citrate.
3. Hyperkalemia
4. Prevention
   correct pH, calcium supply, washed RBC

Blood Priming Protocol

1. pRBC 50 ml + NS 50 ml ⇒ Make Hct 0.45 (0.3?)
2. Add Heparin 100 u.
3. Add 3% CaCl2 250 mg (8 ml) (?)
4. Agitate gently.
5. Add bicarbonate 30 mEq (30 ml).
6. Agitate gently.
7. Circuit prime with the blood.
8. Connect the access and return lines to a 50ml bag of 0.9% saline.
9. Start the PRISMA into closed circuit.
   (BFR 100ml/min, DFR 1000ml/hr, RFFR 200ml/hr)
10. Check pH, Ca^{++}

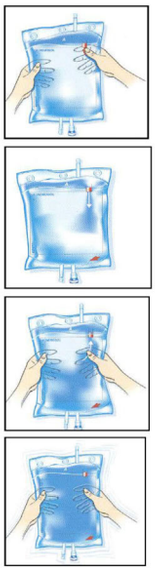
Solution

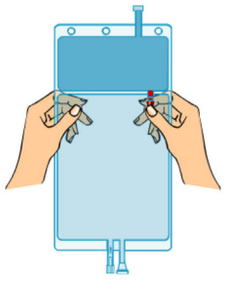
Replacement and Dialysate Fluids

Hemosol bicarbonate

Hemosol B0 사용법

Ionic formula of final solution obtained after transfer of bicarbonate into electrolyte solution	
IONIC FORMULA	mmol / l
Sodium Na^+	140
Calcium Ca^{++}	1.75
Magnesium Mg^{++}	0.50
Chloride Cl^-	109.5
Lactate $C_3H_5O_3^-$	3
Bicarbonate HCO_3^-	**32**
Potassium K^+	0
Theoretical osmolarity (mOsm/l)	287





Na 농도를 바꾸지 말 것!!! → 급격한 Na 농도의 변화는 뇌병변을 유발한다.

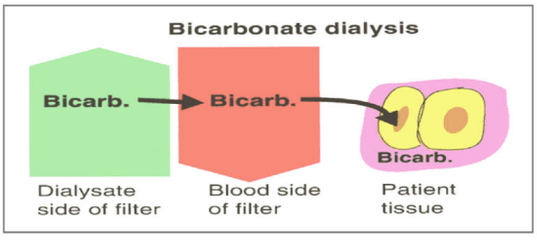
고칼륨혈증 있다고 K free로 줄 필요 없다: 어차피 빨리 교정된다.

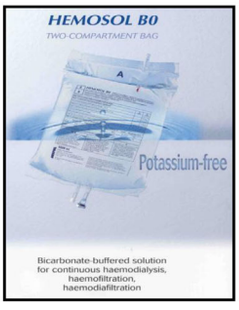
Hypercalcemia가 동반될 경우 생리 식염수에 Ca 제외한 나머지 이온 농도를 맞출 것

Replacement and Dialysate Fluids

Buffer의 종류

❶ Bicarbonate buffer
체내 metabolic conversion이 필요 없고 간이나 심혈관계의 기능부전 시 M. acidosis의 가속화나 심혈관계의 안정성을 위해 반드시 선택되야 하는 buffer.





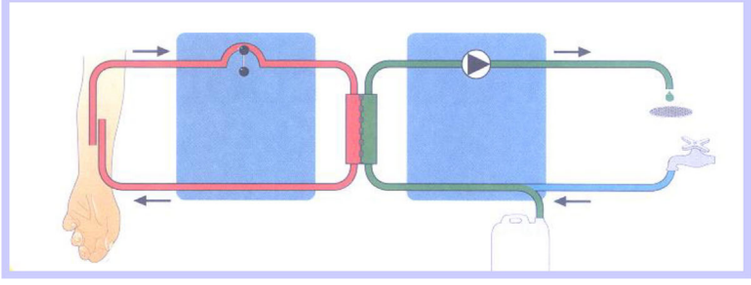
❷ Lactate buffer
체내에 흡수되어 bicarbonate를 생성하는 화합물로, 간이나 다른 장기에서 대사되어 중탄산염이 된다.

	Na	K	Ca	Mg	Cl	HCO	P
Hemosol B0	140	0	1.75	0.5	109.5	32	0
multiBic 4K	140	4	1.5	0.5	113	35	0
Phoxillium	140	4	1.25	0.6	116	30	1.2

Mechanism of Treatment

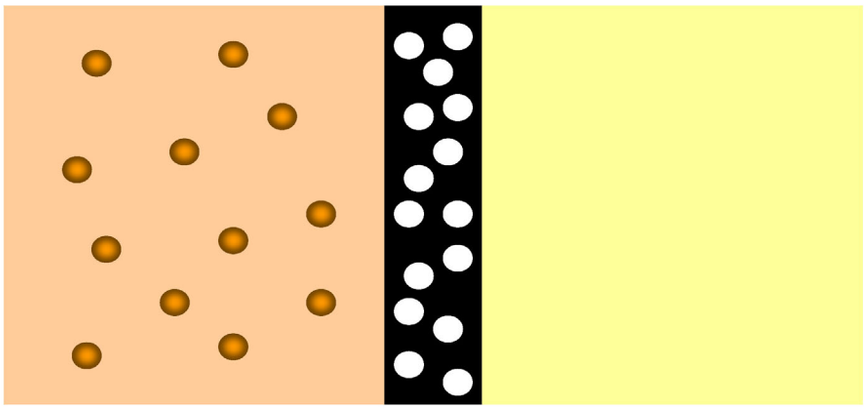
Diffusion
Convection
Adsorption
} Solute removal

Ultrafiltration Fluid removal



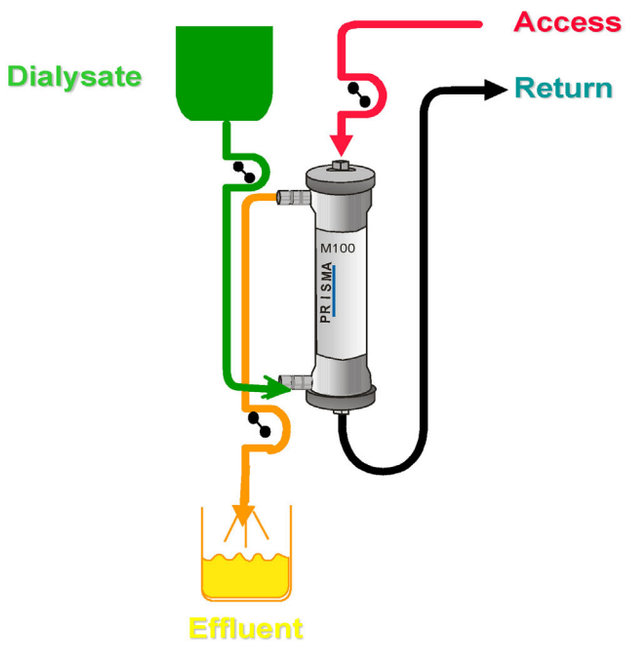
Physiology (1)

1. Diffusion



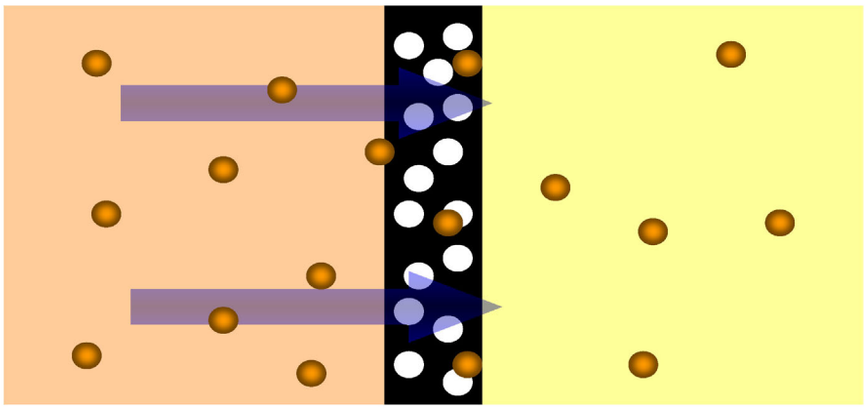
CVVHD

Continuous
Veno-
Venous
Hemo- Dialysis

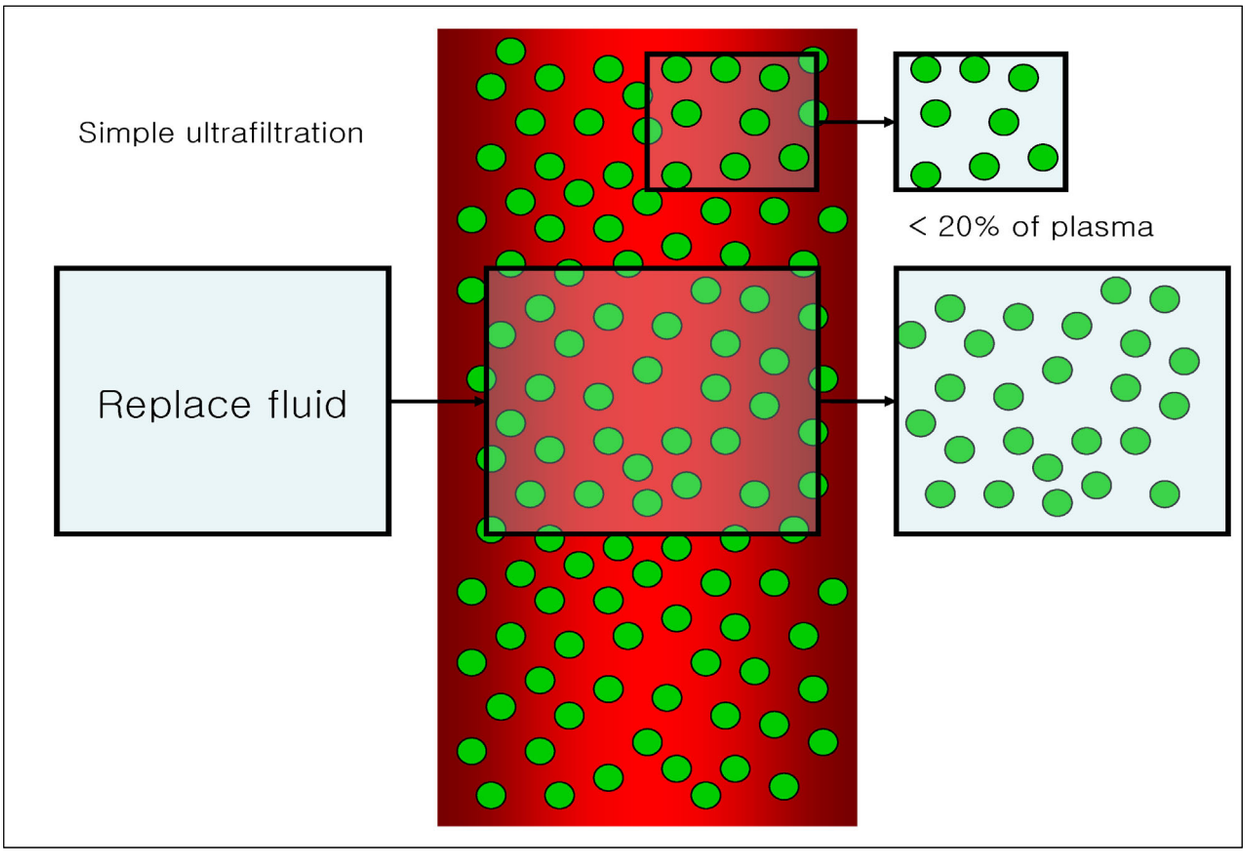


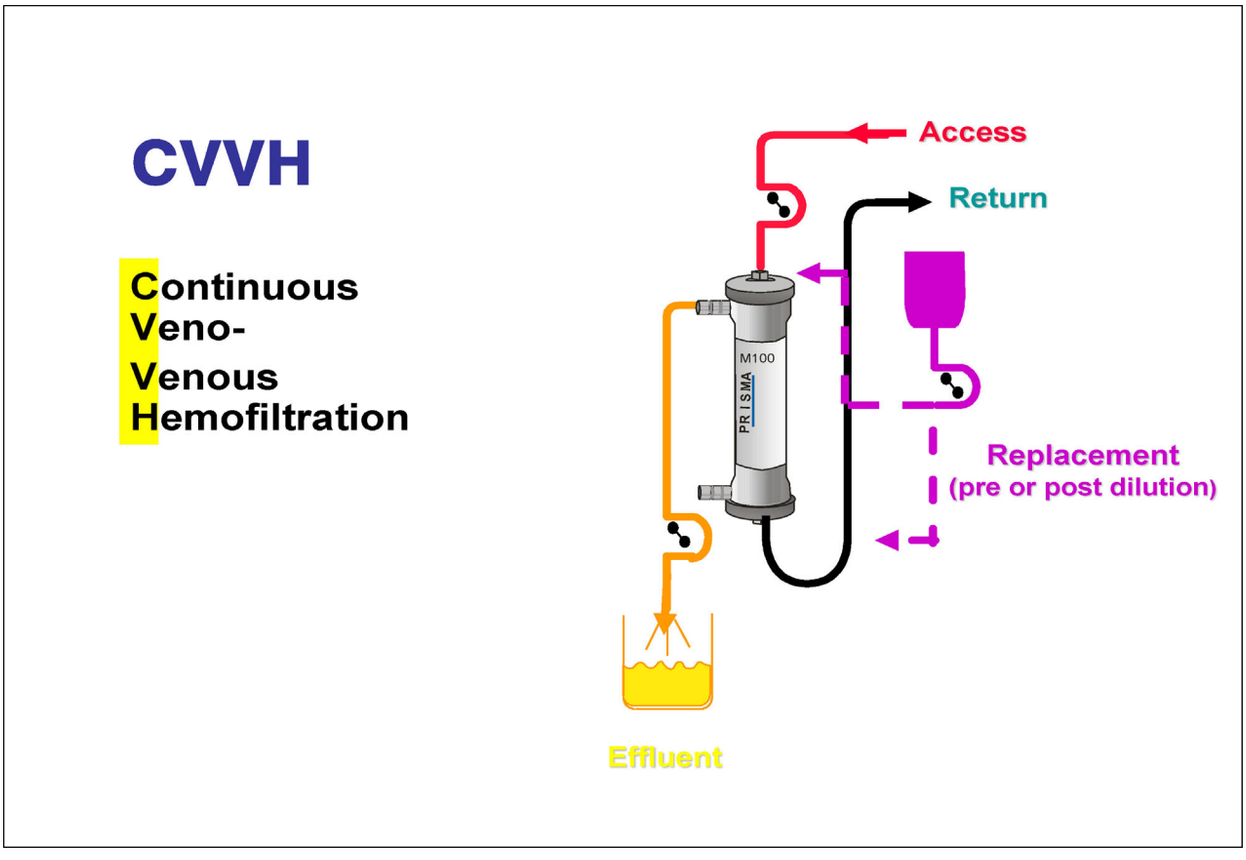
Physiology (2)

2. Ultrafiltraton (convection)



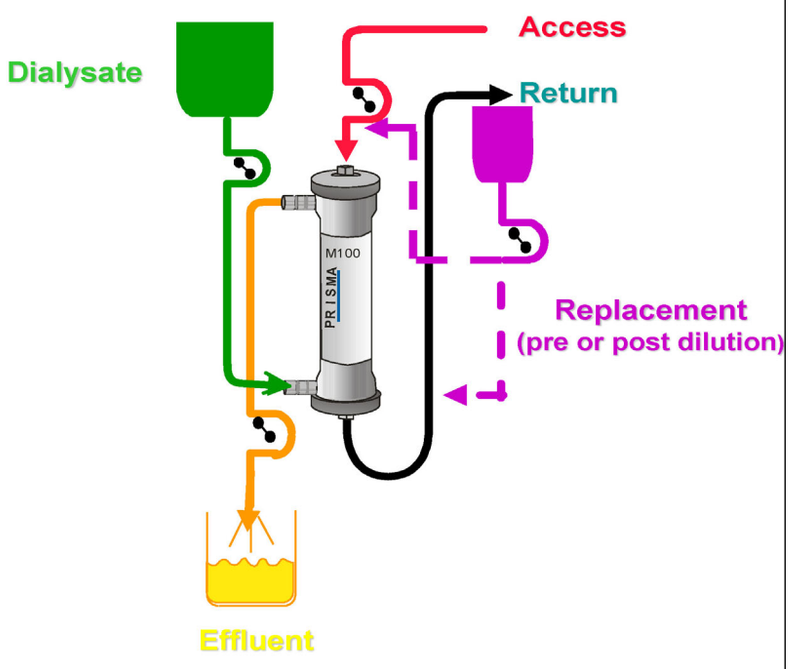
Hydrostatic pressure

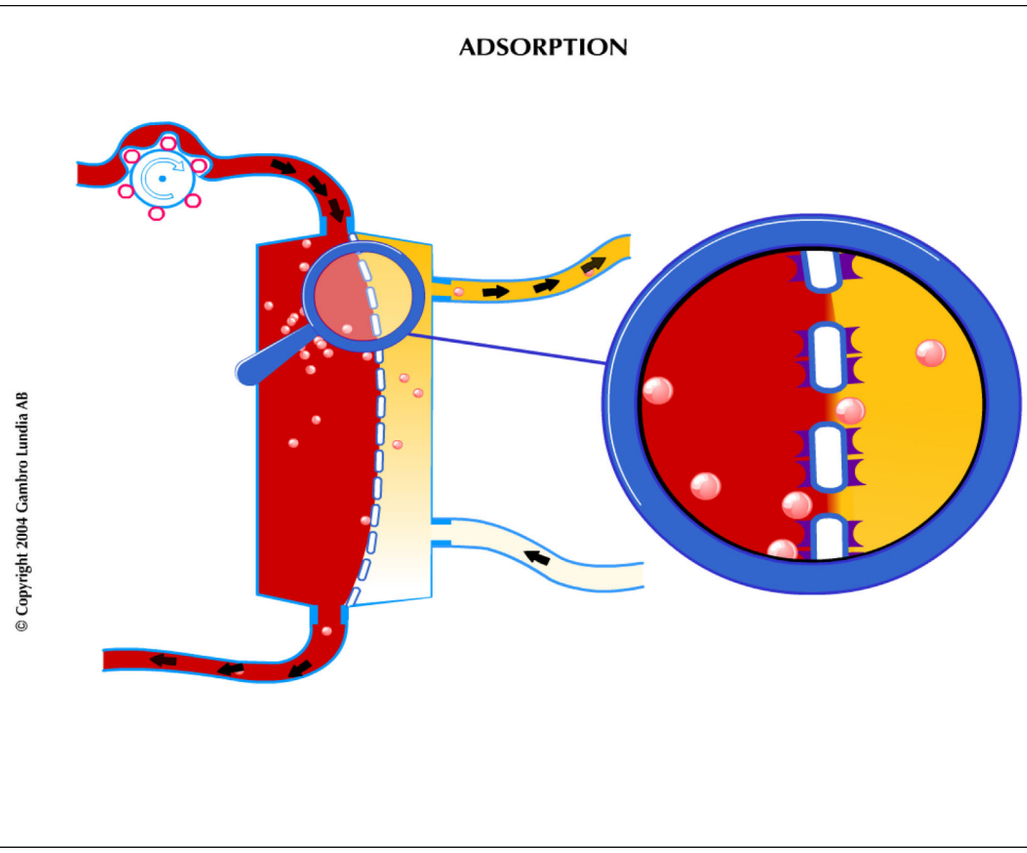

Simple ultrafiltration
< 20% of plasma
Replace fluid

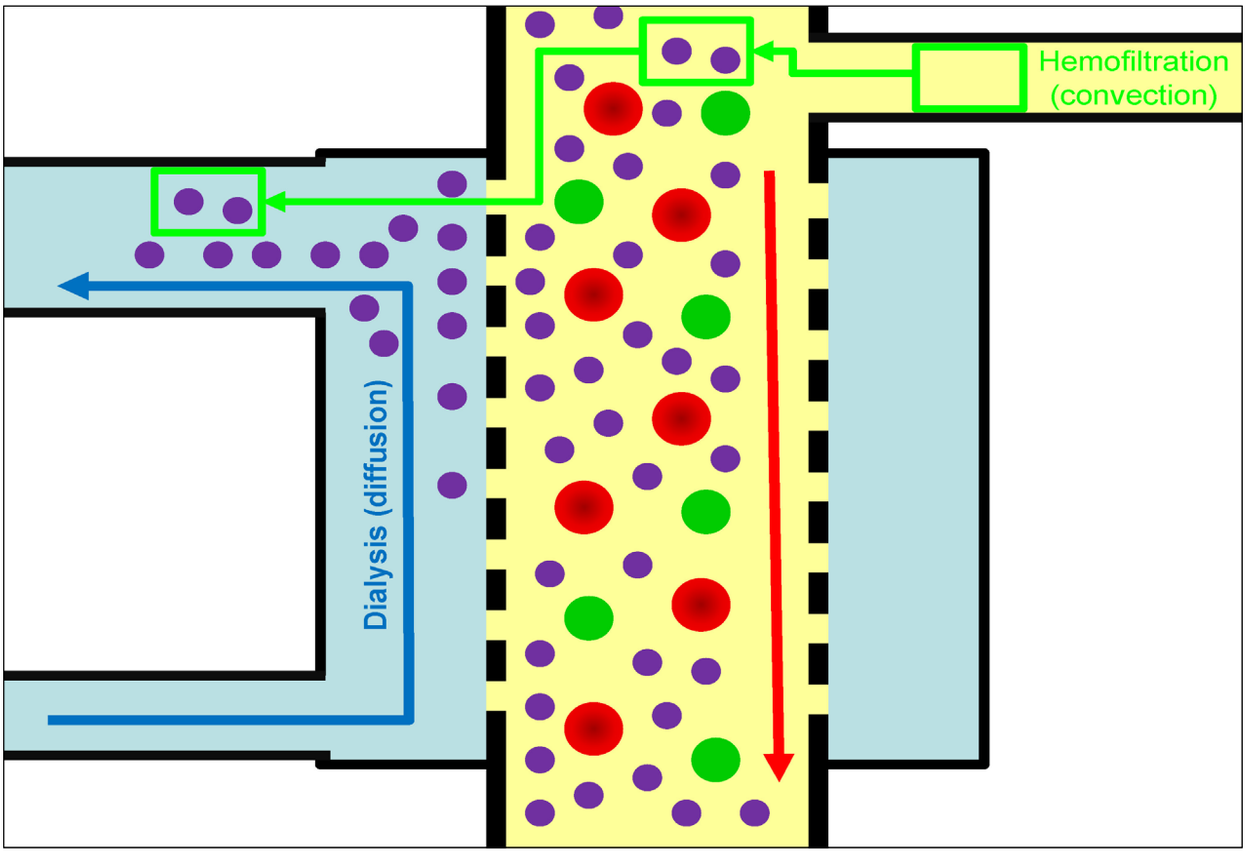

CVVH
Continuous
Veno-
Venous
Hemofiltration
Access
Return
M100
PRISMA
Replacement
(pre or post dilution)
Effluent

CVVHDF

Continuous
Veno-
Venous
Hemo-
Dia-
Filtration







SET FLOW RATE

1. Dialysate flow rate
2. Replace solution flow rate
3. Pt fluid removal rate
4. Blood flow rate

Target dialysis dose?

- IHD (×3/wk): Kt/V ≥ 1.3
- CVVH: not known; UR ≥ 35ml/hr/kg

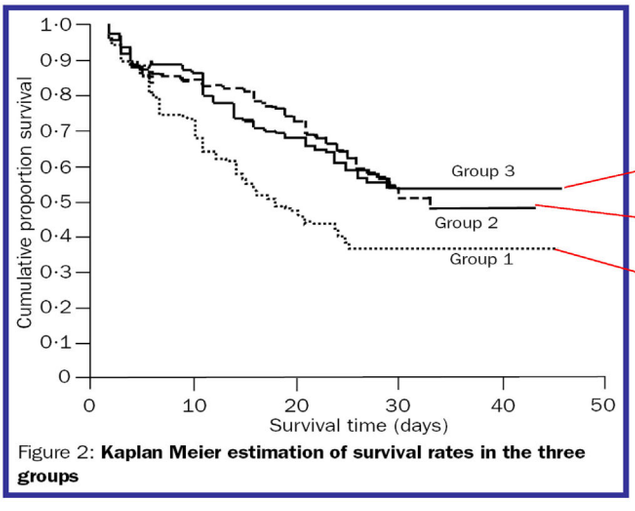


Figure 2: **Kaplan Meier estimation of survival rates in the three groups**

45 ml/hr/kg
35 ml/hr/kg
P=0.87
20 ml/hr/kg
P=0.0007
Kt/V 0.7/day

Ronco et al, *Lancet* 2000

Presciprtion

- Target: GFR 35 ml/min/1.73m^2 (≈ 35 ml/hr/kg)

Urea clearance

1. BFR during conventional CVVHDF is much greater than DFR/RFFR.
2. Dialysate is fully saturated with urea.
   Urea extraction ratio ≒ 1
3. Urea clearance in CVVHDF = DFR + RFFR (+ PFRR)
   cf.) Filter malfunction: clotting etc.
   cf.) High volume hemofiltration in sepsis

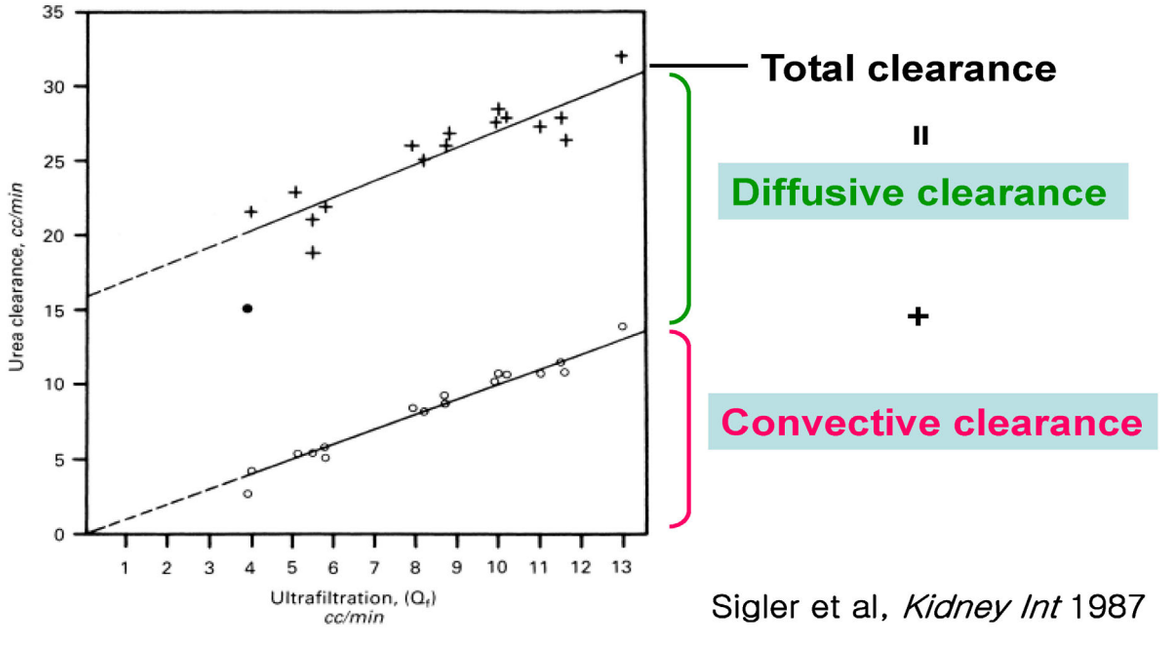
Presciprtion

- Target: GFR 35 ml/min/1.73m^2 (≈ 35 ml/hr/kg)
- Effluent volume: 2000 ml/hr/1.73m^2

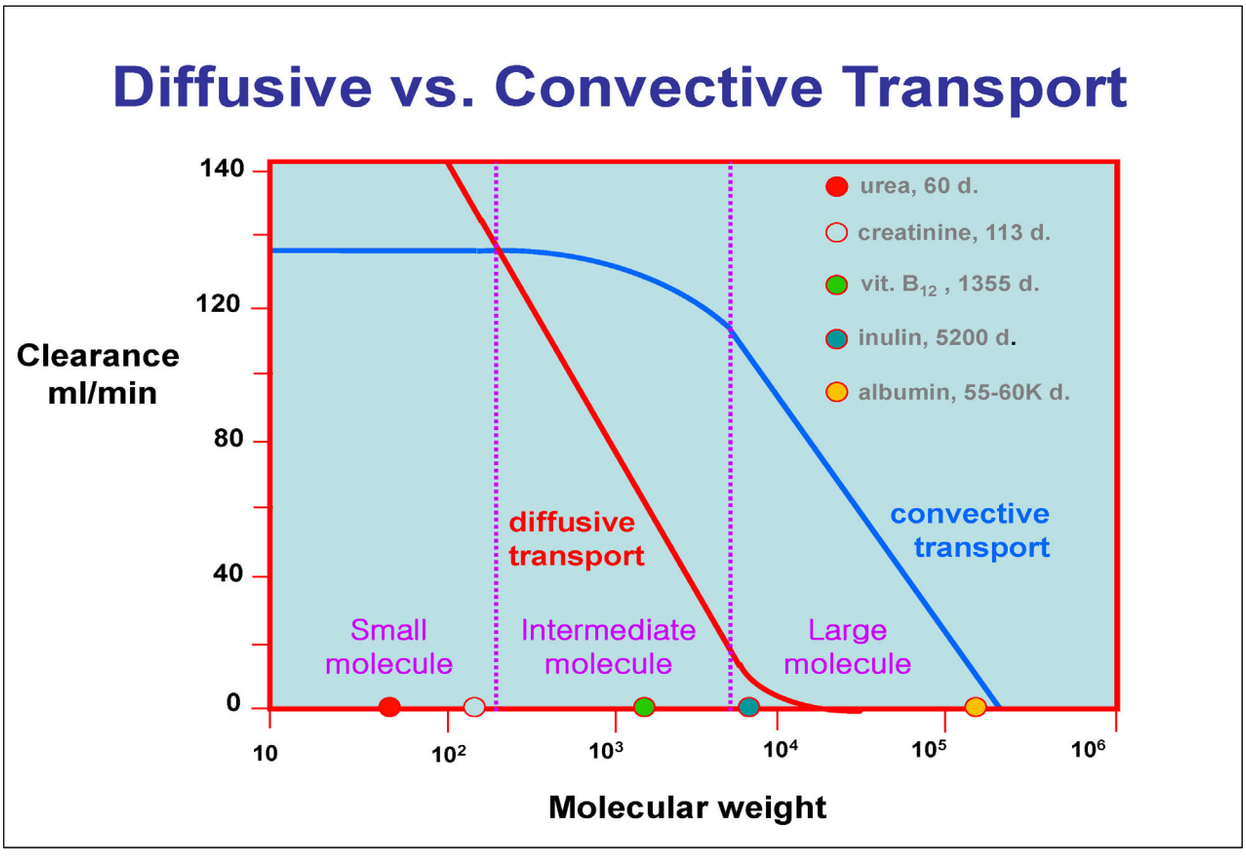
Presciprtion

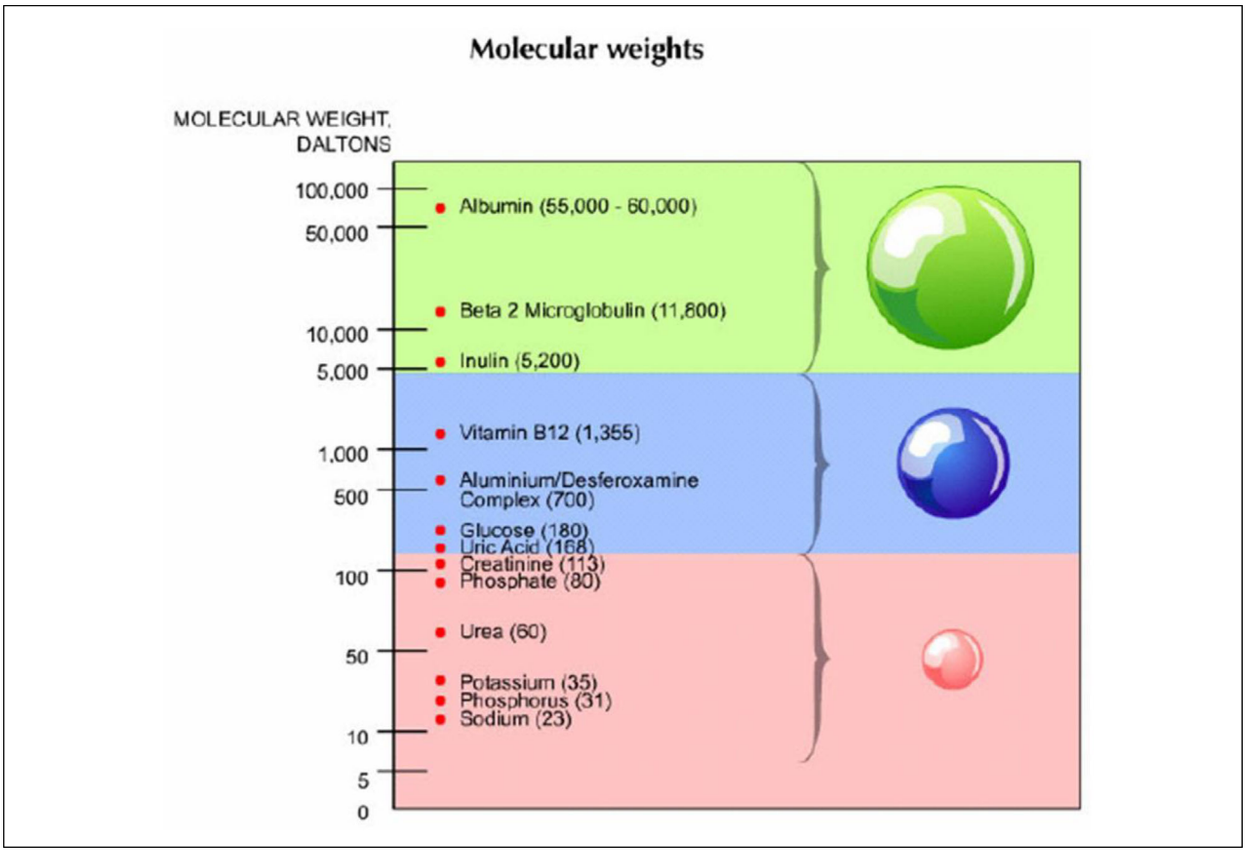
- Target: GFR 35 ml/min/1.73m^2 (≈ 35 ml/hr/kg)
- Effluent volume: 2000 ml/hr/1.73m^2
- Hemofiltration vs Hemodialysis? 50:50

Urea clearance(2)



Sigler et al, *Kidney Int* 1987


Diffusive vs. Convective Transport
Clearance ml/min
140
120
80
40
0
urea, 60 d.
creatinine, 113 d.
vit. B12 , 1355 d.
inulin, 5200 d.
albumin, 55-60K d.
diffusive transport
convective transport
Small molecule
Intermediate molecule
Large molecule
10
10²
10³
10⁴
10⁵
10⁶
Molecular weight


Molecular weights
MOLECULAR WEIGHT, DALTONS
100,000
50,000
10,000
5,000
1,000
500
100
50
10
5
0
Albumin (55,000 - 60,000)
Beta 2 Microglobulin (11,800)
Inulin (5,200)
Vitamin B12 (1,355)
Aluminium/Desferoxamine Complex (700)
Glucose (180)
Uric Acid (168)
Creatinine (113)
Phosphate (80)
Urea (60)
Potassium (35)
Phosphorus (31)
Sodium (23)

Sieving coefficient

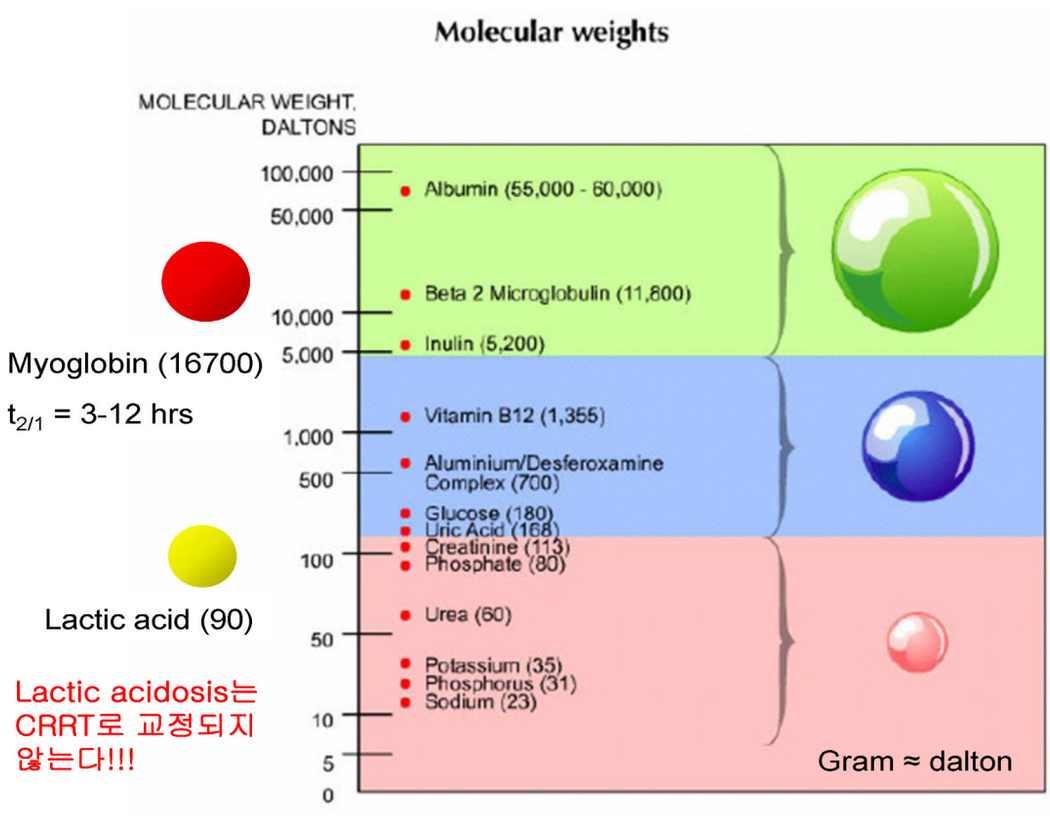
	Prismaflex ST60	Prismaflex ST100	HF6S
Urea	1.0	1.0	1.0
Creatinine	1.0	1.0	1.0
Vit B_{12}	1.0	1.0	1.0
Inuline	0.96	0.96	0.99
ß2Mg			0.63
Myoglobin	0.55	0.55	
Albumin	<0.01	<0.01	<0.01

Presciprtion

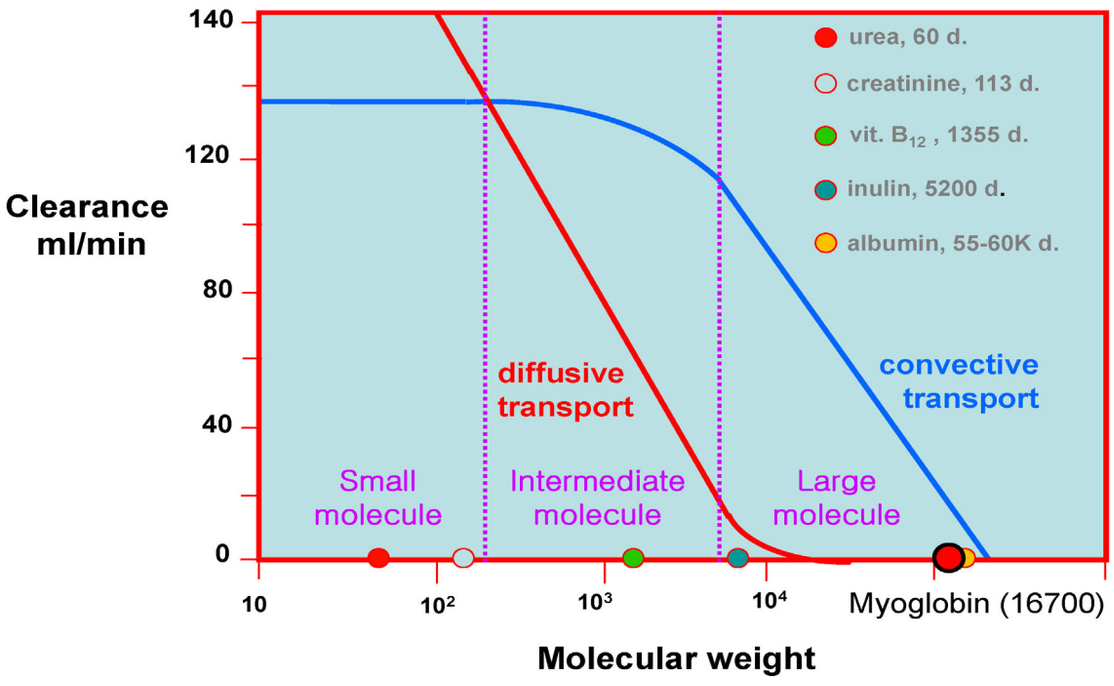
- Target: GFR 35 ml/min/1.73m^2 (≈ 35 ml/hr/kg)
- Effluent volume: 2000 ml/hr/1.73m^2
- Hemofiltration vs Hemodialysis? 50:50
  - CVVH: Replace fluid flow rate 1000 ml/hr/1.73 m^2
  - CVVHD: Dialysate flow rate = 1000 ml/hr/1.73 m^2

Myoglobin

- Myoglobin removal by CVVH in rhabdomyolysis
  - Myoglobin = large molecule
  - Effectively removed by hemofiltration
  - Limit in increasing replace fluid flow rate
  - Myoglobin is not effectively removed by PD or HD.
    (Int J Artif Organs. 1993 16:659-61)
  - Myoglobin rapidly fall in remission state independent of treatment modality.
    (Intensive Care Med. 1994 20:109-12)



Diffusive vs. Convective Transport

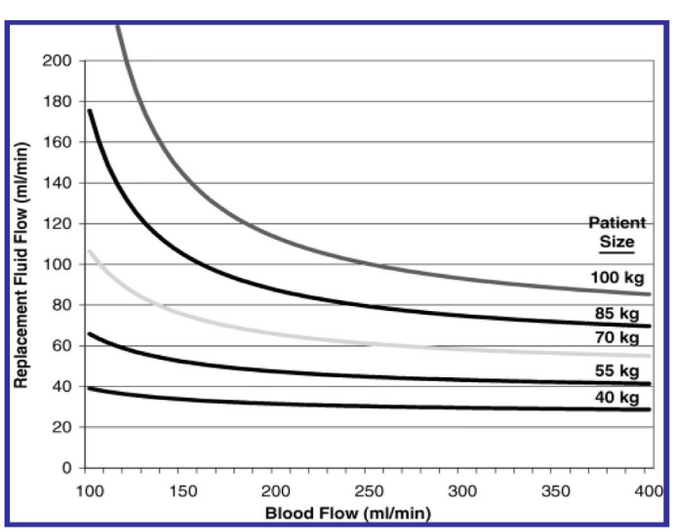


Clearance in predilution CVVH

- $\underline{K}$ = UFR × S × [BFR/(BFR + RFFR)]

Clearance

UFR (ultrafiltration rate) = Pt fluid removal (+ RFFR)

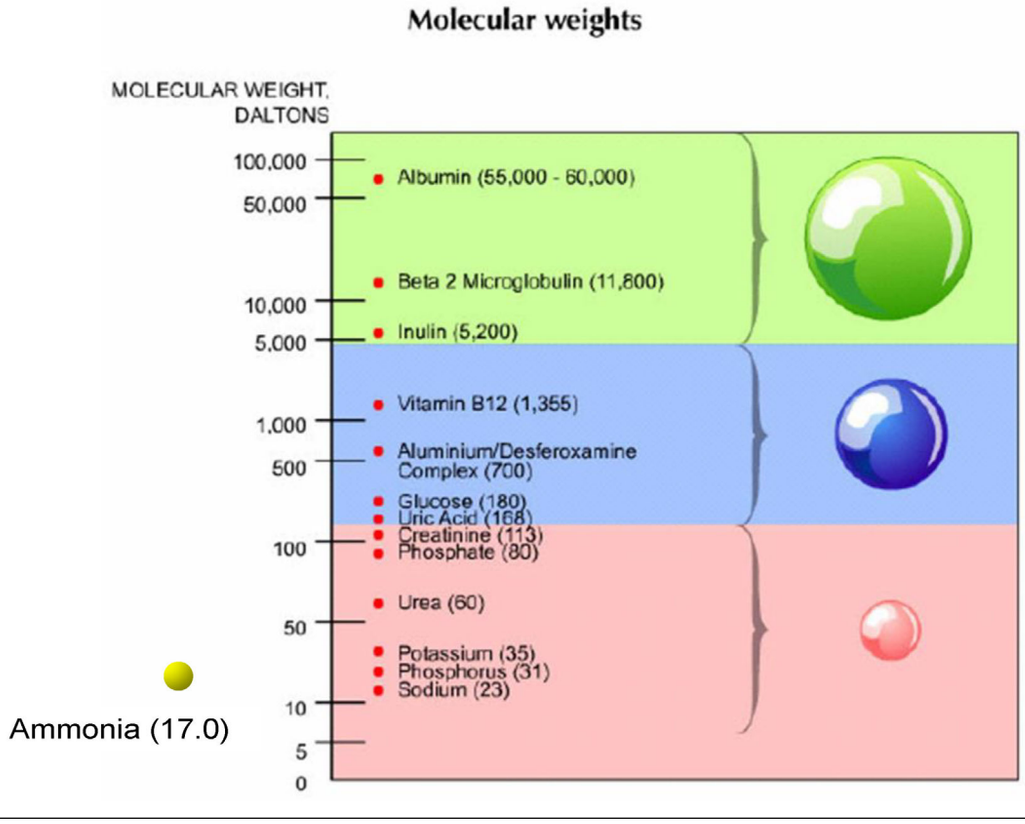


A dose equivalent to 35 ml/hr/kg in postdilution

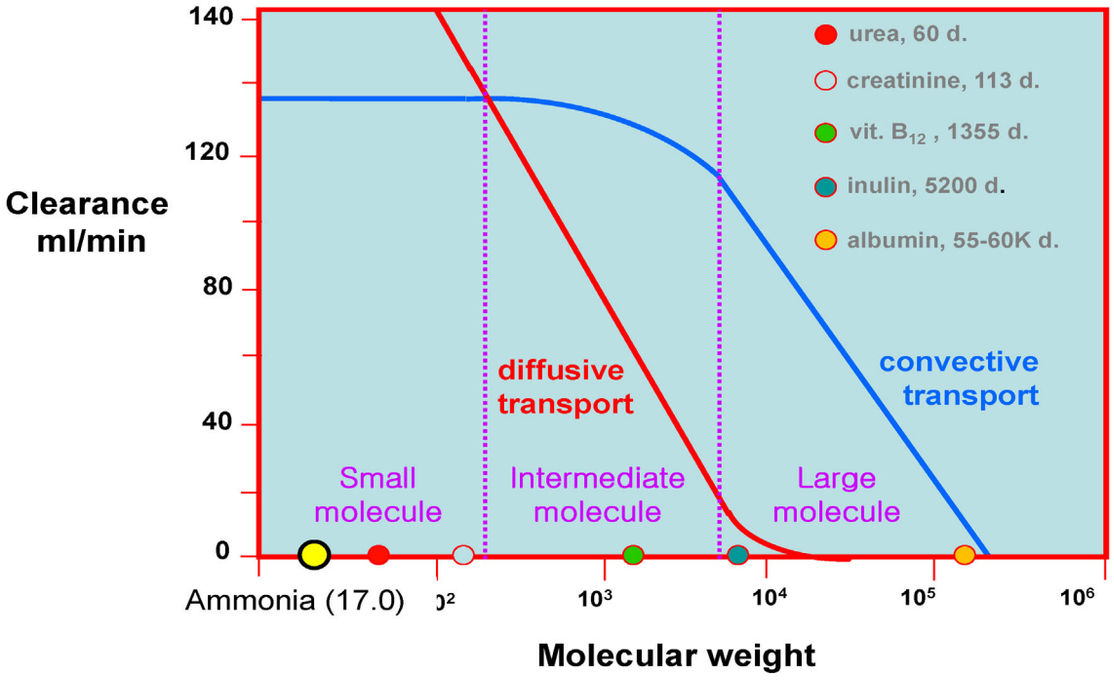
William et al, *Artif Organs* 2003

Ammonia

- Hyperammonemia (ex. Urea cycle defect)
  - Ammonia = small molecule
  - Effectively removed by hemodialysis
  - Dialysate flow rate = 3000 (or more) ml/hr/1.73 m^2
  - Monitor K, P
- Hyperammonemia가 있을 경우 conventional HD를 먼저 시작하여 serum ammonia를 200 mcg/dl 미만까지 낮추고 이후 CRRT를 유지하도록 권장되고 있으나, 현재 국내에 신생아용 HD filter를 구하기 어려우므로 초기에 CRRT를 시작하여 DFR를 높게 유지하는 것이 좋을 것으로 보인다.

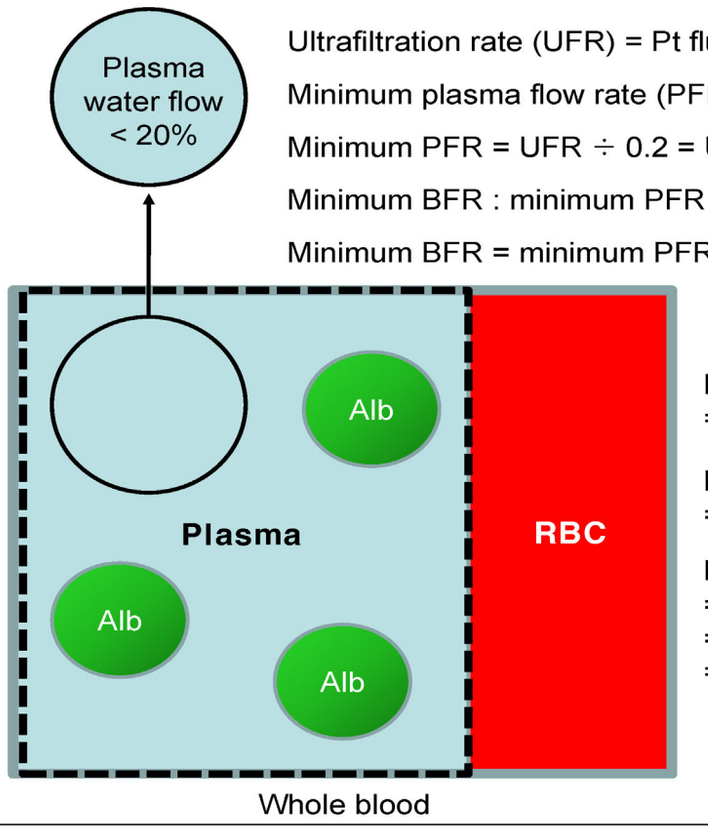


Diffusive vs. Convective Transport



Patient fluid removal

- Total input
  - Main fluid/TPN, Transfusion (RBC, FFP, PC), Albumin
  - Anticoagulation (ACD-A….)
  - Etc.
- Total output
  - Urine, stool, vomitus, drain (G-tube, chest….), etc
- Target weight loss: 5~10% of dry weight per day
  - 전신 부종이 심하거나 폐부종 등의 합병증이 심할 경우 혈압 등의 활력 징후가 괜찮다면 더 많은 양의 수분 제거를 할 수 있다.
- PFR = (Total input – Total output + Target Wt loss) ÷ 24hr



Ultrafiltration rate (UFR) = Pt fluid removal (+ RFFR)

Minimum plasma flow rate (PFR) : UFR = 100% : 20% = 1:0.2

Minimum PFR = UFR ÷ 0.2 = UFR × 5

Minimum BFR : minimum PFR = 1:{1-[Hct(%) /100]}

Minimum BFR = minimum PFR ÷ {1-[Hct(%) /100]}

ex) Hct 45%, UFR = 35 ml/hr/kg

Minimum PFR = UFR × 5
= 35 × 5 = 175 ml/hr/kg

Minimum BFR : minimum PFR
= 1:(1-0.45) = 1:0.55

Minimum BFR
= minimum PFR ÷ {1-[Hct(%) /100]}
= 175 ml/hr/kg ÷ 0.55 = 318 ml/hr/kg
= 5 ml/min/kg

Prescription: Flow Rates

- Ideal blood flow - patient size dependent
  - minimum 2-5ml/kg/min
  - maximum 400ml/min/1.73m^2
    - Neonates 10-12ml/kg/min
      - eg. 4kg 50ml/min
    - Children 5ml/kg/min
      - eg. 15kg 75ml/min
    - Older child 2-5ml/kg/min
      - eg. 45kg 100ml/kg/min
- Replacement/dialysis flow: 1/5 ~ 1/10 of BFR
  - UFR (convection) 2L x BSA / 1.73m^2 / hr
  - Q_D (diffusion) 2L x BSA / 1.73m^2 / hr

예제) 건체중 30 kg (BSA = 1 m^2) Hct 45%

- Effluent volume: 2000 ml/hr/1.73m^2
- Replace fluid flow rate : Dialysate flow rate = 50% : 50%
- **RFFR** = 1000 ml/hr/1.73 m^2 = 1000 × 1 ÷ 1.73 (ml/hr) = 578 ml/hr
  → **600 ml/hr**
- **DFR** = 1000 ml/hr/1.73 m^2 → **600 ml/hr**
- Patient removal rate (**PRR**)
  = (Total input – Total output + Target Wt loss) ÷ 24hr
  = [2000 – 200 + 500 (ml)] ÷ 24hr = 2300 ml ÷ 24hr
  = 96 ml/hr → **100 ml/hr**
- Ultrafiltration rate = PRR + RFFR = 100 + 600 (ml/hr) = 700 ml/hr
- Minimum PFR = UFR × 5 = 700 × 5 (ml/hr) = 3500 ml/hr = 58 ml/min
- Minimum BFR = minimum PFR ÷ {1-[Hct(%) /100]} = 58 ÷ (1-0.45) ml/min
  = 58 ÷ 0.55 ml/min = 105 ml/min
- **BFR** = BWt × 5 ml/min = 30 × 5 ml/min = **150 ml/min** (> 105 ml/min)

Hypokalemia, Hypophosphatemia 잘 동반되므로 관찰할 것!!!

Anticoagulation	Units	Dosage	Monitoring
Free			
Heparin	U/hr	5~10 U/kg/hr	ACT, aPTT
Protamine	mg/hr	1mg/100 U hepain/hr	
ACD-A(Baxter) (Citrate)	ml/hr	1.5 × BFR(ml/min)/hr	iCa
3%$CaCl_2$ 133ml + NS 367ml	ml/hr	40% citrate flow	
Nafamostat mesilate (Futhan)	mg/hr	0.1 mg/kg/hr	ACT, aPTT
Low molecular weight heparins	U/hr	10 U/kg/hr	anti-Xa
Argatroban	mcg/min	2~10 mcg/kg/min	ACT, aPTT
Bivalirudin	mg/hr	0.15-0.25 mg/kg/hr	ACT, aPTT

※ Target range: ACT 300~450, aPTT 45~60 seconds, anti-Xa 0.25~0.35
(filter가 잘 유지되는 경우 target range까지 증량할 필요 없습니다.)
※ Citrate protocol (filter가 잘 유지되는 경우 patient iCa만 맞춰줍니다.)

Filter iCa	Citrate		Patient iCa	Calcium	
(mmol/L)	<20kg	>20kg	(mmol/L)	<20kg	>20kg
0.25	↓5ml/hr	↓10ml/hr	>1.3	↓5ml/hr	↓10ml/hr
0.25-0.39	none	none	1.1-1.3	none	none
0.4-0.5	↑5ml/hr	↑10ml/hr	0.9-1.1	↑5ml/hr	↑10ml/hr
>0.6	↑10ml/hr	↑20ml/hr	<0.9	↑10ml/hr	↑20ml/hr
citrate infusion >200ml/hr → notify Dr			calcium infusion >150ml/hr → notify Dr		

Prismaflex Priming, Circuit and Initiation of CRRT

Sun Yoon

Clinical Specialist

Contents

Prismaflx 시스템

GamCath / Prismaflex Set / Prismaflex Solution

Prismaflex Operation

Baxter KO/MG230/20-0027

Prismaflex 시스템

급성 신부전증 및/또는 체액 과다 환자를 위한 **지속적 신대체 요법***

혈장 성분을 제거해야 하는 질병이 있는 환자를 위한 **혈장 교환술 요법** *

물질을 즉시 흡착하여 제거해야 하는 상태에 있는 환자를 위한 **혈액 관류요법** *

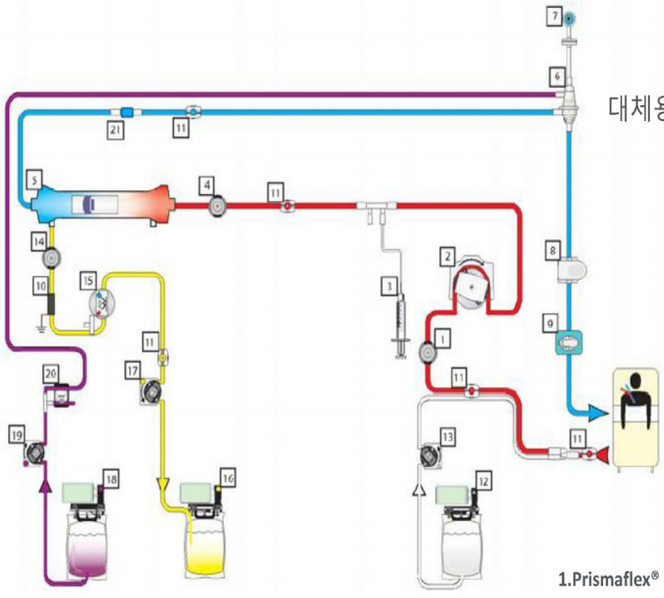
MARS 간 보조 시스템은 급성 또는 만성 간부전 환자의 혈액에서
단백질 결합 독소 및 수용성 독소를 제거하도록 설계**

Baxter KO/MG230/20-0027

1.Prismaflex® 관리자 설명서 * 16p, **116p 3

Prismaflex 시스템_ TPE [Theraputic Plasma Exchange]혈장 교환술*

TPE(혈장교환술)에서 혈장과 혈장 내에 포함된 질병 매개체는 필터 막의 여과를 통해 환자의 혈액에서 제거됩니다. 이러한 혈장 여과 과정을 통해 제거된 혈장량을 보충하기 위해 대체용액이 주입**

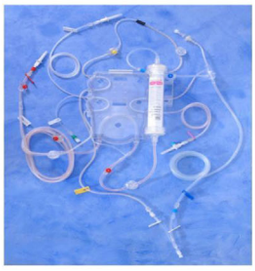


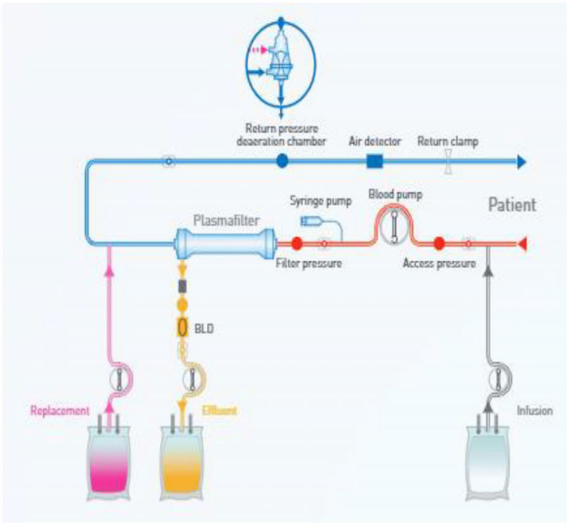
대체용액은 항상 100% 후희석으로 주입***

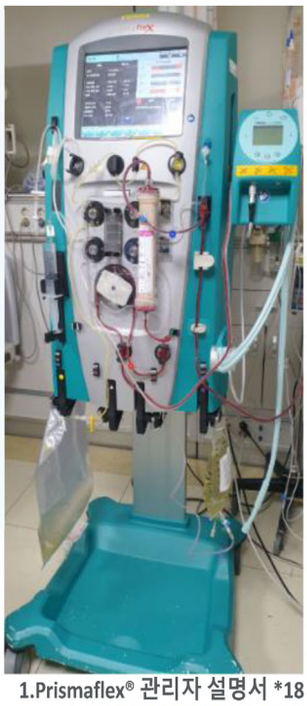
Baxter

1.Prismaflex® 관리자 설명서 *18**127p***36p 그림출처128p | 4

Prismaflex 시스템_ TPE [Theraputic Plasma Exchange]혈장 교환술*



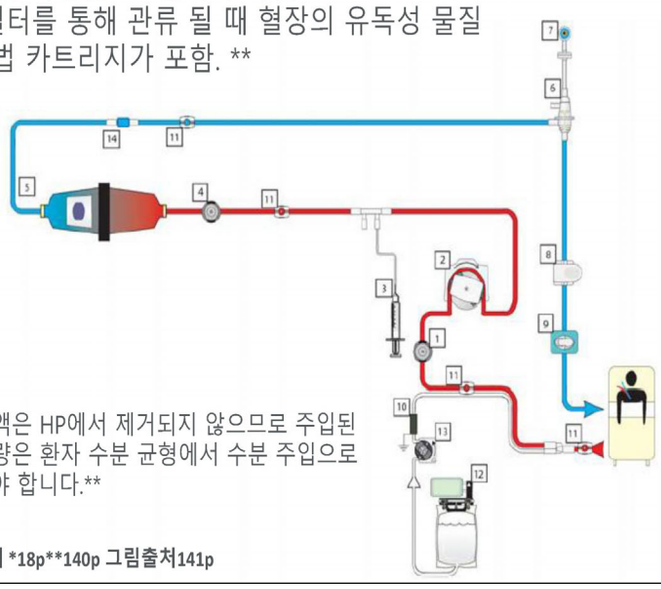




1.Prismaflex® 관리자 설명서 *18
2. 그림: Prismaflex System 브로셔 KO/MG230/20-0026

Prismaflex 시스템_ HP – 혈액 관류 요법 *

환자 혈액은 Prismaflex 일회용 HP 라인 세트를 통해 유도되어 HP 장치를 통과하고, 정화된 혈액은 다시 환자에게 반환. 수분 제거는 수행되지 않음.
Prismaflex 시스템과 함께 사용할 수 있는 다양한 HP 장치가 지원.
이러한 장치에는 환자의 혈액이 흡착 필터를 통해 관류 될 때 혈장의 유독성 물질 및/또는 약물이 흡수되는 혈액 관류 요법 카트리지가 포함. **

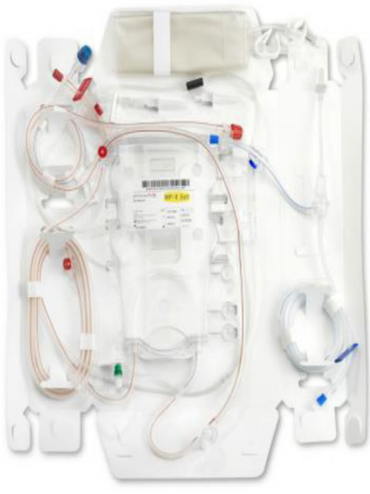


PBP 용액은 HP에서 제거되지 않으므로 주입된 PBP 용량은 환자 수분 균형에서 수분 주입으로 계산해야 합니다.**

1.Prismaflex® 관리자 설명서 *18p**140p 그림출처141p

Prismaflex 시스템_ HP – 혈액 관류 요법 *

Adsorba® 카트리지**
생체 적합 셀룰로스 막에 싸여 있는 활성 탄소 입자가 들어 있는 혈액 관류 카트리지 환자 혈액이 카트리지를 통해 관류 될 때 혈액의 유독성 물질이 탄소 입자에 흡착.



Baxter KO/MG230/20-0027

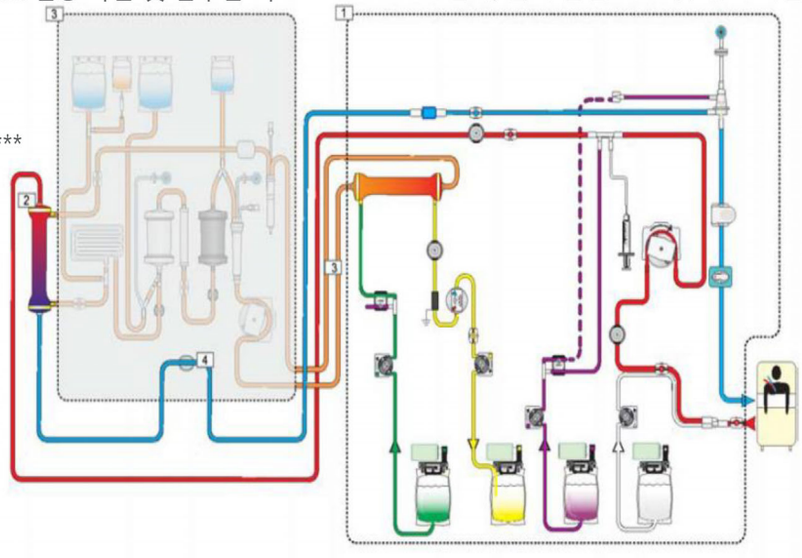
1.Prismaflex® 관리자 설명서 *18p**145p
3. 그림: Set 브로셔_ KO/MG230/20-0024 | 7

Prismaflex 시스템_CRRT MARS® – 인공 간 투석기(MARS)를 지원하는 지속적 신대체 요법*

- CVVHD – 지속적 정정맥 혈액 투석**
- CVVHDF – 지속적 정정맥 혈액 투석 여과**

diaFLUX 연장 라인 및 알부민 회로*** diaFLUX 필터, 혈액 순환 회로 및 유액 라인이 포함***

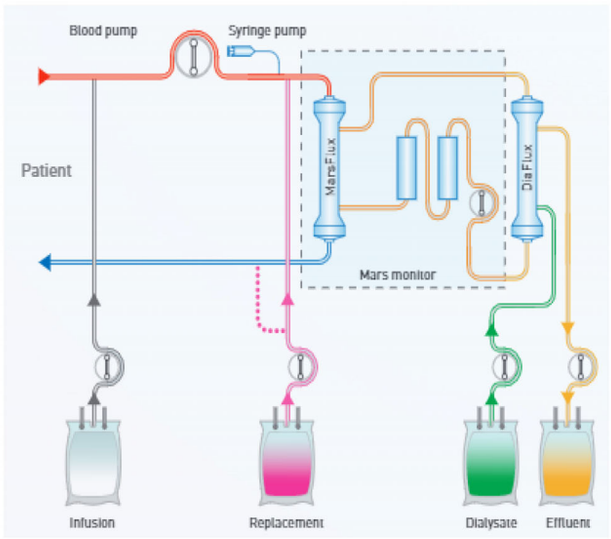
MARSFLUX 필터***



Baxter KO/MG230/20-0027

1.Prismaflex® 관리자 설명서*18p, **116, ***117,그림출처117p | 8

Prismaflex 시스템_CRRT MARS® – 인공 간 투석기(MARS)를 지원하는 지속적 신대체 요법*



Baxter KO/MG230/20-0027

2.그림 Prismaflex System 브로셔_KO/MG230/20-0026 9

Prismaflex 시스템

Prismaflex 제어 장치는 **펌프로 환자의 혈액을 빼내어** Prismaflex 일회용 **세트의 필터**로 통과시킨 후 다시 환자의 정맥류로 돌려보냅니다. 혈액이 필터를 통과할 때 원하는 치료 과정이 이루어집니다. 사용 중인 요법에 따라 이러한 절차에는 수분 제거 및/또는 용질 제거가 포함될 수 있습니다.

CRRT - 지속적 신대체 요법
SCUF – 지속적 저속 초여과
CVVH – 지속적 정정맥 혈액 여과
CVVHD – 지속적 정정맥 혈액 투석
CVVHDF – 지속적 정정맥 혈액 투석 여과

Baxter KO/MG230/20-0027

1.Prismaflex® 관리자 설명서*18p 10

지속적 신대체요법 Prismaflex 시스템 CRRT 요법 선택사항을 제공하기 위해 초여과, 혈액 여과 및 혈액 투석 메커니즘이 사용.

초여과 용질을 포함한 혈장액을 환자의 혈액에서 필터의 반투과성 막을 통해 끌어 냅니다. 배액 펌프는 초여과 비율을 자동으로 제어합니다.

혈액 여과 초여과 방식을 사용하여 용질을 포함한 혈장액을 환자의 혈액에서 필터의 반투과성 막을 통해 끌어 냅니다. 대체용액은 전희석 또는 후희석으로 동시에 혈액 경로로 주입됩니다. 용질 제거는 대류(용질의 막 통과)를 통해 수행됩니다.

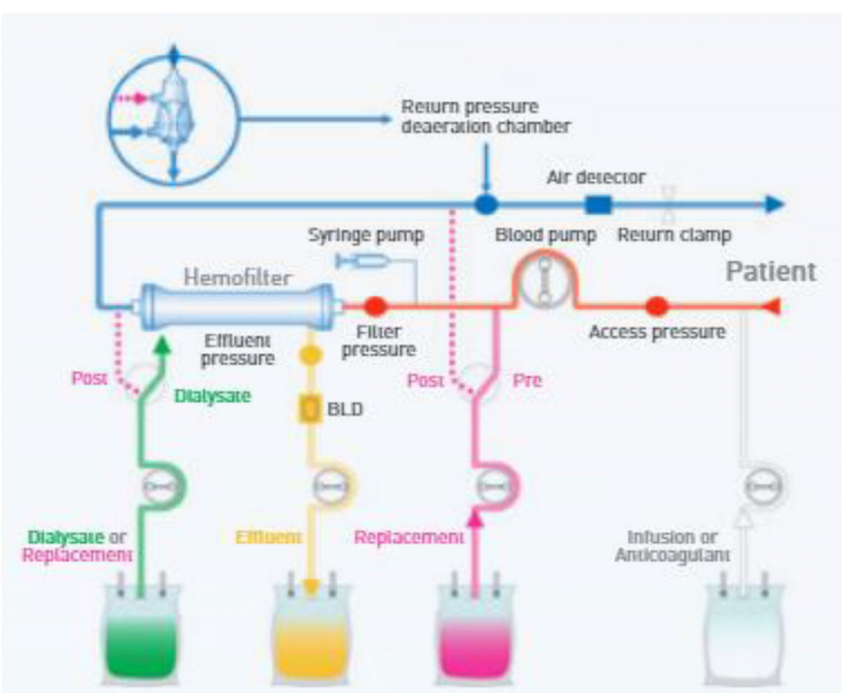
혈액 투석 원치 않는 용질은 환자의 혈액에서 반투과성 막을 거쳐 필터의 유액막을 통해 반대쪽으로 흐르는 투석액으로 가게 됩니다.
원치 않는 용질의 농도는 혈액보다 투석액에서 더 낮기 때문에 용질은 농도가 더 높은 곳(환자의 혈액)에서 낮은 곳(투석액)으로 확산됩니다. 이 확산에 의해 용질이 제거됩니다.

혈액 투석 여과 혈액 투석 여과에서는 혈액 투석과 혈액 여과가 모두 사용됩니다. 용질 제거는 대류와 확산을 통해 수행됩니다.
투석액은 필터의 유액 분획을 통해 주입됩니다. 동시에 배액 펌프는 초여과를 제어하며 대체용액은 혈액 경로로 주입됩니다.

Baxter KO/MG230/20-0027

1.Prismaflex® 관리자 설명서*100p 11

지속적 신대체요법



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2. 그림 Prismaflex System 브로셔 KO/MG230/20-0026 12

Gamcath _혈관 통로

Baxter KO/MG230/20-0027

4. 그림: GamCathe 브로셔_KO/MG230/20-0020 13

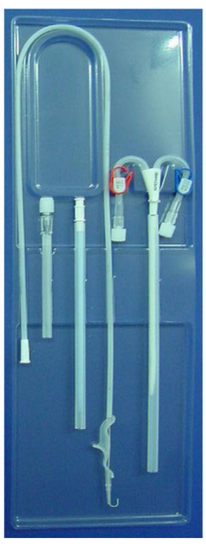
GamCath

제품명	굵기[Fr]	길이[cm]	
GDK- 610	6.5	10	Double Lumen
GDK- 810	8.0	10	
GDK – 1115	11	15	
GDK – 1115J	11	15	
GDK – 1120	11	20	
GDK – 1120J	11	20	
GTK – 1215	12	15	Triple Lumen
GTK - 1215J	12	15	
GTK - 1220	12	20	
GTK – 1220J	12	20	

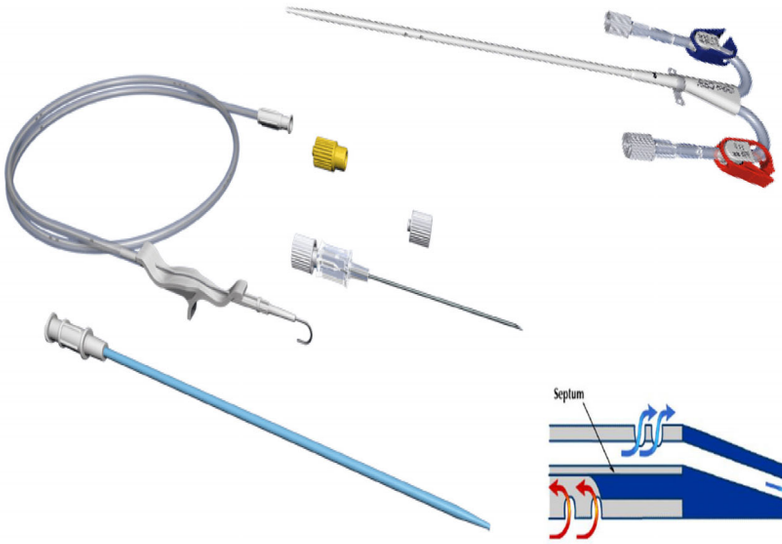
Baxter KO/MG230/20-0027

4. GamCathe 브로셔_KO/MG230/20-0020 14

GamCath -Kit



Kit
Introducer needle
Dilator
Guidewire
Injection caps



Baxter KO/MG230/20-0027

4. 그림: GamCathe 브로셔 KO/MG230/20-0020 15

Prismaflex Set

Baxter KO/MG230/20-0027

3. 그림: Set 브로셔 KO/MG230/20-0024 | 16

Prismaflex sets for CRRT

* EBV : Extracorporeal Blood Volume

Name	총프라이밍량[ml]	*EBV/Kg	혈류범위[ml/min]
HF20	500	58ml/8kg**	20-100[증분 :2ml]

계획되지 않은 환자 수분 손실/ 증가 한도[ml/3h]	환자 수분 제거 범위[ml/h]
60-150	0-500[증분: 5ml]

PBP	투석액	대체액[전희석]	대체액[후희석]
0-1000	0-2500	0-2500[증분:20]	0-2000[증분:20]

실행 모드 중에 모든 세트와 요법에 대해 모니터에서 허용하는 최소 혈류 범위는 10ml/min입니다. 명시된 혈류 범위 하한은 각 세트에서 권장되는 최소 혈류량을 나타냅니다.

1.Prismaflex® 관리자 설명서274p *50P
3. 그림: Set 브로셔 KO/MG230/20-0024

Prismaflex sets for CRRT

체외 혈액량에 특별한 주의를 기울이십시오. 체외 순환 혈액량 대 환자 혈액량 비율이 높은 환자의 경우 의사는 세트를 환자에게 연결하기 전에 적절한 양을 보충하여 체외순환회로를 프라임할 수 있습니다.*

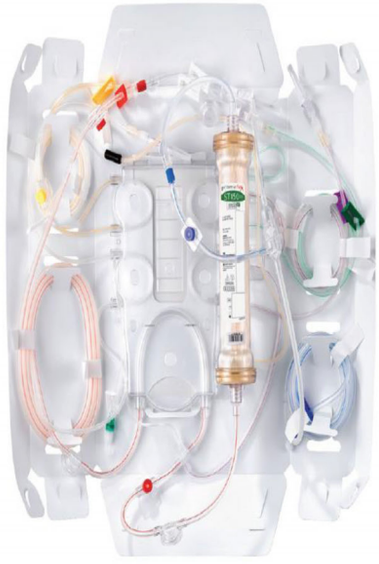
혈액 프라임
프라이밍 완료 화면에 **혈액 프라임** 소트트키가 제공됩니다. 혈액 프라임이 의사의 처방의 일부인 경우 이 소프트키를 사용하여 환자 연결 전에 체외 순환 회로에 혈액을 채우는 것과 관련된 지침 및 기능을 확인하고 사용할 수 있습니다. **

혈액 반환
혈액 프라임된 체외순환회로에서 혈액이 반환될 경우 과혈량증으로 이어질 수 있습니다. 의사의 처방을 확인하십시오.***

1.Prismaflex® 관리자 설명서*26p **115p ***86p
3. 그림: Set 브로셔 KO/MG230/20-0024

Prismaflex sets for CRRT

* EBV : Extracorporeal Blood Volume



Name	총프라이밍량[ml]	*EBV/Kg	혈류범위[ml/min]
ST60	1000	93ml/11kg**	50-180[증분 :5ml]

계획되지 않은 환자 수분 손실/증가 한도[ml/3h]	환자 수분 제거 범위[ml/h]
60-200	0-2000[증분: 5ml]

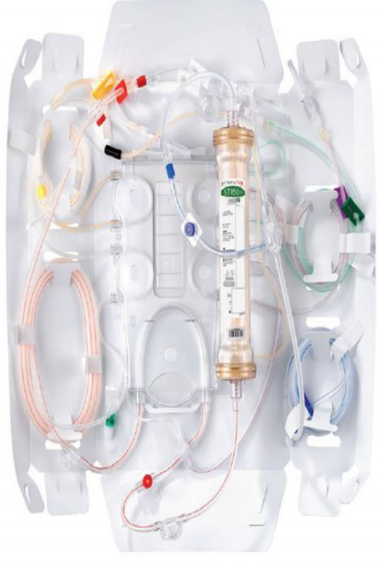
PBP	투석액	대체액[전희석]	대체액[후희석]
0-2000	0-4000	0-4000[증분:50]	0-3000[증분:50]

실행 모드 중에 모든 세트와 요법에 대해 모니터에서 허용하는 최소 혈류 범위는 10ml/min입니다. 명시된 혈류 범위 하한은 각 세트에서 권장되는 최소 혈류량을 나타냅니다.

1.Prismaflex® 관리자 설명서274p**50p
3. 그림: Set 브로셔 KO/MG230/20-0024

Prismaflex sets for CRRT

* EBV : Extracorporeal Blood Volume



Name	총프라이밍량[ml]	*EBV/Kg	혈류범위[ml/min]
ST100	1000	152ml/30kg**	80-400[증분 :5ml]

계획되지 않은 환자 수분 손실/증가 한도[ml/3h]	환자 수분 제거 범위[ml/h]
100-400	0-2000[증분: 10ml]

PBP	투석액	대체액[전희석]	대체액[후희석]
0-4000	0-8000	0-8000[증분:50]	0-6000[증분:50]

실행 모드 중에 모든 세트와 요법에 대해 모니터에서 허용하는 최소 혈류 범위는 10ml/min입니다. 명시된 혈류 범위 하한은 각 세트에서 권장되는 최소 혈류량을 나타냅니다.***

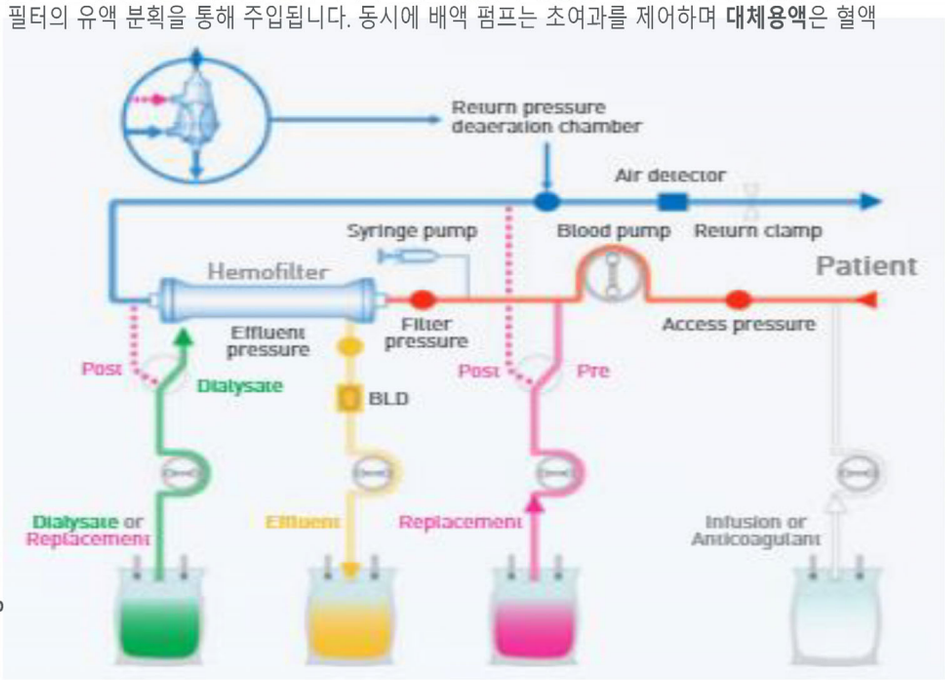
1.Prismaflex® 관리자 설명서 275p**50p***274p
3. 그림: Set 브로셔 KO/MG230/20-0024

Prismaflex Solution

Baxter KO/MG230/20-0027 21

Prismaflex Solution

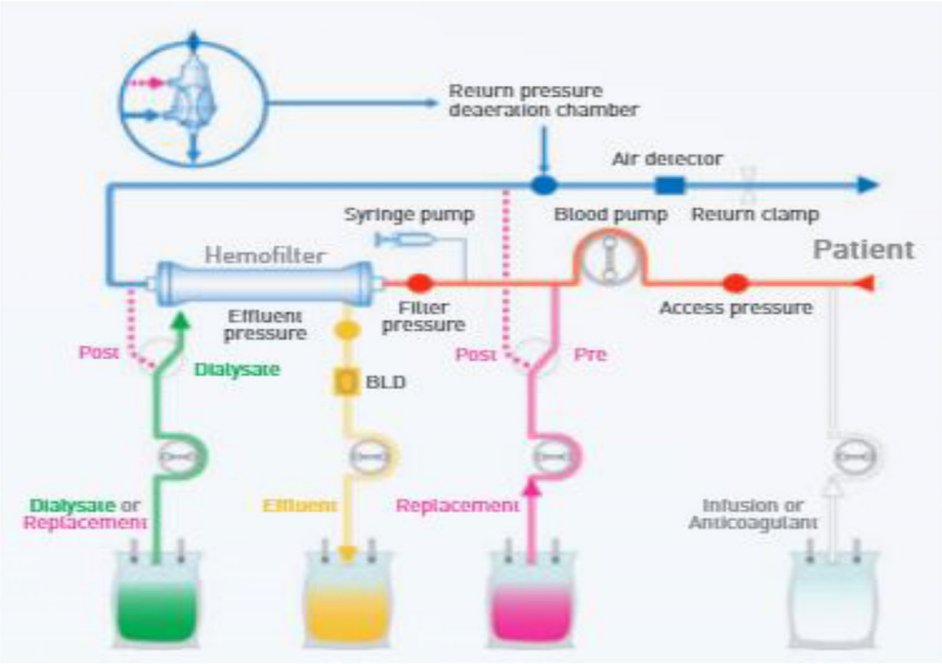
혈액 투석 여과 혈액 투석 여과에서는 혈액 투석과 혈액 여과가 모두 사용됩니다. 용질 제거는 **대류와 확산을 통해** 수행됩니다. **투석액**은 필터의 유액 분획을 통해 주입됩니다. 동시에 배액 펌프는 초여과를 제어하며 **대체용액**은 혈액 경로로 주입됩니다.*



1.Prismaflex® 관리자 설명서*100p
2. 그림 Prismaflex System 브로셔
KO/MG230/20-0026

Baxter KO/MG230/20-0027 22

Prismaflex Solution



2. 그림 Prismaflex System 브로셔 KO/MG230/20-0026 | 23

Prismaflex Solution

Hemosol B0 [5]
헤모졸비제로

Prismasol 2 [6]
프리즈마졸2

Prismasol 4 [6]
프리즈마졸4

Phoxilium [7]
폭실리움

5. Hemosol B0브로셔 KO/MG230/20-0021
6. Prismasol2_4브로셔 KO/MG230/20-0025
7. Phoxilium브로셔 KO/MG230/20-0023 | 24

Prismaflex Solution

(unit : mmol/L)

Components	Hemosol B0 [5]	Prismasol 2 [6]	Prismasol 4 [6]	Phoxillium [7]
Na^+	140	140	140	140
K^+	0	2	4	4
Cl^-	109.5	111.5	113.5	116
Ca^{2+}	1.75 [7mg/dl]	1.75	1.75	1.25 [5mg/dl]
HCO^3	32	32	32	30
Lactate	3	3	3	0
Phosphate	0	0	0	1.2[3.715mg/dl]
Mg^{2+}	0.5 [1.2mg/dl]	0.5	0.5	0.6[1.4598mg/dl]
Glucose	0	6.1	6.1	0
Osmolality (mOsm/L)	287	297	301	293

5. Hemosol B0 KO/MG230/20-0021
6. Prismasol2_4 KO/MG230/20-0025
7. Phoxilium KO/MG230/20-0023

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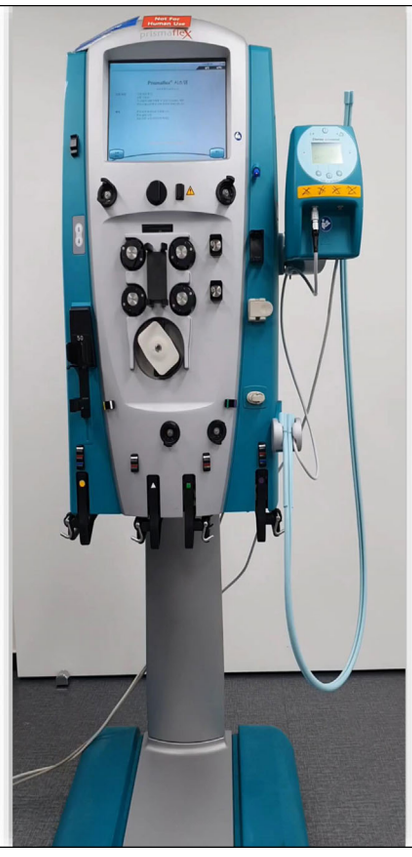
Prismaflex 시작



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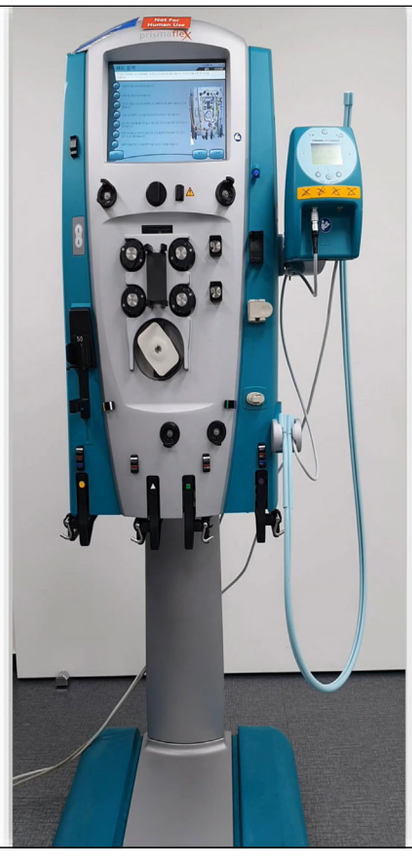
Prismaflex 세트장착



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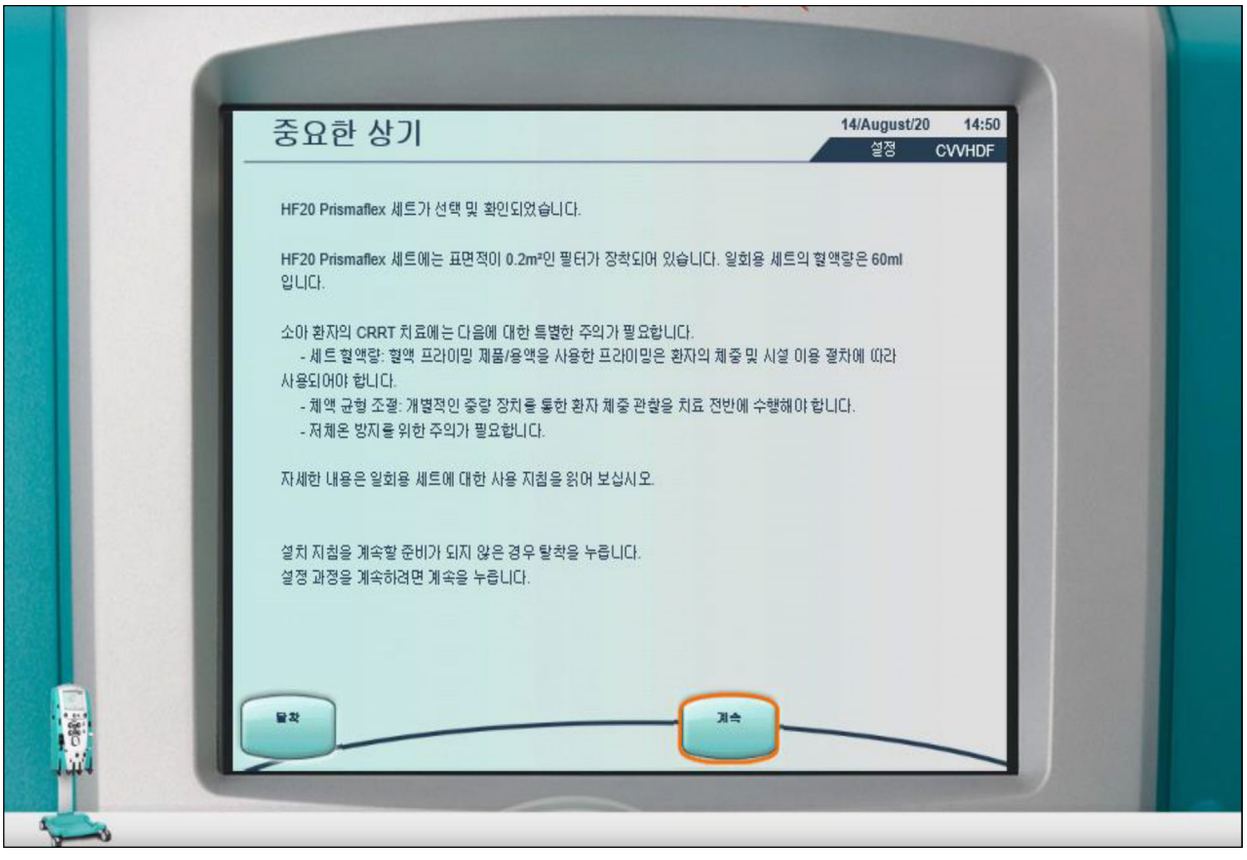
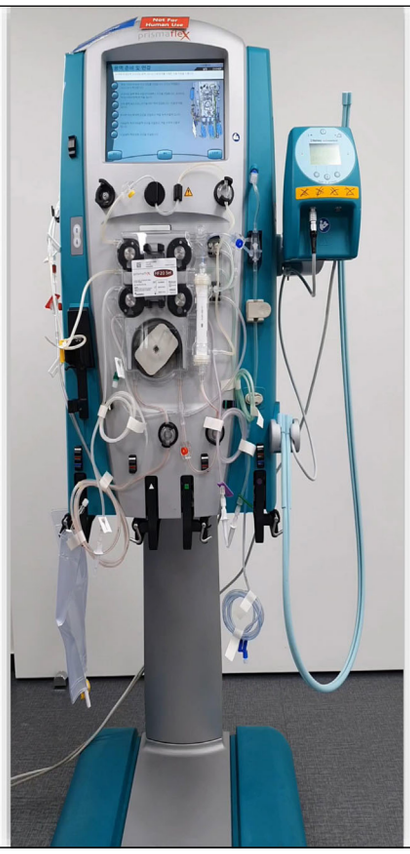


용액 준비 및 연결
주사기 장착
프라임+검사
유량설정



Solution & Catheter 연결 시,
병원 규정에 따른 무균술을
시행해야 합니다.

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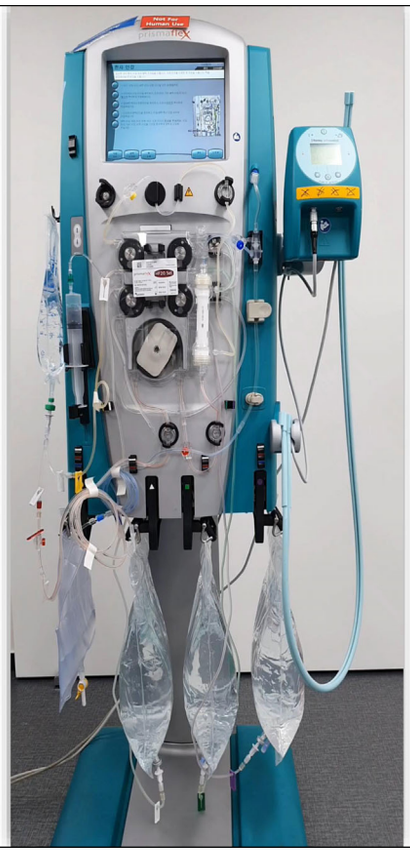
Primsflex 시작



Solution & Catheter 연결 시,
병원 규정에 따른 무균술을
시행해야 합니다.

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http://www.prismaflexguide.co.kr/

Baxter

Prismaflex
사용자가이드동영상

Baxter Prismaflex
동영상 가이드

Baxter KO/MG230/20-0027 31

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Thank You!

Baxter.com

참고 자료

1. Prismaflex 8.XX version 관리자 설명서 KO/MG230/20-0032
2. Prismaflex System 브로셔 KO/MG230/20-0026
3. Prismaflex Set 브로셔 KO/MG230/20-0024
4. GamCath 브로셔 KO/MG230/20-0020
5. Hemosol B0 KO/MG230/20-0021
6. Prismasol2_4 KO/MG230/20-0025
7. Phoxilium KO/MG230/20-0023
8. 동영상 E-mail로 승인을 득함

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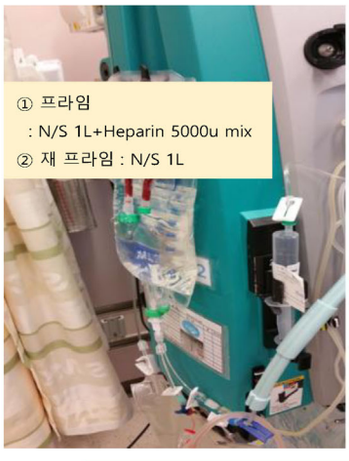
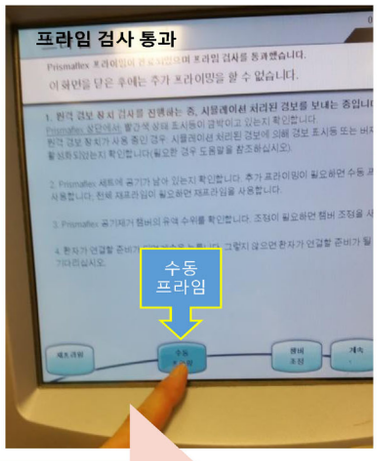
Alarm Troubleshooting

최 앵 자

삼성서울병원

Neonatal CRRT Priming





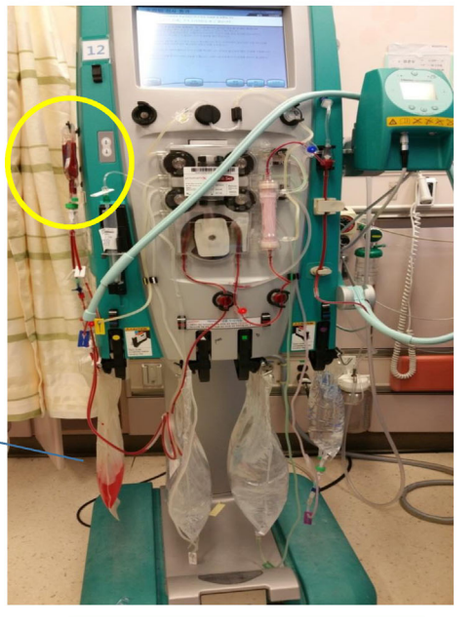
N/S Priming
& 프라임 검사

Priming용 수액 교체
(N/S 50ml + RBC 50ml mix)

→ 필터에 혈액이 채워 질 때 까지 수동 priming 누름

체외 순환 혈액량이 전체 혈액의 10% 초과 시 **Blood priming**

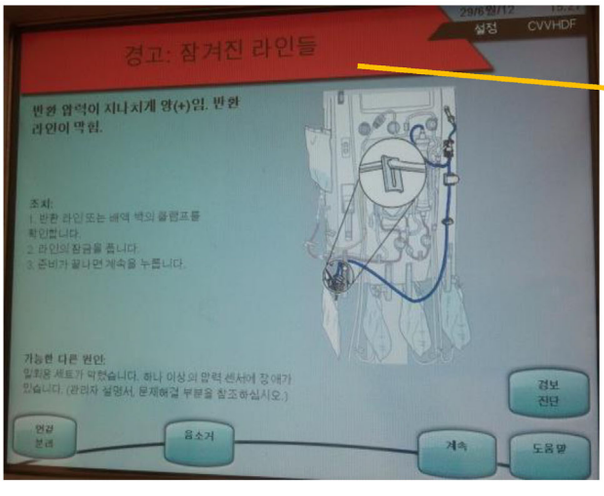
Neonatal CRRT Priming



Effluent bag으로
priming 용액이 나옴.

Blood priming 후 연결

Priming 시 알람 발생



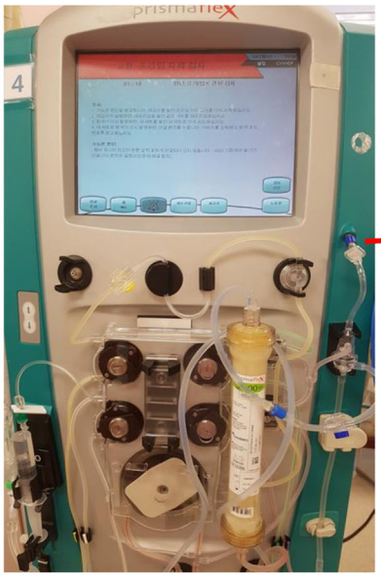
프라임 중에
투석/보충액이
터치 된 경우도
발생 가능함

- 잠겨진 라인들
- 라인 교차

라인 확인 후 교정

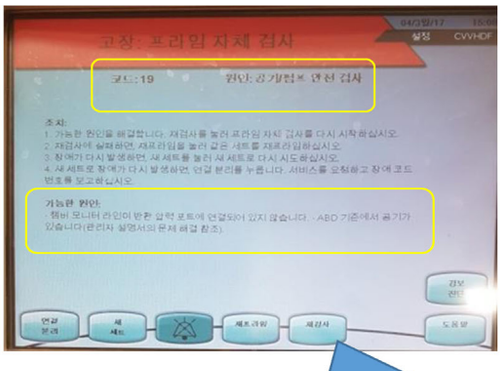
재 프라임 실시

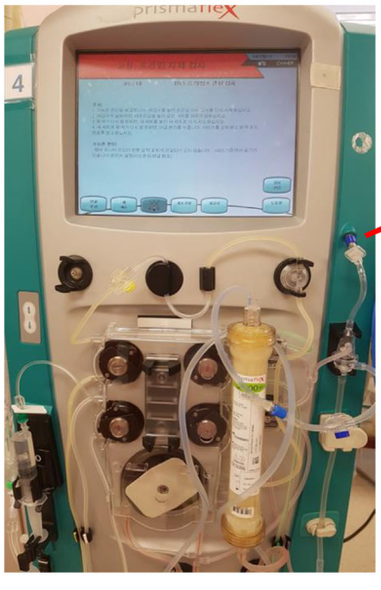
프라임 자체 검사



- 라인이 잠겨 있는지 확인
- 누출 여부 확인

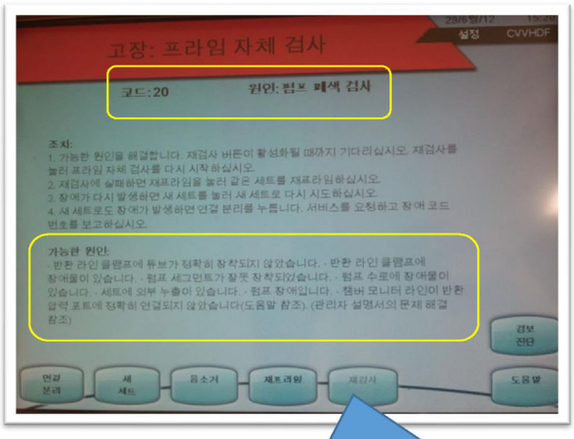
프라임 자체 검사

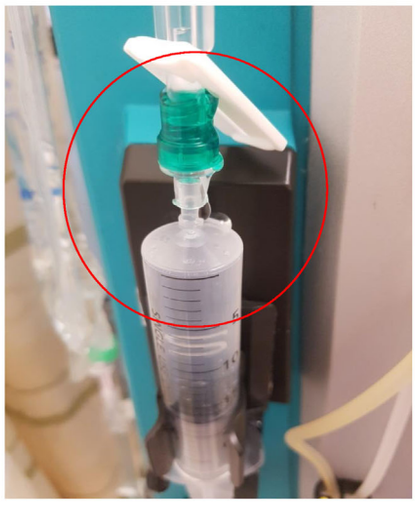




- 반환 라인 확인
  : 반환 압력 포트 부위 연결 재확인
⇒ 재검사

프라임 자체 검사





- 반환 라인 확인 / 재검사
- 항 응고제 주사기 점검
- 세트에 외부 누출 확인

CRRT

❖ CRRT 장비 : 압력 모니터링 (정상과 비정상을 반영 하는 압력 측정)의 변화 시 알람 발생.

⇒ 알람 발생 : 환자 안전을 보호하는 중요한 역할 (Baldwin & Fealy, 2009).

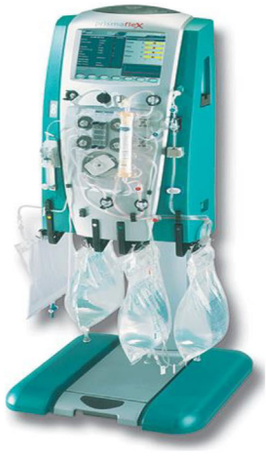
❖ **Factors Affecting Pressures**

- Individual patient characteristics
  - Blood pressure
  - Size
  - General condition
  - Hematocrit
- Location and condition of vascular access and catheter size
- Therapy being delivered and flow rates applied

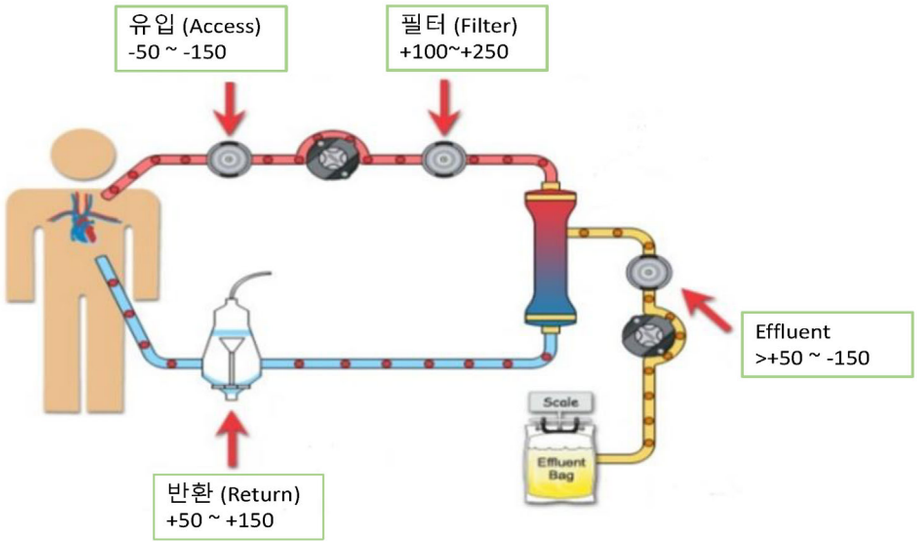
CRRT 알람

❖ 알람 발생 : 환자 안전을 보호하는 중요한 역할
- ➢ 고장음(malfunction): 기계의 고장을 알림.
- ➢ 주의 경보음(advisory): 필요한 작업을 알림.
- ➢ 경고음(caution과 warning) : **환자의 안전과 관계된 알람.**

❖ 경고음: CRRT 동안 즉각적인 처치가 요구되는 알람 (Dirkes & Hodge,
- 유입 알람
- 반환 알람
- 필터 응고 알람
- 유속 알람
- 공기 감지 알람
- 혈액 누출 감지 알람



CRRT Pressure Monitoring

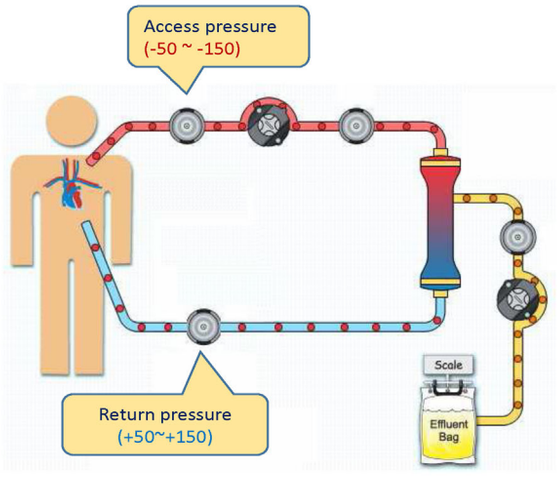


CRRT 장비의 이해

유입, 반환

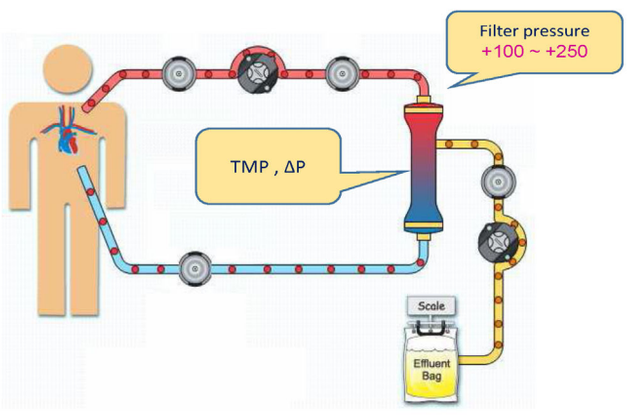
❖ 원인

- line이 꺾이거나 꼬인 경우
- catheter가 clot으로 막힌 경우
- 환자의 BP가 낮은 경우
- BFR이 catheter 직경에 비해 너무 높은 경우
- Catheter function 저하된 경우



필터 응고

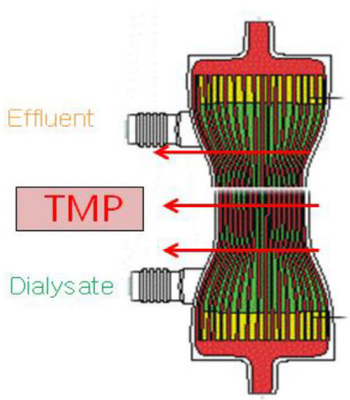
1) 필터에 Clot 있는 경우
2) 시간당 지나치게 많은 fluid가 제거되거나 공급되는 경우
3) Return catheter function이 떨어지는 경우



TMP (Transmembrane pressure)

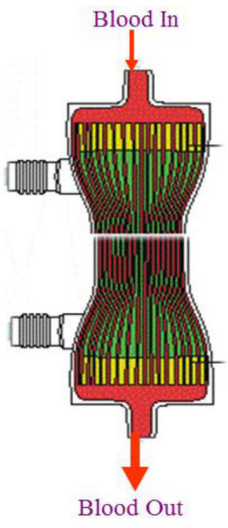
- 혈액내의 수분이 막을 통해 배액쪽으로 빠져 나갈 때 투과막에 걸리는 압력으로 Effluent, filter, return pr 값을 반영

$$TMP = \frac{(\text{Filter P} + \text{Return P})}{2} - \text{Effluent P}$$



- Clotting =초기값보다 100mmHg 증가
  Clotted = 450mmHg이상

ΔP Filter Pressure

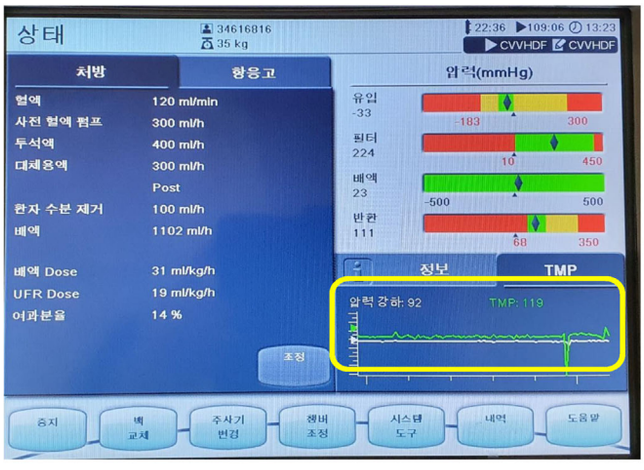


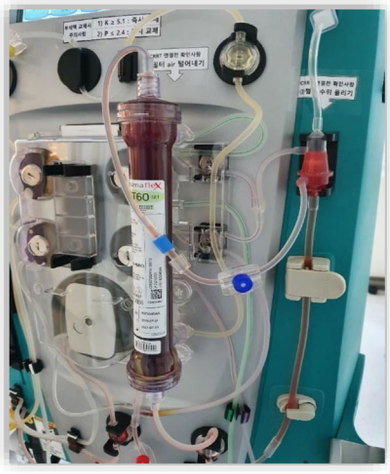
Filter Pressure
- Return Pressure
Filter Pressure Drop

Start	*24 hrs after*
100mmHg	200mmHg
-90mmHg	-110mmHg
10mmHg	90mmHg

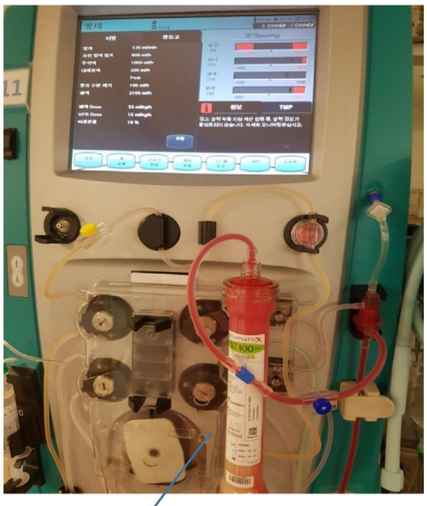
TMP high

- 현재 BFR에 비해 UFR이 많은 경우
- Filter에 Clot이 많은 경우

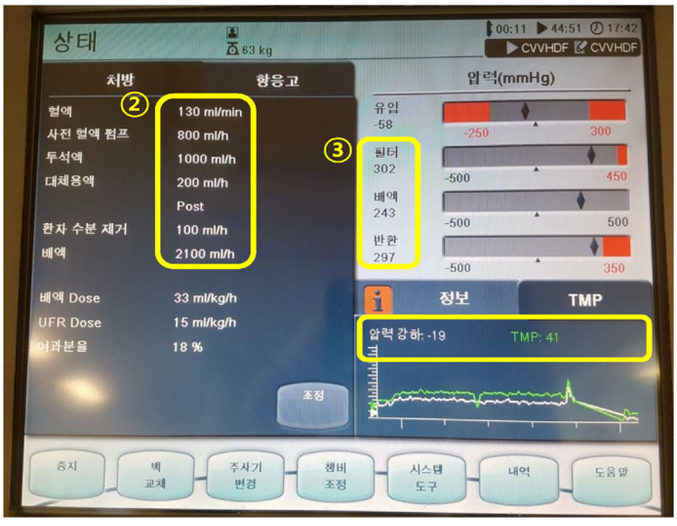




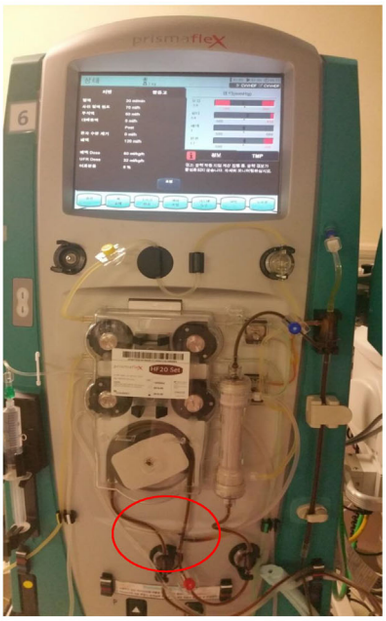
필터 응고 확인

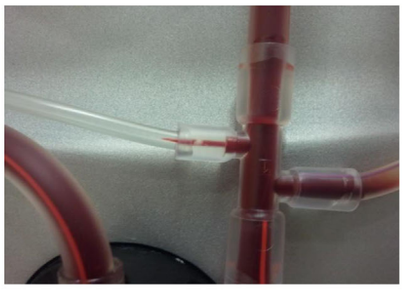


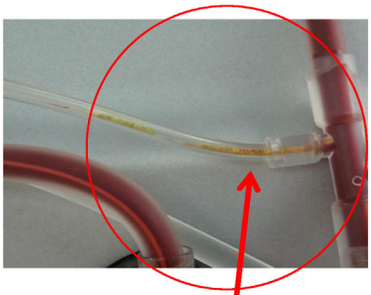
① 필터 상태 확인
– N/S irrigation



항응고제 유입 부위



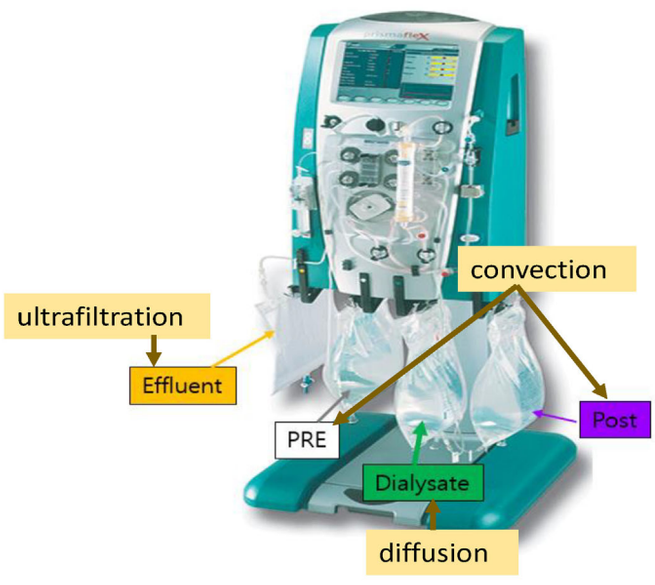




응고 확인

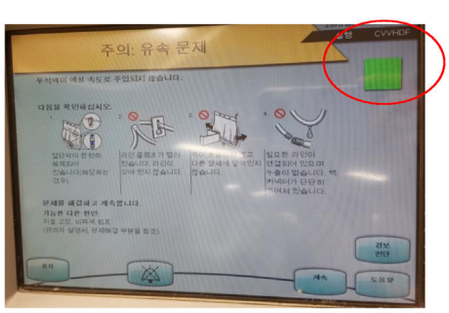
Nafamostat 사용 시 확인

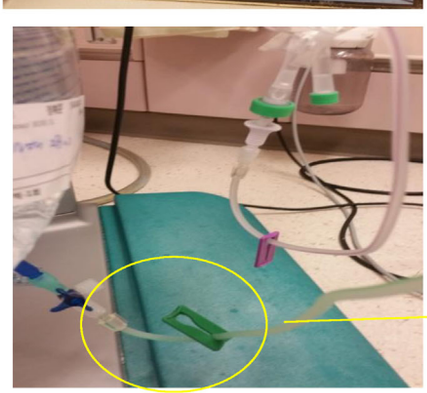
유속 알람



▶ 유속 알람 발생 시 Check point
- 유속 방해 요인 확인
- 무게 변화 요인 확인

유속문제 / 수분 증가 한도 도달

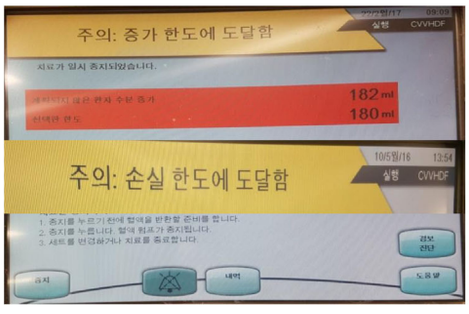




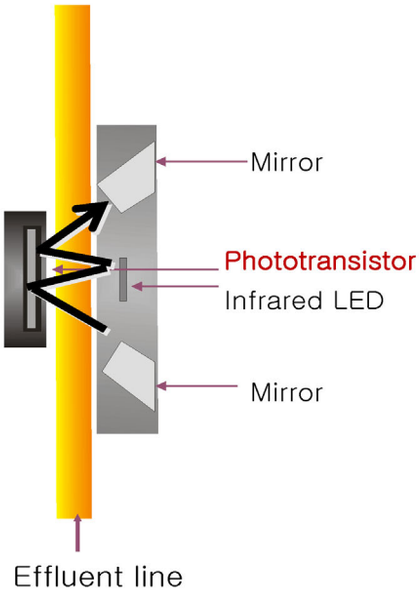
유속

무게

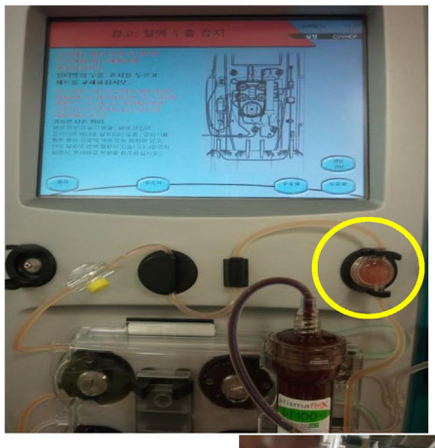
수분 증가 / 손실 한도 도달



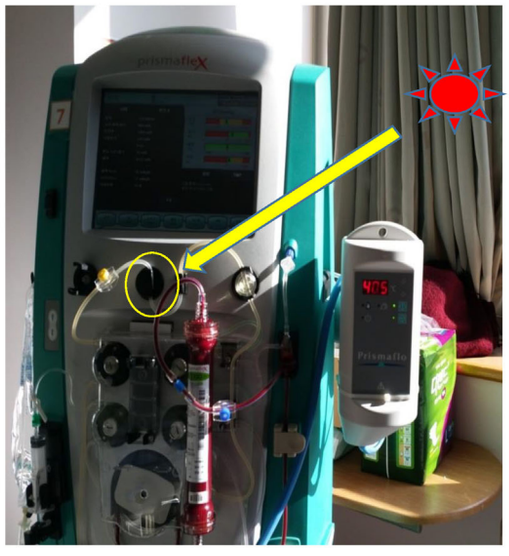
혈액 누출 감지기



혈액누출 감지 알람

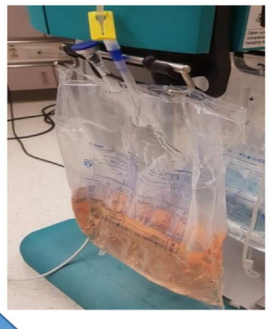


혈액 누출 확인

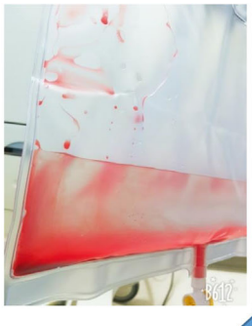


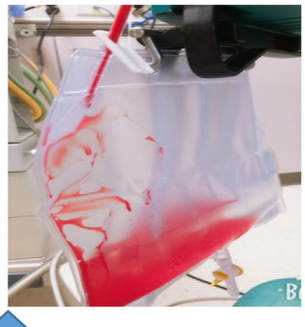
혈액누출감지기 오류

혈액 누출 감지 – Effluent Bag color 확인



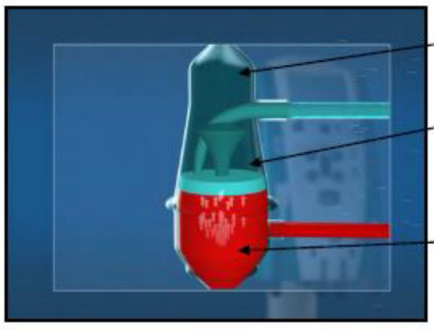
Rhabdomyolysis
- 사용 가능





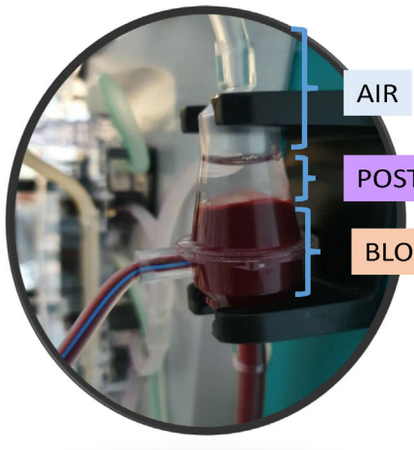
Blood Leak : 혼탁
- 세트 교체 필요

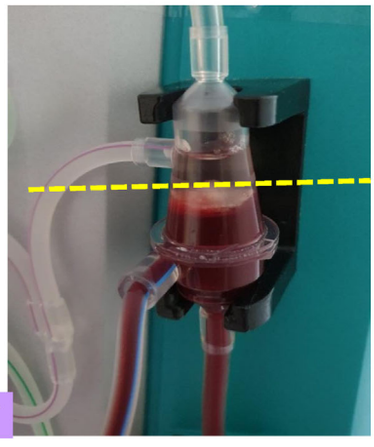
공기 감지 알람



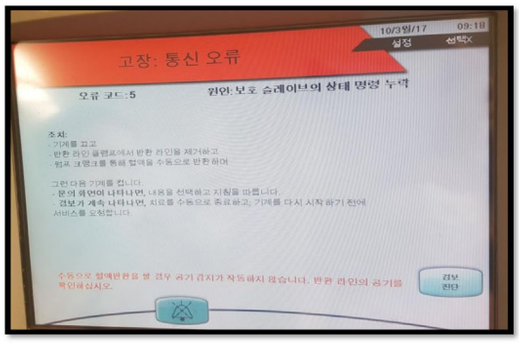
▶Post fluid가 없을 경우 혈액이 공기와 접촉
⇒ 반환 chamber 부위의 혈액 응고 발생

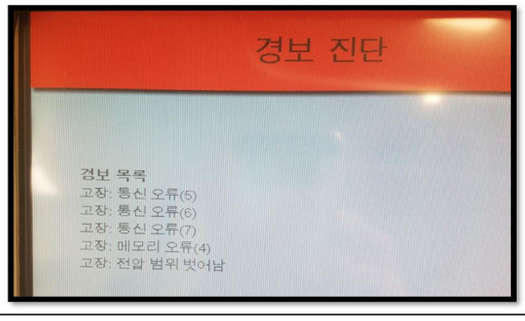
공기 감지 알람





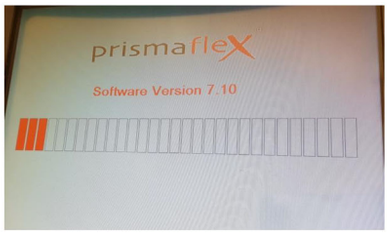
일반 시스템 장애/ 통신 오류

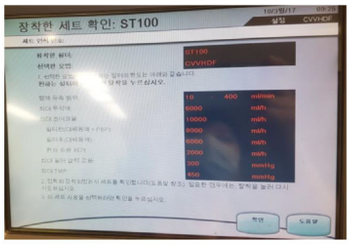


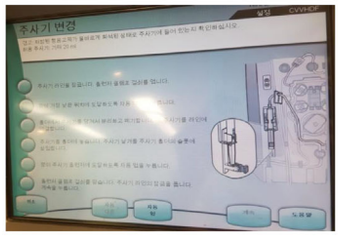


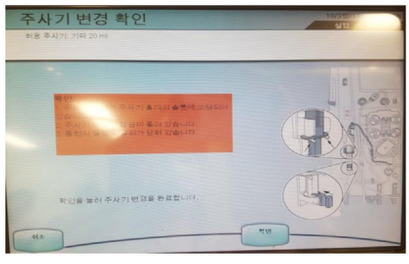
▶ 전원 오프 → ON

일반 시스템 장애/ 통신 오류

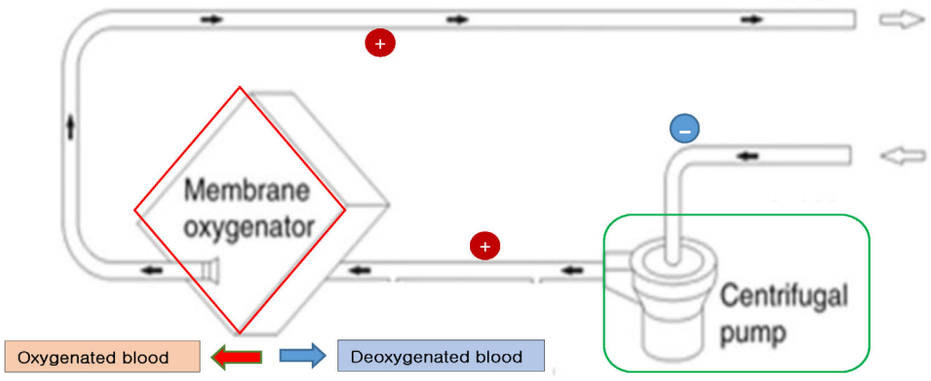






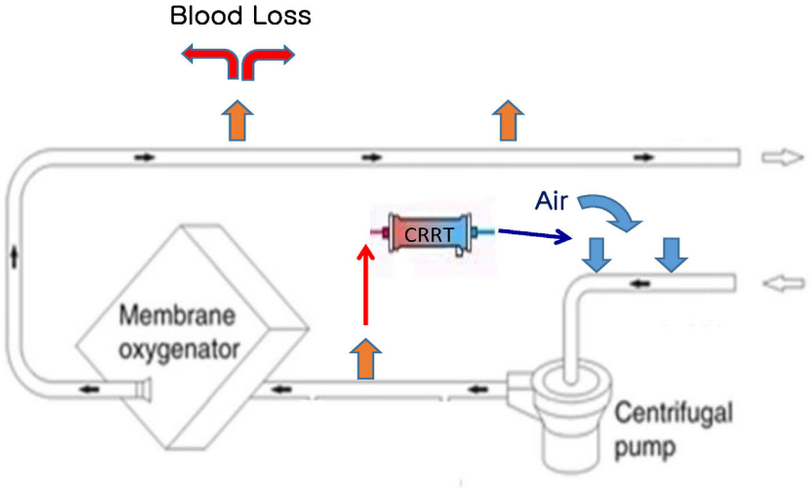


ECMO & CRRT



	PRE	POST
PUMP	음압	양압
Oxygenator	Deoxygenated blood	Oxygenated blood

ECMO & CRRT



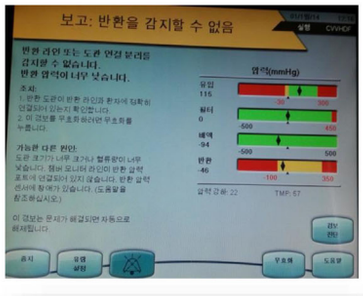
Troubleshooting

Negative pressure : AIR

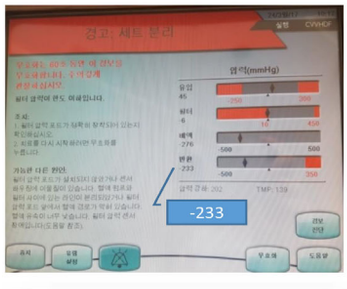
positive pressure : high pressure

Return too negative

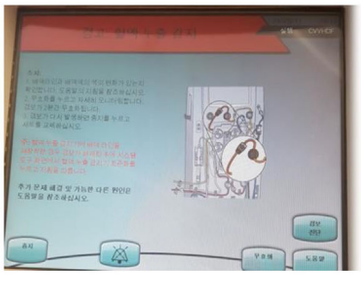
알람 : 반환을 감지할 수 없음

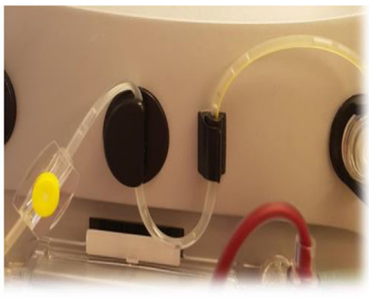


경고: 세트 분리



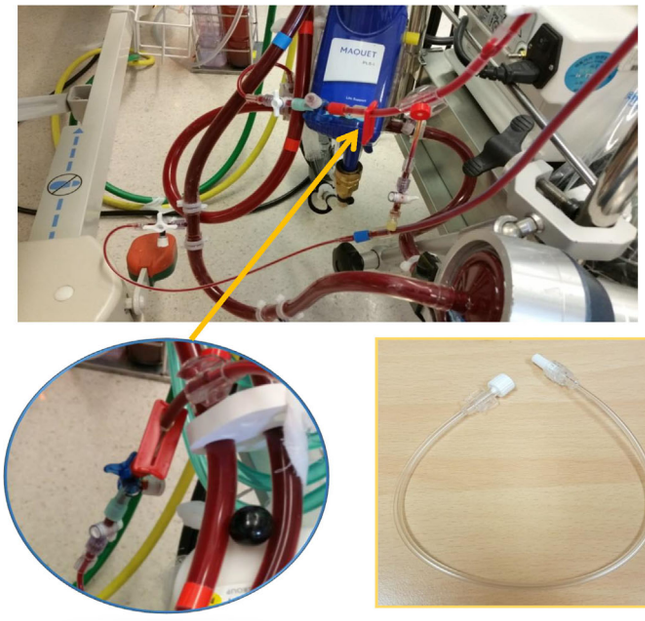
경고: 혈액 누출 감지



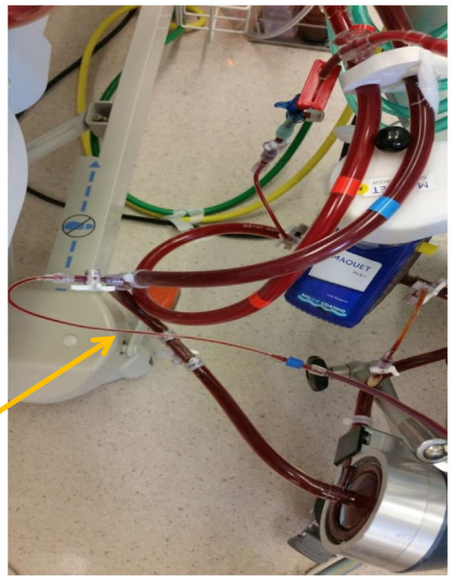


CRRT & ECMO 연결방법

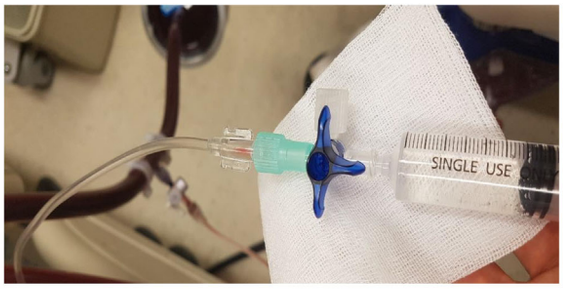
잠금 장치 이용 방법

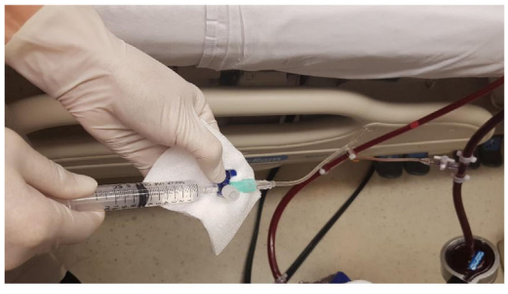


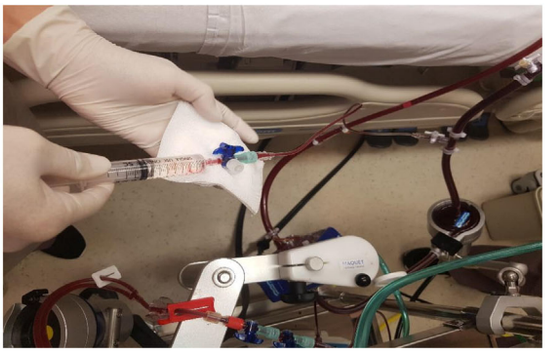
Pressure line 이용 방법



CRRT & ECMO 연결방법



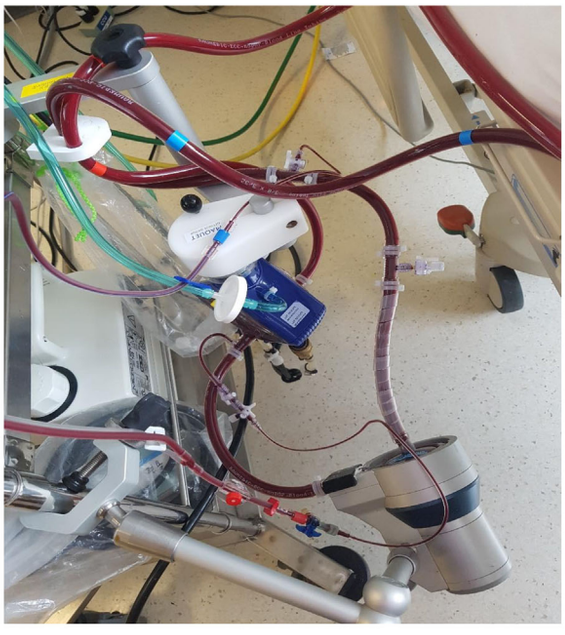


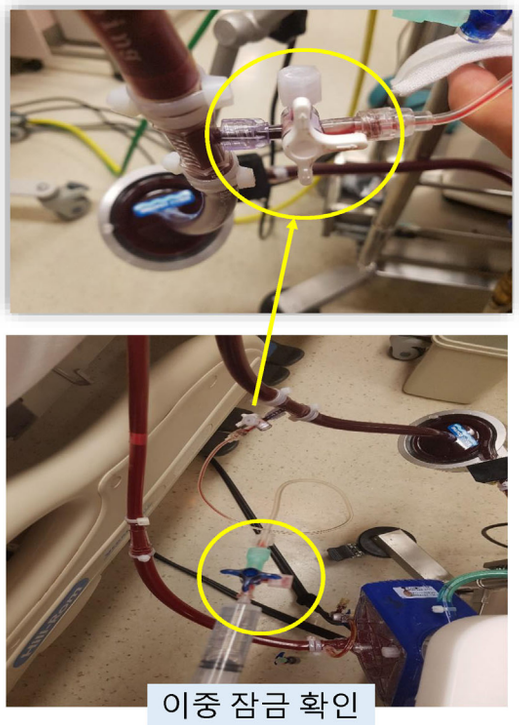


▶ECMO 압력의 영향으로 Syringe가 뒤로 밀릴 수 있다.

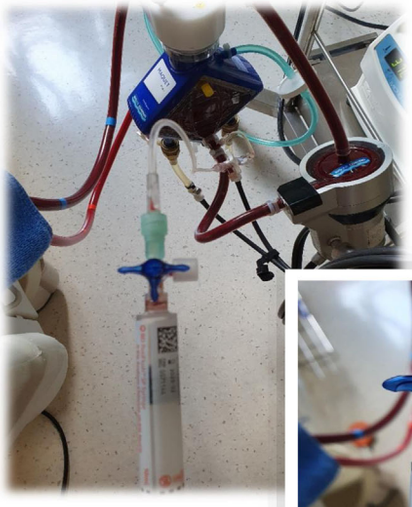
⇒한 손으로 3-way를 고정
& 다른 한 손으로 주사기를 잡는다.

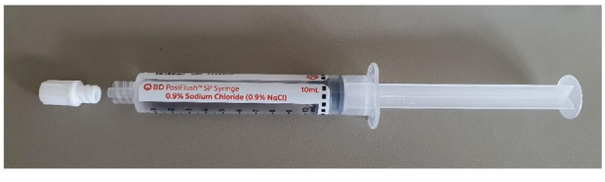
CRRT & ECMO 연결방법

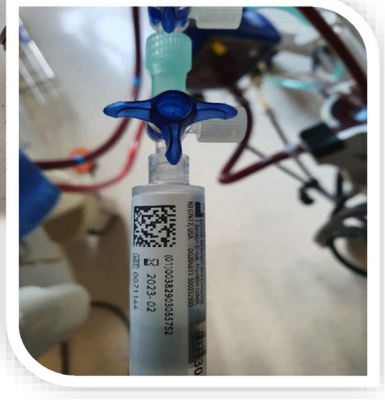


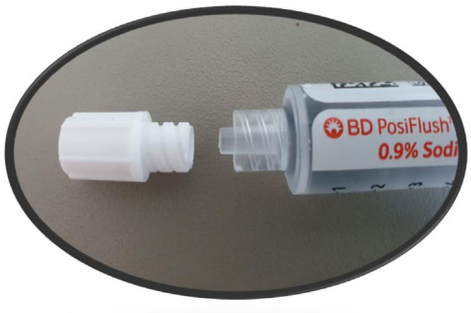


CRRT & ECMO 연결방법

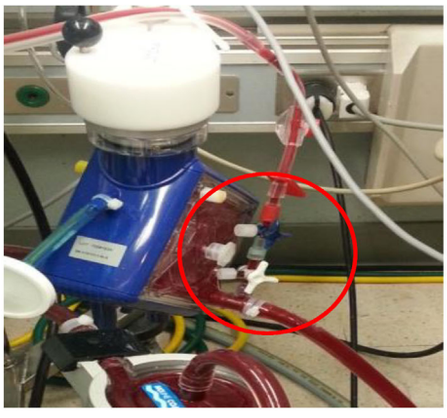


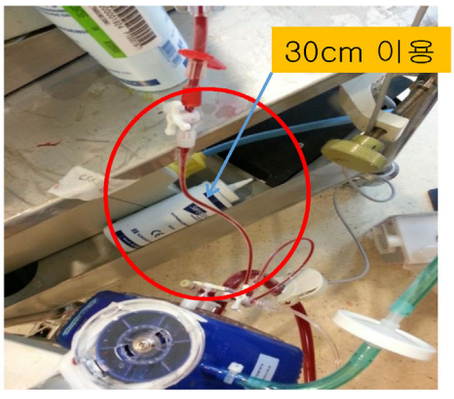


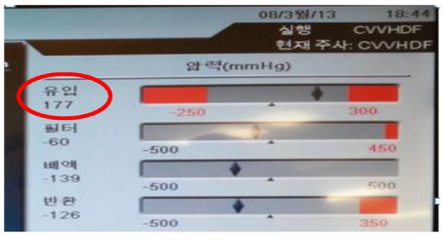


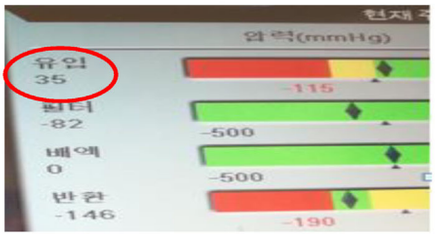


CRRT & ECMO : pressure 조절









II. CRRT in Specific situations

좌장: 조민현(경북의대)

CRRT for sepsis-induced AKI

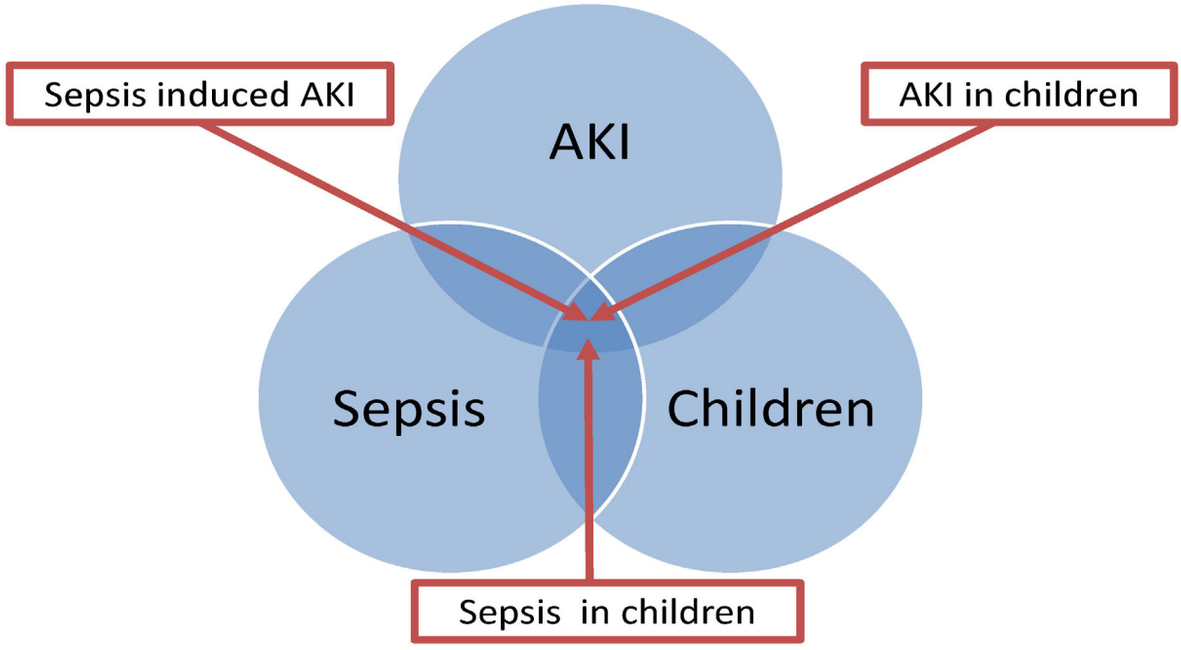
Yeonhee Lee

The Catholic Uinversityof Korea, St. Mary's hospital
Department of pediatrics, division of nephrology

Contents

- Sepsis induced AKI
- Pathophysiology of SI-AKI
- Management of SI-AKI
- Timing of CRRT
- Dose of CRRT
- Special filter membrane

Sepsis induced AKI



What is sepsis?

- **There are two definitions and diagnostic criteria used for sepsis**

SIRS in the presence of infection was introduced in 1992 in CHEST

Sepsis
2/4 SIRS criteria
in the presence of infection

→ **Severe sepsis**
Sepsis + Organ failure

→ **Septic shock**
Sepsis + hypotension

Spesis-3 criteria were proposed by a specialist taskforce in 2016

Sepsis
Increase in SOFA score of ≥2

→ **Septic shock**
Sepsis + circulatory, cellular, and metabolic abnormalities

- **Pediatric sepsis - Modified SIRS criteria**

(2/4, one of which must be abnormal temperature or leukocyte count)
The International Consensus Conference on Pediatric Sepsis in 2005

JAMA. 2016 Feb; 315(8): 801–10.
Pediatr Crit Care Med. 2005 Jan;6(1):2-8

SIRS criteria vs SOFA score

- SIRS criteria

≥ 2 out of 4, High probability of sepsis	
Body temperature (℃)	< 36 or > 38
White blood cell count (/uL)	< 4,000 or > 12,000
Heart rate (beats/min)	> 90
Respiratory rate (breaths/min)	> 20

- SOFA(Sepsis – 3)

Age	Tachycardia/ Bradycardia (beats/min)	Respiratory rate (breaths/ min)	WBC count (x1000/mm)	Systolic BP (mm Hg)
0-1wks	> 180/ <100	>50	>34	< 65
1wks-1mo	> 180/ <100	>40	>19.5 or <5	<75
1mo-1yr	> 180/ <90	>34	>17.5 or <5	<100
2-5yr	> 140/NA	>22	>15.5 or <6	<94
6-12yr	> 130/NA	>18	>13.5 or <4.5	<105
13-18yr	> 110/NA	>14	>11 or <4.5	<117

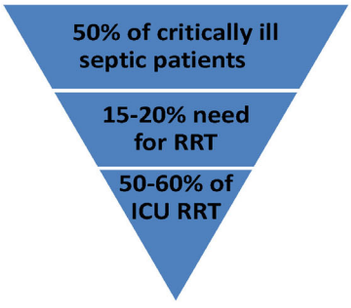
< 500 < 200

- Pediatric sepsis

NEJM. 2015;327:1629-38.

JAMA. 2016 Feb; 315(8): 801–10.

Sepsis-induced acute kidney injury



- SI- AKI is the first cause of AKI in the ICU
- SI-AKI is linked with risk of CKD and death
- SI-AKI associated mortality rates remain high
- About 50–60% of ICU patients receiving RRT not surviving their hospital admission

Curr Opin Crit Care 2018, 24:483–492

Pathophysiology of SI-AKI

Pathophysiology of SI-AKI

1. Renal blood flow ↓ → Tubular epithelial cell death, or acute tubular necrosis → SI-AKI

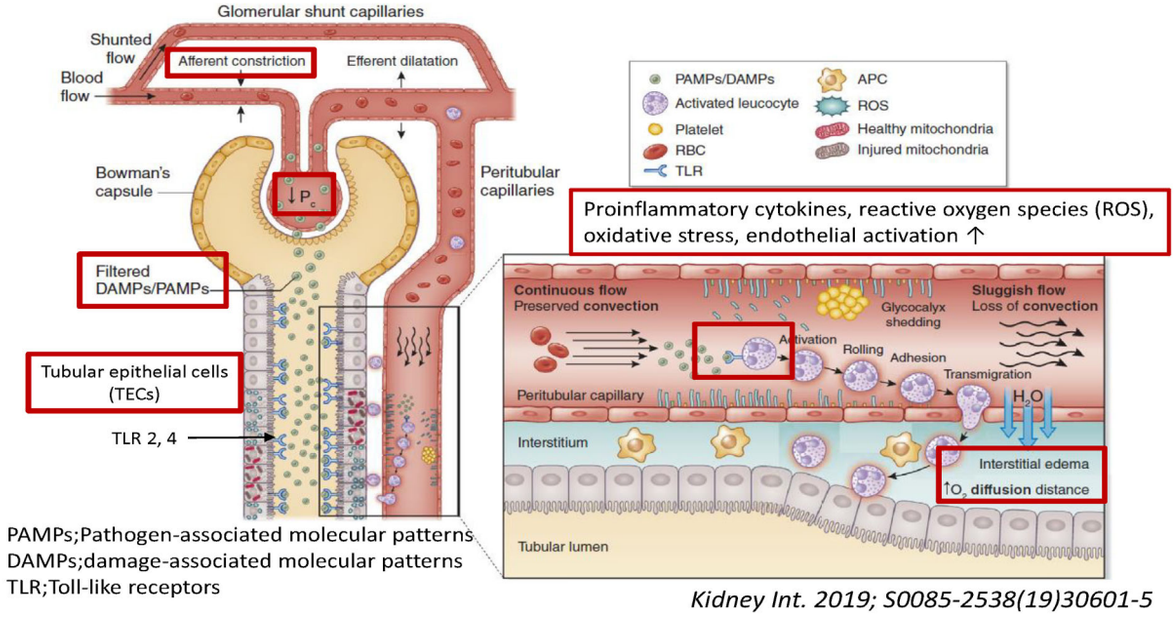
(e.g., sepsis, major surgery, heart failure, and hypovolemia) are all associated with hypo-perfusion and shock, and ischemic injury can cause extensive cell death (e.g., ATN)

Renal blood flow ↑ → A heterogeneous, focal, and patchy tubular injury, with minimal tubule-epithelial cell death (<5%), apical vacuolization, minor focal mesangial expansion → SI-AKI

2. Three mechanism
Inflammation
Microcirculatory dysfunction
Metabolic reprogramming

Kidney Int. 2019; S0085-2538(19)30601-5

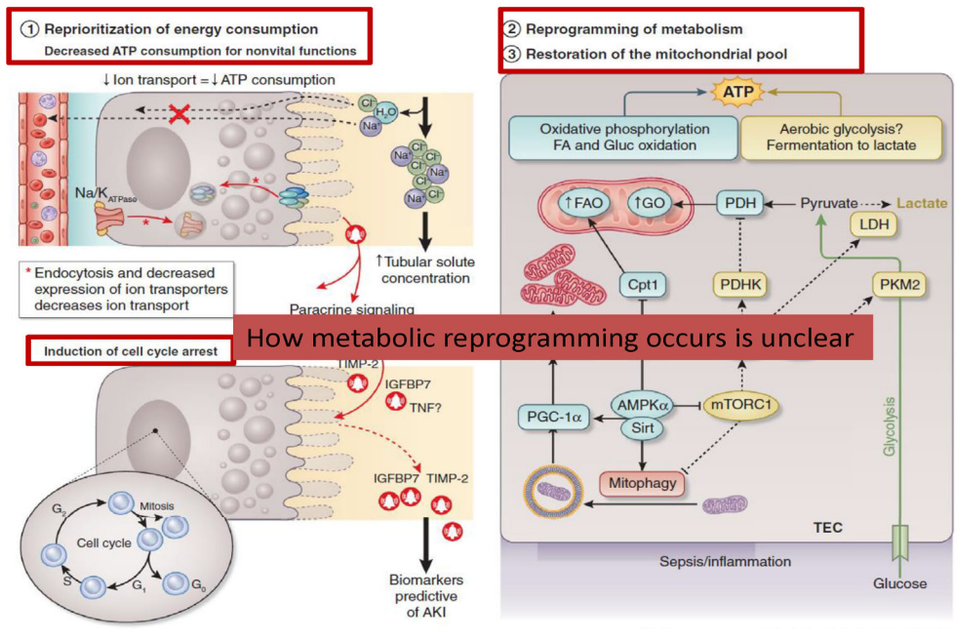
Microcirculatory, inflammatory alterations



PAMPs;Pathogen-associated molecular patterns
DAMPs;damage-associated molecular patterns
TLR;Toll-like receptors

Kidney Int. 2019; S0085-2538(19)30601-5

Metabolic reprogramming

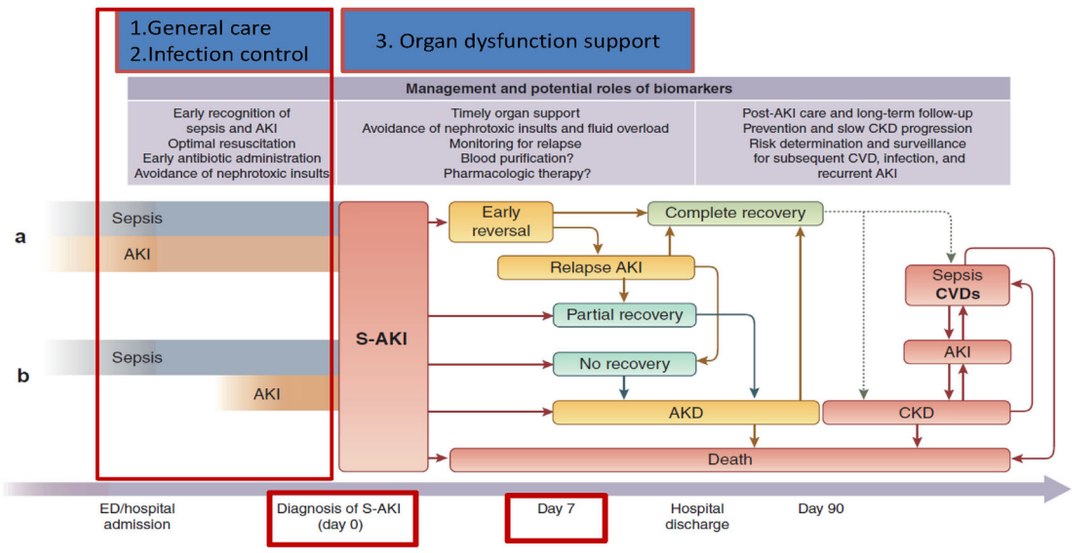


How metabolic reprogramming occurs is unclear

Kidney Int. 2019; S0085-2538(19)30601-5

Management of SI-AKI

Management of SI-AKI



Kidney Int. 2019; S0085-2538(19)30601-5

Management of sepsis in children

First-hour goals:
Restore and maintain heart rate thresholds, capillary refill >2 seconds, and normal blood pressure

0 min

Recognize decreased mental status and perfusion.
Begin high flow O_2 and establish IO/IV access according to PALS.

5 min

If no hepatomegaly or rales / crackles then push 20 mL/kg isotonic saline boluses and reassess after each bolus up to 60 mL/kg until improved perfusion. Stop for rales, crackles or hepatomegaly. Correct hypoglycemia and hypocalcemia.
Begin antibiotics.

15 min

Fluid refractory shock?

Begin peripheral IV/IO inotrope infusion, preferably Epinephrine 0.05 – 0.3 µg/kg/min
Use Atropine / Ketamine IV/IO/IM if needed for Central Vein or Airway Access

Titrate Epinephrine 0.05 – 0.3 µg/kg/min for Cold Shock.
(Titrate central Dopamine 5 – 9 µg/kg/min if Epinephrine not available)
Titrate central Norepinephrine from 0.05 µg/kg/min and upward to reverse Warm Shock.
(Titrate Central Dopamine ≥ 10 µg/kg/min if Norepinephrine not available)

60 min

Catecholamine-resistant shock?

If at risk for Absolute Adrenal Insufficiency consider Hydrocortisone.
Use Doppler US, PICCO, FATD or PAC to Direct Fluid, Inotrope, Vasopressor, Vasodilators
Goal is normal MAP-CVP, $ScvO_2$ > 70%* and CI 3.3 – 6.0 L/min/m²

Crit Care Med 2017;45:1061–1093

Management of AKI in children

- **Fluid management**
  Check I/O, Daily weight, vital signs, heart rate, blood pressure
- **Avoidance of further renal injury**
  Use of adjusting the dose in the patient's renal function status
  Avoid contrast-induced nephropathy
- **Specific intervention**
  Diuretics, Renal dose dopamine, human natriuretic peptide nesiritide, growth factor, erythropoietin, free-radical scavenger
- **Nutrition**
  Enteral nutrition has an advantage over parenteral nutrition

Child Kidney Dis 2015; 19(2): 71-78

Timing of CRRT

CRRT for AKI (KDIGO guideline)

- 5.1.1: Initiate RRT emergently when life-threatening changes in fluid, electrolyte and acid-base balance exist. (Not Graded)
- 5.1.2: Consider the broader clinical context, the presence of conditions that can be modified with RRT, and trends of laboratory tests, rather than single BUN and creatinine thresholds alone, when making the decision to start RRT. (Not Graded)

2012 KDIGO. VOL 2 | SUPPLEMENT 1 | MARCH 2012

Indication of CRRT

The debate between **'rescue'** indications for RRT start in patients with severe AKI (acidosis, hyperkalemia, uremia, oliguria/anuria, volume overload) and **a proactive** RRT initiation is still ongoing.

Life-threatening indications	No trials to validate these criteria.
Hyperkalemia	Dialysis for hyperkalemia is effective in removing potassium; however, it requires frequent monitoring of potassium levels and adjustment of concurrent medical management to prevent relapses.
Acidemia	Metabolic acidosis due to AKI is often aggravated by the underlying condition. Correction of metabolic acidosis with RRT in these conditions depends on the underlying disease process.
Pulmonary edema	RRT is often utilized to prevent the need for ventilatory support; however, it is equally important to manage pulmonary edema in ventilated patients.
Uremic complications (pericarditis, bleeding, etc.)	In contemporary practice it is rare to wait to initiate RRT in AKI patients until there are uremic complications.
Nonemergent indications	
Solute control	BUN reflects factors not directly associated with kidney function, such as catabolic rate and volume status. SCr is influenced by age, race, muscle mass, and catabolic rate, and by changes in its volume of distribution due to fluid administration or withdrawal.
Fluid removal	Fluid overload is an important determinant of the timing of RRT initiation.
Correction of acid-base abnormalities	No standard criteria for initiating dialysis exist.
Renal support	This approach is based on the utilization of RRT techniques as an adjunct to enhance kidney function, modify fluid balance, and control solute levels.
Volume control	Fluid overload is emerging as an important factor associated with, and possibly contributing to, adverse outcomes in AKI. Recent studies have shown potential benefits from extracorporeal fluid removal in CHF. Intraoperative fluid removal using modified ultrafiltration has been shown to improve outcomes in pediatric cardiac surgery patients.
Nutrition	Restricting volume administration in the setting of oliguric AKI may result in limited nutritional support and RRT allows better nutritional supplementation.
Drug delivery	RRT support can enhances the ability to administer drugs without concerns about concurrent fluid accumulation.
Regulation of acid-base and electrolyte status	Permissive hypercapnic acidosis in patients with lung injury can be corrected with RRT, without inducing fluid overload and hypernatremia.
Solute modulation	Changes in solute burden should be anticipated (e.g., tumor lysis syndrome). Although current evidence is unclear, studies are ongoing to assess the efficacy of RRT for cytokine manipulation in sepsis.

AKI, acute kidney injury; BUN, blood urea nitrogen; CHF, congestive heart failure; SCr, serum creatinine; RRT, renal replacement therapy.

2012 KDIGO. VOL 2 | SUPPLEMENT 1 | MARCH 2012

Timing of CRRT for SI-AKI

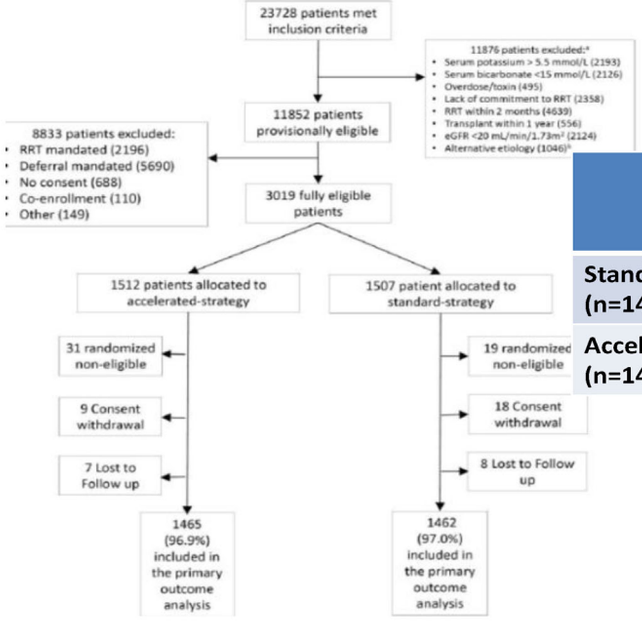
Table 2 | Timing for RRT in S-AKI

Trial	Setting	Percentage of sepsis	Modality of RRT	Timing of RRT initiation: Early strategy	Timing of RRT initiation: Delayed strategy	Outcome
Gaudry *et al.*[147] (AKIKI)	Adults, ICU patients with AKI (multicenter)	80%	IHD/CRRT	Median time 2 h (IQR: 1–3 h) after randomization or 4.3 h (IQR: 2.7–5.9 h) after documented KDIGO stage 3 AKI, $N = 311$	Median time 57 h (IQR: 25–83 h) after randomization, $N = 308$ (51% received RRT)	No difference in 60-day mortality (48.5% vs. 49.7%), *post hoc* analysis in patients with septic shock (56%) showed similar results, more patients with CRBSI and hypophosphatemia in early group, adequate diuresis with no need for RRT were observed earlier in delayed group.
Zarbock *et al.*[148] (ELAIN)	Adults, ICU patients, 47% with cardiac surgery (single center)	21%	CVVHDF	Median time 6 h (IQR: 4–7 h) after documented KDIGO stage 2 AKI, $N = 112$	Median time 25.5 h (IQR: 18.8–40.3 h) after documented KDIGO stage 2 AKI (within 12 h after KDIGO stage 3 AKI), $N = 119$ (91% received RRT)	Significantly lower 90-day mortality in early group (39.3% vs. 54.7%), no difference in renal recovery at 90 days, 95% of study population were surgical patients and small number of patients with sepsis. In follow-up analysis found significantly reduced rate of $MAKE_{365}$ (64.9% vs. 89.1%) and 1-year mortality (50.2% vs. 69.8%) in early group.
Barbar *et al.*[149] (IDEAL-ICU)	Adults, patients with septic shock and severe AKI (multicenter)	100%	IHD/CRRT	Median time 7.6 h (IQR: 4.4–11.5 h) after RIFLE-F, $N = 246$	Median time 51.5 h (IQR: 34.6–59.5 h) after documented AKI or meet emergency RRT criteria (K >6.5 mmol/l, pH < 7.15, fluid overload), $N = 242$ (51% received RRT)	No difference in 90-day mortality (58% vs. 54%), more days of RRT and less RRT-free days in early group, more patients with hyperkalemia in delayed group, similar fluid balance, 29% of patients in delayed group had spontaneous recovery.
STARRT-AKI (NCT01557361)	Adults, ICU patients with severe AKI (RIFLE-I, oliguria, pNGAL ≥400 ng/ml (multicenter)	N/A	IHD/SLED/CRRT	"Accelerated" initiation: RRT will be initiated within 12 h of fulfilling eligibility	"Standard" initiation: participants will be monitored over 7 days to identify indications for RRT (K ≥6.0 mmol/l, bicarbonate ≤10 mmol/l, PaO_2/FiO_2 <200 and bilateral infiltrates on CXR, persistent AKI >72 h after eligibility)	N/A

AKIKI, Artificial Kidney Initiation in Kidney Injury trial; CRBSI, catheter-related bloodstream infection; CRRT, continuous renal replacement therapy; CVVHDF, continuous venovenous hemodiafiltration; CXR, chest x-ray; ELAIN, Early Versus Late Initiation of Renal Replacement Therapy in Critically Ill Patients With Acute Kidney Injury trial; ICU, intensive care unit; IDEAL-ICU, Initiation of Dialysis Early Versus Delayed in the Intensive Care Unit trial; IHD, intermittent hemodialysis; IQR, interquartile range; KDIGO, Kidney Disease: Improving Global Outcomes; $MAKE_{365}$, major adverse kidney events by 365 days; N/A, not applicable; pNGAL, plasma neutrophil gelatinase-associated lipocalin; RIFLE, Risk, Injury, Failure, Loss of Kidney Function, End-Stage Kidney Disease classification; RRT, renal replacement therapy; S-AKI, sepsis-associated acute kidney injury; SLED, sustained low efficiency dialysis; STARRT-AKI, Standard Versus Accelerated Initiation of Dialysis in Acute Kidney Injury trial.

Kidney Int. 2019; S0085-2538(19)30601-5

clinical trial
Standard Versus Accelerated Initiation of Dialysis in AKI [STARRT-AKI]

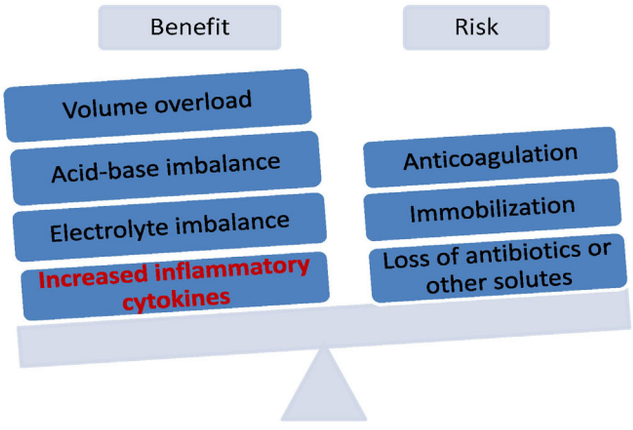


	Mortality at 90days	KRT dependence	Any adverse Event
Standard (n=1464)	43.7%	6%	17%
Accelerated (n=1465)	43.9%	10%	23%

N Engl J Med 2020 Jul 16;383(3):240-251.

Indication of proactive initiation CRRT?

- **The patients with sepsis without advanced stage of AKI ?**



Dose of CRRT

CRRT setting

- **Type of CRRT**
  [ ] CVVHDF [ ] CVVHD [ ] CVVHF
- **Filter**
  [ ] HF20 [ ] ST60 [ ] ST100 [ ] ST150
- **Priming solution**
  [ ] RBC [ ] NS [ ] 5% albumin [ ] Others
- **Blood flow rate**
  From 3 to ~10 ml/kg/min, depending on age (min. 24ml/min)
- **Dialysis fluid flow rate(DFR) + Replacement fluid flow rate (RFR Pre/Post)**
  Filtration replacement fluid or dialysate rate (2100 ml/1.73m^2/hr)
- **Patient flulid removal rate (PFRR)**
  Input/hr-output/hr+ 0ml/hr → (+ max. 2ml/kg/hr)

Dose of CRRT

Author/ study	Type	Sample	Comparison/intervention	Outcomes
ATN trial	Multicenter RCT	1124 critically ill patients with AKI	Pre-dilution CVVHDF 35 ml/kg/hr or si x sessions/week of SLEDD/IHD versus pre-dilution CVVHDF 20 ml/kg/hr or t hree sessions/week of SLEDD/IHD	**No significant difference of survival rate** (46 and 48%)
RENAL trial	Multicenter RCT	1508 critically ill patients with AKI	Post-dilution CVVHDF 40 ml/kg/hr ver sus 25 ml/kg/hr	**No significant difference of survival rate** (55 and 55%)

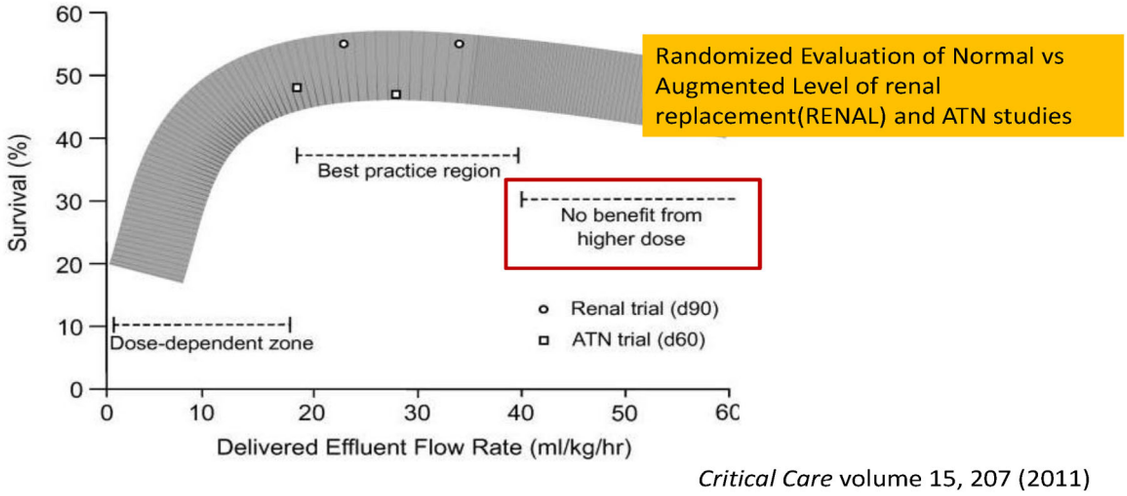
The KDIGO guidelines proposed the optimal dose of CRRT of 20–25 mL/kg/hr Considering about filter clotting, concentration polarization of the filter, and other factors including access-related problems which diminish the treatment time

CRRT : Effluent dose of 20-25(30)mL/kg/hr (Effluent volume 2000ml/hr/1.73m2)

Critical Care volume 15, 207 (2011)

Dose of CRRT ?

- **CRRT : Effluent dose of 20-25(30)mL/kg/hr**
  (Effluent volume 2000ml/hr/1.73m2)



Randomized Evaluation of Normal vs Augmented Level of renal replacement(RENAL) and ATN studies

Critical Care volume 15, 207 (2011)

Special filter membrane

ST 60/ST 100/ST 150

Name	Filter size	*EBV/Kg
HF20	0.2㎡	60ml/8kg
ST60	0.6㎡	93ml/11kg
ST100	1.0㎡	152ml/30kg
ST150	1.5㎡	189ml/30kg

* EBV : Extracorporeal Blood Volume

The polyarylethersulfone (PAES) membrane

Surface-treated polyacrylonitrile =ST AN69

CASE REPORT Open Access

Effects of continuous renal replacement therapy with the AN69ST membrane for septic shock and sepsis-induced AKI in an infant: a case report with literature review of cytokine/mediator removal therapy in children

Naoto Nishizaki[1*], Riko Ueno[1], Yuki Nagayama[1], Hanako Abe[1], Akina Matsuda[1], Akira Mizutani[1], Kaoru Obinata[1], Tadaharu Okazaki[2] and Toshiaki Shimizu[3]

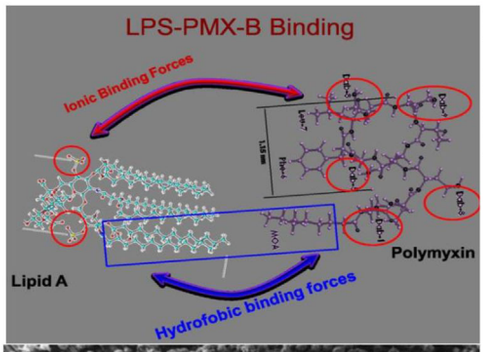
Abstract

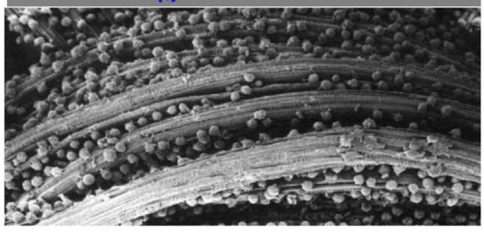
Background: Septic shock is a life-threatening condition and one of the most common causes of acute kidney injury (AKI). The acrylonitrile-co-methallyl sulfonate surface-treated (AN69ST) membrane used in severe sepsis was formally launched in Japan in 2014, as a non-renal indication. This membrane provides hemofiltration in dialysis and improves hemodynamics in patients with sepsis and hypercytokinemia. However, the clinical literature regarding continuous renal replacement therapy (CRRT) with the AN69ST membrane is very limited, especially in infants.

Case presentation: A 3-month-old female infant weighing 4.2 kg was hospitalized for septic shock and AKI secondary to necrotizing enterocolitis. Although she underwent palliative surgery, her vital signs did not recover from shock, and she developed reduced urine output. Her pediatric sequential organ failure assessment score was 10 points. Thus, we strongly suspected septic shock and sepsis-induced AKI, which were refractory to conservative treatment, and we decided to introduce CRRT with the AN69ST membrane for both renal replacement and anti-hypercytokinemic indications. After initiating CRRT for 72 h, her blood pressure increased sufficiently to maintain urine output, and improvements in the electrolyte abnormalities and metabolic acidosis were observed. Notably, her serum inflammatory cytokine levels decreased in parallel with improvement in her general condition. Despite successfully recovering from the AKI and being stable enough to allow discontinuing CRRT, she died of multiple organ dysfunction syndrome 3 weeks after CRRT was discontinued.

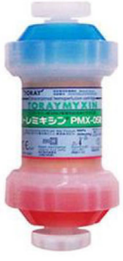
Renal Replacement Therapy (2020) 6:34

Polymyxin-B (TORAYMYXIN®)





Product type	PMX-20R	PMX-05R
Length	225 mm	133 mm
Diameter (max)	63 mm	55 mm
Priming volume	135 ± 5 ml	40 ± 3 ml
Launch year in EU market	2002	2019



Immobilizing **PMX** to **polystyrene-derived fibers**

Critical Care volume 18, 309 (2014)
https://cs2.toray.co.jp

Polymyxin-B (TORAYMYXIN®)

Table 2 Variables changes 72 h after PMX-HP

From: Polymyxin-B hemoperfusion in septic patients: analysis of a multicenter registry

Patients	t_0 N = 357	t_{72} N = 299	p (Wilcoxon)
SOFA score	12.4 ± 4.2	10.5 ± 5.3	*<0.001*
Cardiovascular SOFA	3.32 ± 1.29	2.16 ± 1.77	*<0.001*
Renal SOFA	2.23 ± 1.62	1.84 ± 1.77	*0.013*
Hepatic SOFA	1.22 ± 1.28	1.19 ± 1.30	0.80
Respiratory SOFA	2.40 ± 1.06	1.95 ± 0.95	*<0.001*
Coagulation SOFA	1.33 ± 1.29	1.67 ± 1.38	*0.004*
Inotropic score	30 (11.9–72.5)	6.0 (0.0–22)	*<0.001*
Lactate, mmol/L	3.4 (1.9–6.0)	1.9 (1.3–2.9)	*<0.001*
Platelets, $10^3/\mu L$	117 (56–220)	86 (40–163)	*<0.001*

Normally distributed data are expressed as mean ± SD and non-normally distributed data as median (interquartile range)
Italics indicates significant *p* values

Intensive Care(2016) 6:77

정부혁신 보다나은 정부 | 다양한 복지서비스 복지로에서 한번에 | 평생친구

<수술·처치 분야 건강보험 적용>

항목	사용목적	관행가(평균)		환자본인부담
후두마스크(재료, 31개)	응급환자대상 후두경 없이 구	3만9000원		1만8000원
폴리믹신B 고정화 섬유를 이용한 혈액관류요법	그람음성균에 의한 패혈증 환자 내독소 제거하는 혈액투석	행위	63만5000원	62만4000원
		재료 (1개)	430만6000원	339만5000원
체외 간 지지요법	간부전 환자의 암모니아 등 독소 제거	행위	108만2000원	80만8000원
		재료 (2개)	409만5000원	355만3000원

1) 내독소혈증 또는 의심되는 그람음성균 감염
2) 아래 2가지 이상의 조건에 해당될 경우
- 구강체온시 >38℃ 혹은 <36 ℃
- 빈맥(>90회/min)
- 빈호흡(>20회/min) 또는 PaCO2<32mmHg
- 백혈구수치(>12,000개/mm3 또는 <4,000개/mm3 또는 10% 이상의 간상핵 호중구)
3) 혈관 수축제를 필요로 하는 패혈증 쇼크

* 보험적용가격, 환자본인부담: 상급종합병원, 입원 기준

oXiris

Name	Filter size	*EBV/Kg
oXiris	1.0㎡	193ml/30kg
ST150	1.5㎡	189ml/30kg

* EBV : Extracorporeal Blood Volume

Surface-treated polyacrylonitrile =ST AN69 + PEI (polyethyleneimine)

Larger molecular weight molecules by membrane binding

RESEARCH ARTICLE

Background

Endotoxin induces an inflammatory response, with secondary release of cytokines, which can progress to shock and multiple organ failure. We explored whether continuous renal replacement therapy (CRRT) using a modified membrane (oXiris) capable of adsorption could reduce endotoxin and cytokine levels in septic patients.

Methods

Sixteen patients requiring CRRT for septic shock-associated acute renal failure and who had endotoxin levels >0.03 EU/ml were prospectively randomized in a crossover double-blind design to receive CRRT with an oXiris filter or with a standard filter. Endotoxin and cytokine levels were measured at baseline and 1, 3, 8, 16 and 24 hours after the start of CRRT. Norepinephrine infusion rate and blood lactate levels were monitored.

Results

During the first filter treatment period, endotoxin levels decreased in 7 of 9 (77.8%) oXiris filter patients, but in only 1 of 6 (16.7%) standard filter patients ($P = 0.02$). Levels of tumor necrosis factor (TNF)-α, interleukin (IL)-6, IL-8 and interferon (IFN)γ decreased more with the oXiris filter than with the standard filter. Lactate concentration decreased with oXiris (-1.3[-2.2 to -1.1] mmol/l, $P = 0.02$), but not with the standard filter (+0.15[-0.95 to 0.6]). The norepinephrine infusion rate was reduced during oXiris CRRT, but not during standard filter CRRT. In the second filter treatment period, there was no significant reduction in endotoxin or cytokine levels in either group.

Conclusions

CRRT with the oXiris filter seemed to allow effective removal of endotoxin and TNF-α, IL-6, IL-8 and IFNγ in patients with septic shock-associated acute renal failure. This may be associated with beneficial hemodynamic effects.

Which filter is better in SI-AKI ?

Adsorption	Property/mechanism of action	Comment
Polymyxin B Hemoperfusion	Synthetic membrane coated with polymyxin B that binds endotoxin	Improved hemodynamic parameter and monocyte and neutrophil function with controversy on survival benefit
CytoSorb	Porous polymer beads; adsorption of cytokines, myoglobin, free hemoglobin, bilirubin/bile acid	Reduce circulating IL-6, improve hemodynamics, no survival benefit
oXiris	Surface-treated AN69 membrane with PEI and coated with heparin; adsorption of endotoxin and cytokines	Reduced SOFA score at 48 h Ongoing RCTs are investigating the effectiveness of this treatment (ENDoX, NCT01948778; oXiris, NCT02600312).
HA-330	Neutral microporous resin; adsorption of cytokines, complements, free hemoglobin	Improved hemodynamics and organ function, shortened ICU stay, and reduced ICU mortality
LPS adsorbers	Synthetic polypeptide bound to porous polyethylene discs; adsorption of endotoxins	A case series in patients with gram-negative sepsis reported improvement of hemodynamics and decreased endotoxin level but no effect on survival.
CPFA	Combined plasma separation with adsorption and hemodialysis; removes inflammatory mediators	No survival benefit, technical issue (clotted), high cost. Additional RCTs are pending (COMPACT 2, NCT01639664;ROMPA, NCT02357433).

Kidney Int. 2019; S0085-2538(19)30601-5

Current choice of Filter in children

	HF20	ST60	ST100	Polymyxin-B
Body weight	> 8Kg	> 11Kg	> 30Kg	PMX-05R child
BSA (m^2)	0.2	0.6	1.0	
Membrane	PAES	AN69ST	AN69ST	PMX-B
Set blood volume(ml)	60	93	152	40(+/- 3)
Cost (won)	103,320	103,320	103,320	4,980,000

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3) 혈관 수축제를 필요로 하는 패혈증 쇼크

Summary

- Sepsis-induced acute kidney injury (SI-AKI) is currently accounted as the first cause of AKI in the ICU
- A "unified theory" of SI-AKI
  Hypo-perfusion
  Inflammation, Microcirculatory dysfunction, Metabolic reprogramming
- Management of SI-AKI
  Optimal resuscitation, antibiotics, avoidance of nephrotoxic insults
  Avoidance of fluid overload, pharmacologic therapy, Blood purification
- Timing of CRRT
  The optimal time to start RRT in the setting of SI-AKI is still undefined
  [STARRT-AKI] not associated with a lower risk of death at 90 days
- Special filter membrane : ST60 filter, Toraymyxin , Oxiris

CRRT application in Infants

안 요 한

서울대학교병원 소아청소년과

Content

- CRRT in infants
  - Indication
  - Primary disease
  - Outcome
  - Factors for survival
- Prescribing CRRT in infants
- New machines and filters

CRRT in Children up to 10kg

Table 1. Patient Diagnoses at CRRT Initiation

Diagnosis	No. of Patients	%
Congenital heart disease	14	16.5
Metabolic disorder	14	16.5
Multiorgan dysfunction	13	15.3
Sepsis syndrome	12	14.1
Liver failure	9	10.6
Malignancy	5	5.9
Congenital nephrotic syndrome	4	4.7
Congenital diaphragmatic hernia	3	3.5
Hemolytic uremic syndrome	2	2.3
Heart failure	2	2.3
Obstructive uropathy	1	1.2
Renal dysplasia	1	1.2
Other	5	5.9
Total	85	100

Table 2. Indications for CRRT Initiation

Indication	No. of Patients	%
Combined volume overload and biochemical abnormalities of renal failure	46	54
Volume overload	15	18
Metabolic imbalance unrelated to renal failure (eg, hyperammonemia)	12	14
Biochemical abnormalities of renal failure	8	9
Other (eg, medication overdose)	3	4
Volume overload and hyperammonemia	1	1
Total	85	100

- 5 children's hospitals, 1993-2001
- Retrospective study, 86 patients (16 pts ≤3 kg)

Symons JM et al. Am J Kidney Dis (2003)

Survival by Diagnosis

Diagnosis	All	>3 kg	≤3 kg
Congenital heart disease	36%	36%	33%
Metabolic disease	**71%**	**71%**	-
Multiorgan dysfuction	**15%**	**11%**	**25%**
Sepsis	42%	42%	-
Liver failure	22%	22%	-
Malignancy	**0%**	**0%**	**0%**
Congenital diaphragmatic hernia	**0%**	**0%**	**0%**
Heart failure	50%	50%	0%
Renal disease	50%	50%	0%

Symons JM et al. Am J Kidney Dis (2003)

Survivors vs. Nonsurvivors

	Weight (kg)	Days on CRRT	No. of Pressors
All patients			
Survivors	5.54 (2.3–10)	8.31 (1–46)	1.03
Nonsurvivors	5.15 (1.5–10)	7.35 (1–43)	1.47
Patients ≤ 3 kg			
Survivors	2.80 (2.3–3)	16.50 (4–46)	1.5
Nonsurvivors	2.42 (1.5–3)	4.42 (1–9)	1.25
Patients > 3 kg			
Survivors	5.93 (3.1–10)	7.14 (1–33)	0.96*
Nonsurvivors	5.95 (3.2–10)	8.21 (1–43)	1.6*

NOTE. Values expressed as mean (range).
*$P < 0.03$.

Symons JM et al. Am J Kidney Dis (2003)

Prospective cohort study

THE JOURNAL OF PEDIATRICS • www.jpeds.com ORIGINAL ARTICLES

Continuous Renal Replacement Therapy for Children ≤10 kg: A Report from the Prospective Pediatric Continuous Renal Replacement Therapy Registry (ppCRRT registry)

David J. Askenazi, MD, MSPH[1], Stuart L. Goldstein, MD[2], Rajesh Koralkar, MBBS, MPH[1], James Fortenberry, MD[3], Michelle Baum, MD[4], Richard Hackbarth, MD[5], Doug Blowey, MD[6], Timothy E. Bunchman, MD[7], Patrick D. Brophy, MD[8], Jordan Symons, MD[9], Annabelle Chua, MD[10], Francisco Flores, MD[11], and Michael J. G. Somers, MD[4]

- 84 children ≤10kg, 2001-2005
- Bwt 4.4 (1.3-10) kg, age 69 days (1 day-2.9 years)

Askenazi D et al. J Pediatr (2013)

Survival by Primary Disease

Primary diagnosis	N (%)	Survive, n (%)	P value
Sepsis	25 (30)	9 (36)	0.37
Cardiac disease	16 (19)	6 (38)	0.59
Inborn error of metabolism	**13 (15)**	**8 (62)**	**0.15**
Hepatic	**9 (11)**	**0 (0)**	**<0.01**
Oncology	6 (7)	3 (50)	0.73
Pulmonary	5 (6)	3 (60)	0.44
Renal*	**5 (6)**	**4 (80)**	**0.09**
Other**	5 (6)	3 (75)	0.19

*ARPKD, cortical necrosis, renal agenesis, congenital NS, unknown cause of CKD
**nephrotoxin, congenital diaphramatic hernia, Omenn's syndrome, post BMT

Askenazi D et al. J Pediatr (2013)

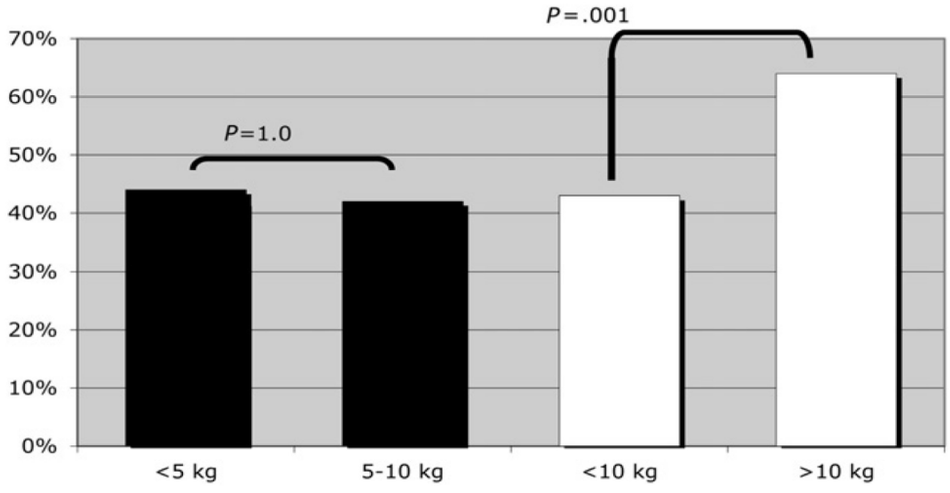
Risk Factors for Mortality

Variables	Adjusted OR	P value
PRISM II score at CRRT	**1.1 (1.0-1.2)**	**0.02**
FO group		
<10%	Ref	
10%-20%	0.9 (0.17-4.67)	0.25
>20%	**4.8 (1.3-17.7)**	**0.01**
Urine output at CRRT	**0.72 (0.53-0.97)**	**0.04**

$$Percent\ fluid\ overload\ (\%FO) = \frac{Fluid\ input\ (L) - Fluid\ out\ (L)}{\text{ICU admission weight (kg)}} \times 100$$

Askenazi D et al. J Pediatr (2013)

Survival Data by Weight



Askenazi D et al. J Pediatr (2013)

CRRT in Neonates <3kg

- NICU at Samsung Medical Center, 2007-2010
- Age 5 days (38^{+2} weeks – 23 days), Bwt 2.73 kg (2.60-2.98)

No	GA	Age	Bwt	S-Cr	Disease	PRISM III	Outcome
1	36^{+2}	3	2.71	2.36	DIC, MODS	22	Death
2	38^{+2}	23	2.83	1.72	NEC, sepsis, MODS	14	Death
3	30^{+3}	38^{+2}*	2.63	2.92	Sepsis, MODS	15	Death
4	25	5*	2.98	0.82	Sepsis, MODS	14	Death
5	**38^{+6}**	**17**	**2.74**	**3.11**	**Atypical HUS**	**9**	**Survival**
6	**36^{+4}**	**5**	**2.6**	**2.30**	**Metabolic disease**	**14**	**Survival**
7	**39**	**9**	**2.65**	**0.93**	**Metabolic disease**	**9**	**Survival**
8	**38^{+3}**	**4**	**2.92**	**0.44**	**Metabolic disease**	**2**	**Survival**

Sohn YB et al. Korean J Pediatr (2012)

CRRT in NICU

- 34 neonates
- NICU of Samsung Medical Center, 2007-2014

- CRRT
  - Prisma or Prismaflex
  - 6.5Fr double lumen catheter
  - M10 hemofilter (2007-2010), HF20 (2010-)
  - Blood flow rate: 5-10 mL/kg/min
  - No anticoagulation → heparin if hemofilter life span <12h

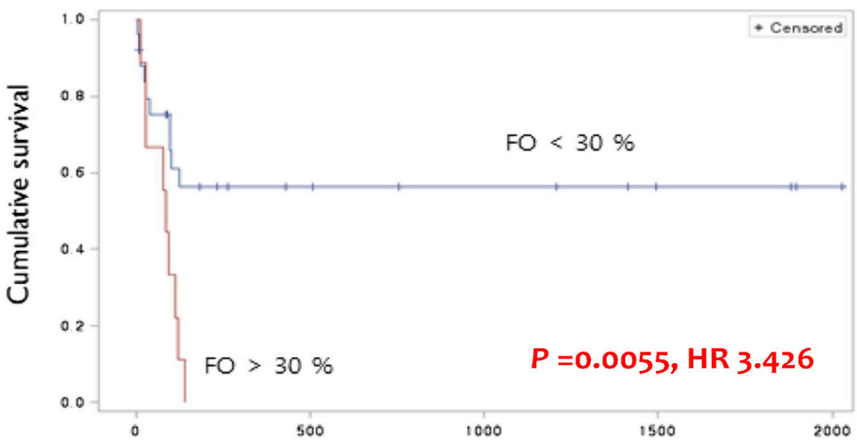
Lee ST et al. Pediatr Nephrol (2016)

Patient Characteristics

	Preterm (n=15)	Term (n=19)
GA (weeks)	30 (27-36)	38 (38-40)
Bwt on NICU admission (kg)	2.7 (2.2-3.0)	2.9 (2.7-3.6)
Age at CRRT initiation (days)	65 (6-97)	6 (4-18)
Indications for CRRT		
Inborn errors of metabolism	2 (13%)	**7 (37%)**
Sepsis	**5 (33%)**	0
Gastrointestinal	**5 (33%)**	2 (11%)
Cardiac anomaly	0	1 (5%)
Hypoxic ischemic	0	1 (5%)
Renal	1 (7%)	2 (11%)
Oncology	0	1 (5%)
Mortality	**12 (80%)**	**5 (26.3%)**

Lee ST et al. Pediatr Nephrol (2016)

Fluid Overload and Mortality



$$\%FO = \frac{Bwt\ at\ CRRT\ initation - Bwt\ at\ NICU\ admission}{\text{Bwt at NICU admission}} \times 100$$

Lee ST et al. Pediatr Nephrol (2016)

Risk factors for Mortality

	HR	95% CI	P value
Urine output at the end of CRRT	**0.578**	**0.361-0.926**	**0.0225**
S-Cr level at CRRT initiation	0.698	0.423-1.152	0.1596
Bwt at NICU admission	1.071	0.492-2.233	0.8633
Fluid overload of ≥30% at CRRT initiation	1.599	0.581-4.398	0.3634
Preterm (GA <37 weeks)	0.519	0.127-2.127	0.3622
Blood flow rate of CRRT	1.218	0.881-1.685	0.2325

Lee ST et al. Pediatr Nephrol (2016)

Prescribing CRRT for Infants

- Vascular access
- Hemofilter
- Modality
- Anticoagulation
- Special considerations

Vascular access

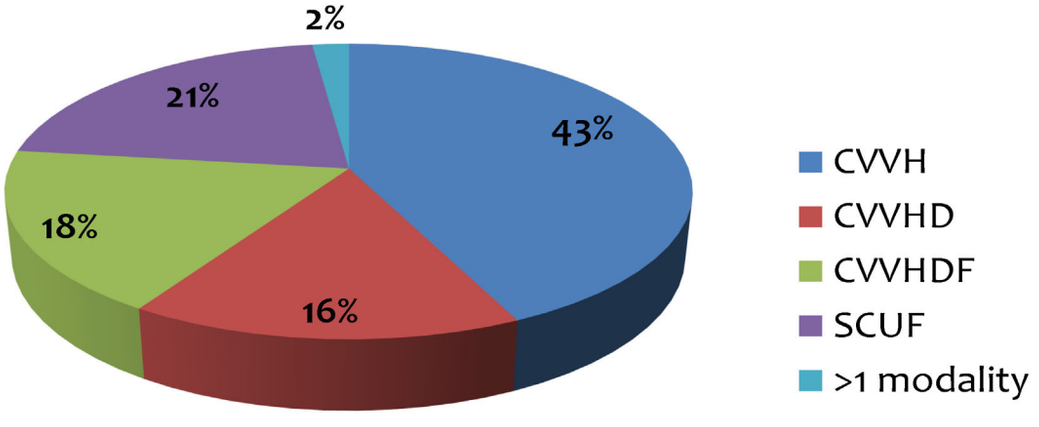
- Catheter size: 6.5 Fr dual lumen
- Location
  - 1st Rt IJV
  - 2nd Femoral
  - 3rd Lt IJV

Hemofilter

	Filter	Bwt (kg)	Surface area (m^2)	Priming vol (mL)	RBC priming*
Prismaflex	**HF20**	**8-10**	**0.2**	**60**	**<8kg**
	ST60	10-30	0.6	93	<12kg
	ST100	>30	1.0	152	<19kg
MultiFiltrate	**Kit paed**	**<20**	**0.2**	**72**	**<9kg**
	Kit midi	20-40	0.75	135	<17kg

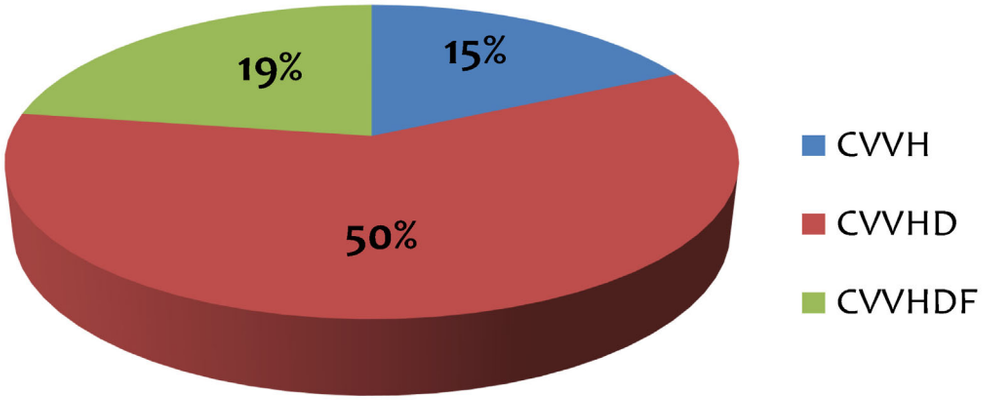
* Priming volume > Blood volume 10% (Bwt 0.8%)

CRRT Modality (1993-2001)



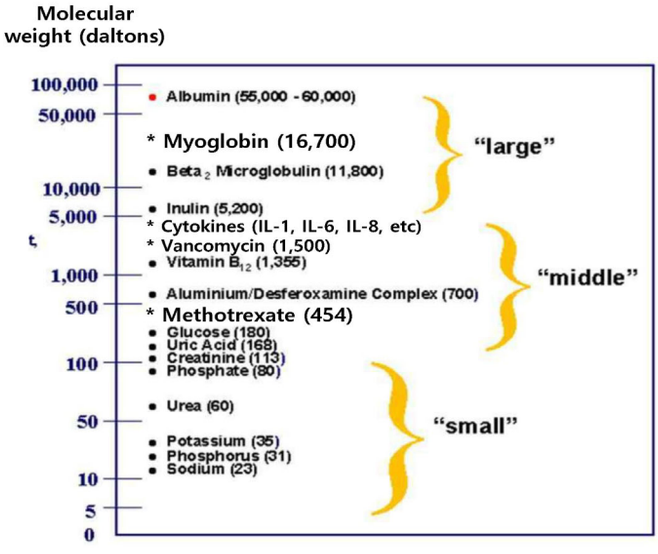
Symons JM et al. Am J Kidney Dis (2003)

CRRT Modality (2001-2005)



Askenazi D et al. J Pediatr (2013)

CVVH vs. CVVHD

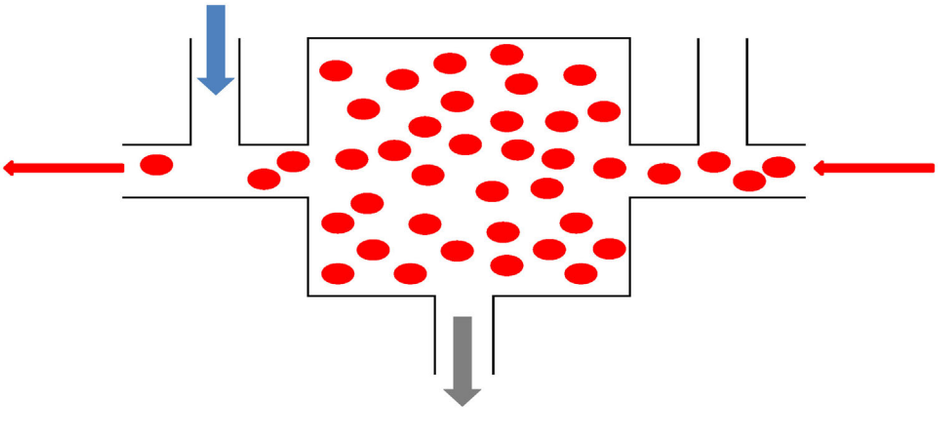


- Hemofiltration
  - **Middle/Large molecules**
  - Replacement fluid flow rate
- Hemodialysis
  - **Small molecules**
  - Dialysate flow rate

Anticoagulation

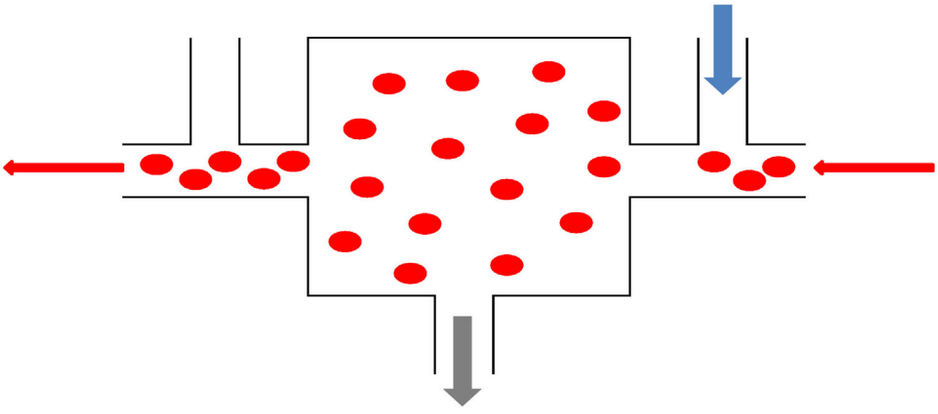
- Heparin
- Futhan
- No anticoagulation
  - Indication
    - PLT <50k, PT INR >2, aPTT >60 sec
    - Active bleeding, severe hepatic dysfuction, liver TPL
  - Strategies
    - Well-functioning vascular access
    - High blood flow rate
    - Pre-dilution replacement fluid

Post-dilution (Replacement fluid)



- Advantage: higher solute removal
- Disadvantage: higher chances of filter clotting

Pre-dilution (Replacement fluid)



- Advantage: Lesser chances of filter clotting
- Disadvantage: Lesser solute removal

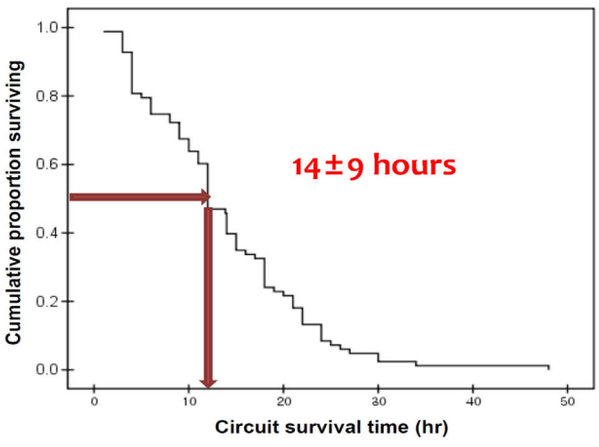
CRRT Circuit Data

	≤5 kg (N = 170)	>5 kg (N = 251)	*P* value
Anticoagulation protocol			<.001
Citrate	76 (45%)	155 (62%)	
Heparin	94 (55%)	96 (38%)	
Prime			<.001
Blood	164 (96.5%)	202 (80%)	
Saline	5 (3%)	29 (12%)	
Albumin	1 (0.5%)	20 (8%)	
Parameter			
Blood flow* (mL/kg/min)	12 (7.9-15.6)	6.6 (4.8-8.8)	<.001
Daily effluent volume* (mL/h/1.73 m^2)	3328 (2325-4745)	2321 (1614-2895)	<.001
Circuit life	28 (11-67)	37 (16-67)	.15

Askenazi D et al. J Pediatr (2013)

CRRT in NICU

2007-2010



2007-2014

	Preterm (n=15)	Term (n=19)
Duration (days)	6 (4-12)	4 (2-8)
Hemofilter life (hours)	**56±16**	**47±19**

Sohn YB et al. Korean J Pediatr (2012)
Lee ST et al. Pediatr Nephrol (2016)

Special considerations

- Large extracoporeal volume compared to small patients
  - Blood priming at initiation
- Hypothermia
  - Heating system

- Potential complications
  - Volume related problems
  - Biochemical and nutritional problems
  - Hemorrhage
  - Infection
  - Technical problems

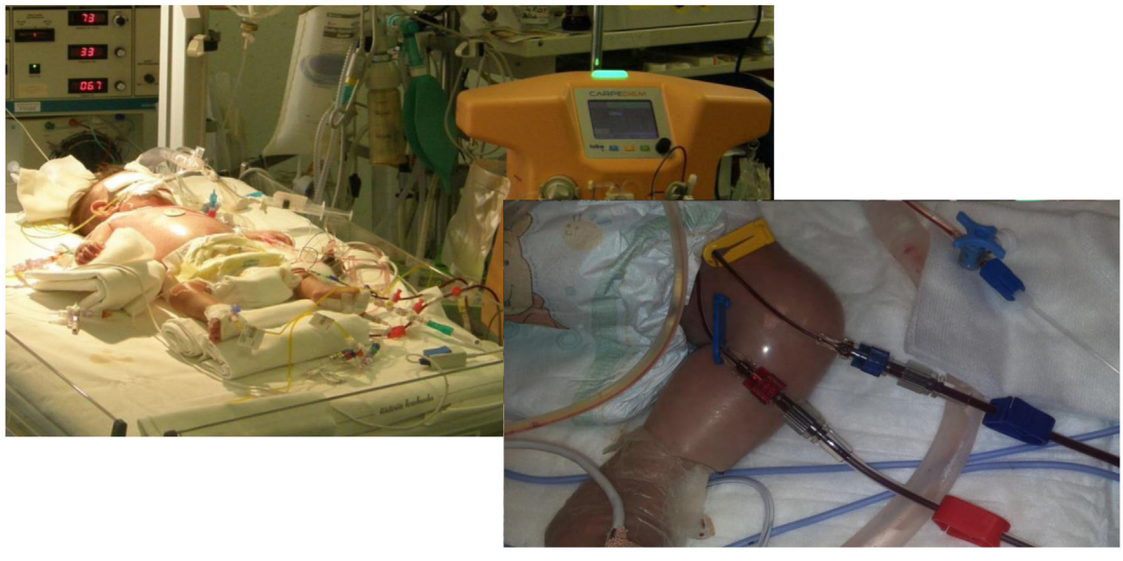
New CRRT machine for infants

Fig. 3 The **Ca**rdio-**R**enal, **Pe**diatric **Di**alysis **E**mergency **M**achine (CARPEDIEM) measures 44 (L) × 43 (H) ×23 (W) cm, weighs 13 kg, and is specifically designed as a miniaturized, transportable device

- Bwt : 2.0-9.9 kg
- BSA : 0.15-0.5 m^2
- Blood vol : 200-1000mL
- Blood flow rate: 2-50mL/min
- Filter: 0.075, 0.15, and 0.25 m^2
- Priming vol: 27, 34 and 45 mL
- 4-4.5Fr dual lumen catheter

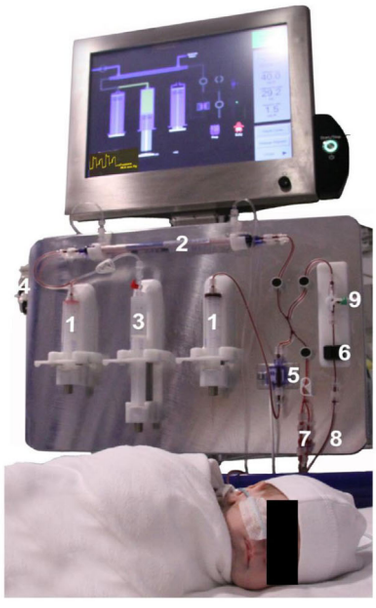
Ronco C et al. Pediatr Nephrol (2012)

CRPEDIEM



Francesco Garzotto et al. Presented as poster in CRRT 2013
Stefano Picca. Oral presentation in CRRT 2015
Ronco C et al. Lancet (2014)

Newcastle Infant Dialysis Ultrafiltration System (NIDUS)



- Priming vol: 6.5 mL
- Filter: 0.045 m^2
- Blood flow rate: 20 mL/min
- Bwt: 800g-8kg
- 4Fr single lumen catheter

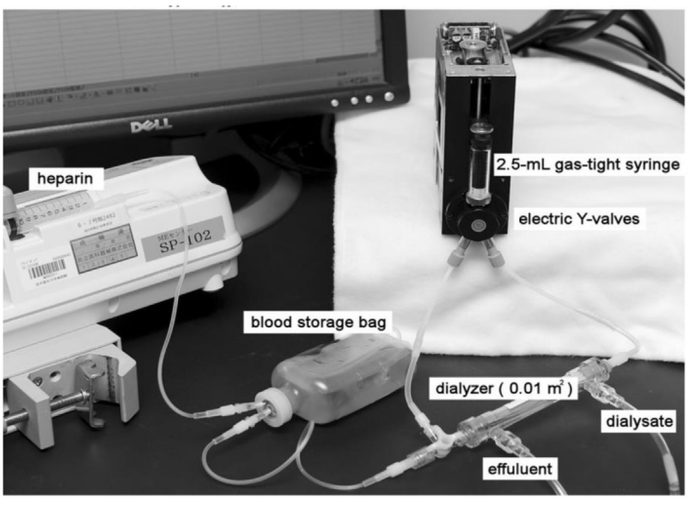
Lui ID et al. Pediatr Nephrol (2013)

Aquadex™ machine

- Priming vol: 33 mL
- Filter: 0.12 m^2
- Blood flow rate: 10-40 mL/min
- CVVH

Askenazi D et al. Pediatr Nephrol (2016)

Ultra-small volume circuit



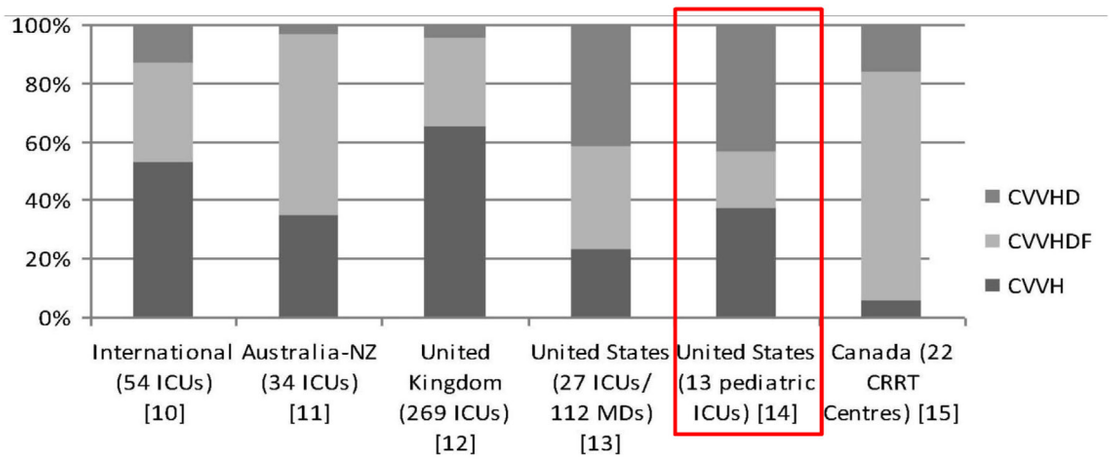
- Plasouto iQ21
- Priming vol: 3.2 mL
- Filter: 0.01 m^2

Nishimi S et al. Pediatr Nephrol (2016)

New machines and filters

	HF20	CARPEDIEM	NIDUS	Aquadex™	Plasouto iQ21
Surface area (m^2)	0.2	0.075/0.15/0.25	0.045	0.12	0.01
Priming volume (mL)	60	27/34/45	6.5	33	3.2
Blood flow rate (mL/min)	20-100	2-50	20	10-40	
Bwt (kg)	8-20	2-10	0.8-8	<15	
Catheter size	6.5 Fr	4-4.5Fr	6.5-7 Fr	6-8 Fr	?
Mode	CVVH CVVHD CVVHDF	CVVH CVVHD?	CVVHD IHD	CVVH	In Vitro

Mode of CRRT



Friedrich JO et al. Crit Care (2012)

Effect of HF vs HD RRT on Mortality

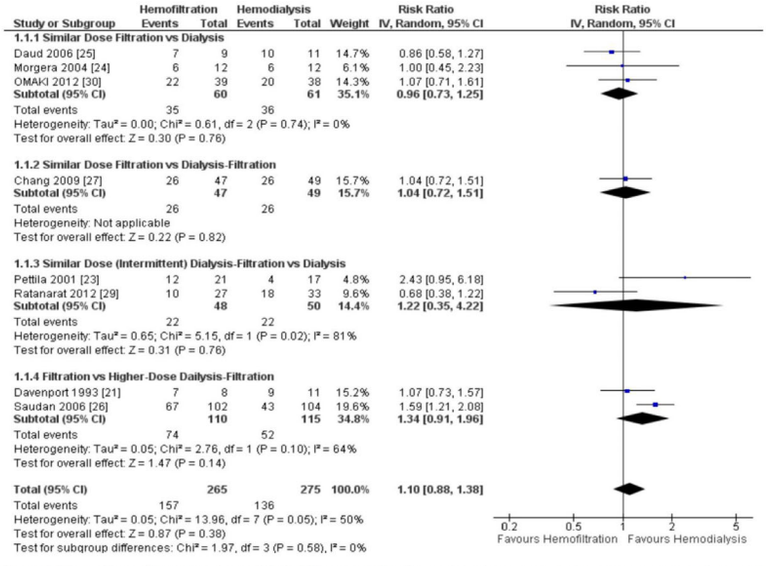


Figure 2 Effect of hemofiltration vs. hemodialysis RRT on mortality. The pooled risk ratio was calculated using a random-effects model. Weight refers to the contribution of each study to the overall estimate of treatment effect. Abbreviations: CI, confidence interval; IV, inverse variance.

Friedrich JO et al. Crit Care (2012)

Effect of HF vs HD RRT on Filter Life

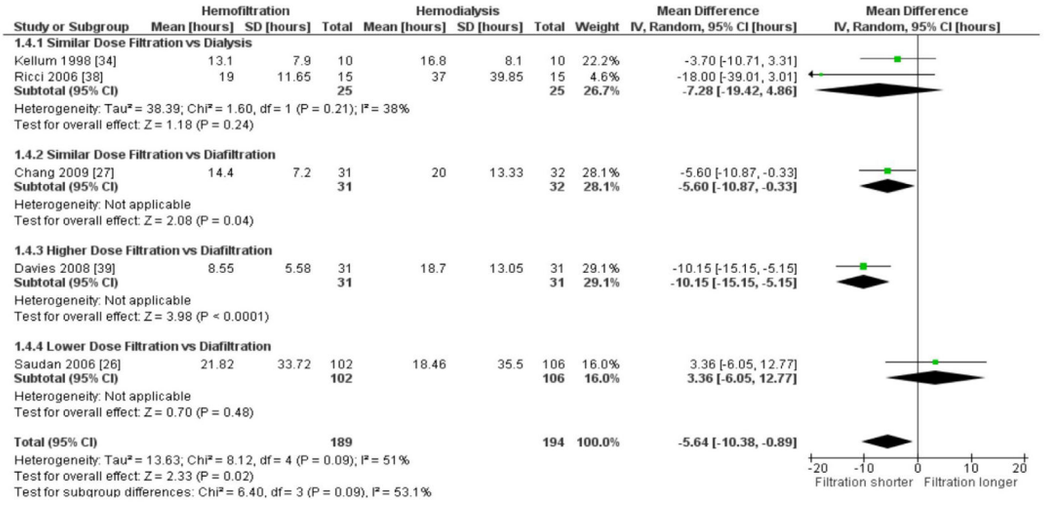


Figure 3 Effect of hemofiltration vs. hemodialysis on filter life. The pooled mean difference was calculated using a random-effects model. Weight refers to the contribution of each study to the overall estimate of treatment effect.

Friedrich JO et al. Crit Care (2012)

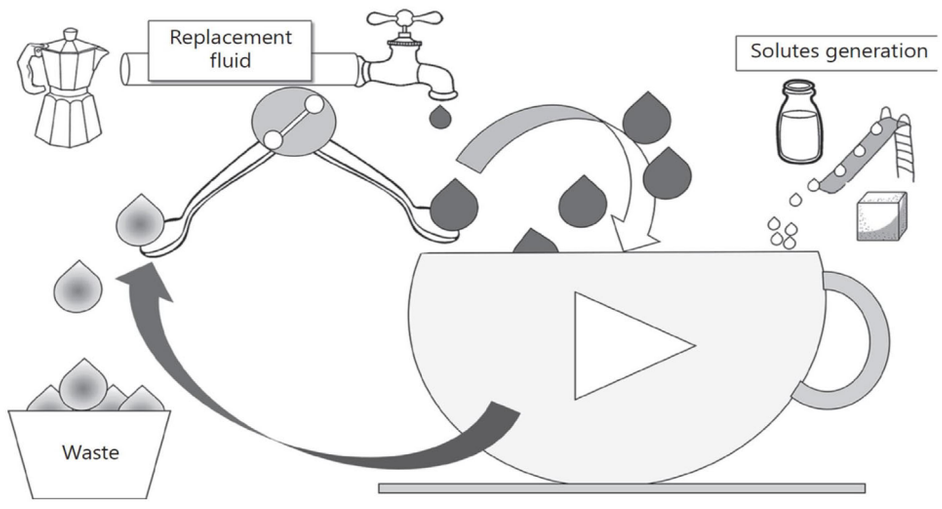
Clearance HF vs. HD

Table 4 Clearance measurements of hemofiltration vs.

Molecular substance	Number of trials; number of patients randomized	Change in clearance hemofiltration vs hemodialysis[a]			
		Effect estimate	95% confidence interval	*P*-value	Heterogeneity (I^2)
Smaller molecules					
Urea (60 Da)	4 [33,36-38]; 49	+1%[b]	-2% to +3%	0.60	0%
Phosphate (95 Da)	1 [37]; 18	0%[c]	-4% to +4%	1.00	n/a
Creatinine (113 Da)	3 [33,37,38]; 43	+1.8%[b]	-0.4% to +4.1%	0.12	0%
Uric acid (168 Da)	2 [33,37]; 28	+4%	+1% to +7%	0.01	0%
Larger molecules					
Vancomycin (1.8 kDa)	1 [33]; 10	+18%	+8% to +28%	0.0003	n/a
β_2-microglobulin (11.8 kDa)	2 [37,38]; 33	+94%[d]	+78% to +112%	<0.0001	0%
IL-1 Receptor Agonist (16-18 kDa)	1 [24]; 12	+77%[e,f]	+24% to +153%	0.002	n/a
Retinol Binding Protein (21.2 kDa)	1 [37]; 18	+42%	+4% to +94%	0.03	n/a
IL-6 (26 kDa)	2 [24,34]; 22	+6%[f,g]	-62% to +191%	0.91	89%

Friedrich JO et al. Crit Care (2012)

Action of Hemofiltration



Ricci Z et al. Blood Purif (2018)

CVVHpre/CVVHpost/CVVHD

Table 2. Urea and creatinine clearance data with standard deviations for all three modalities with a blood flow rate of 60 mL/min and a fluid rate (either dialysate or replacement fluid) of 600 mL/hr, which is 16.7% of the blood flow rate

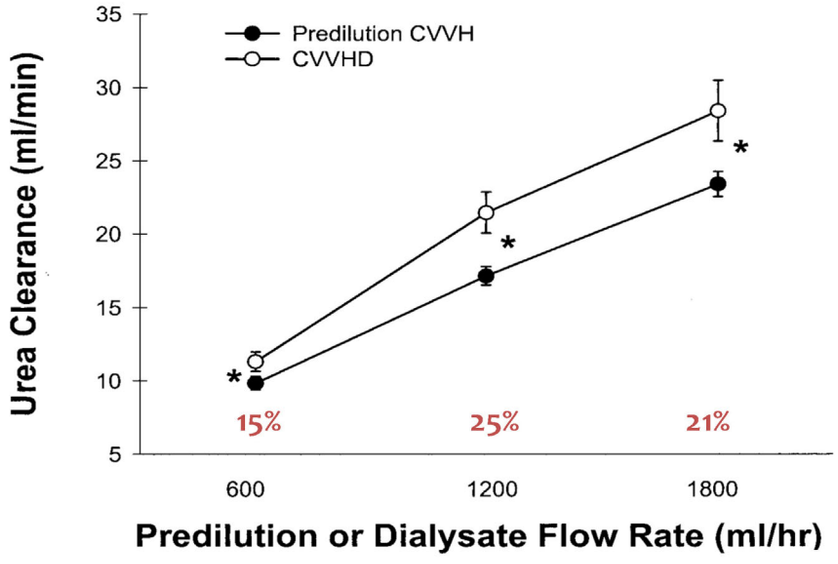
Modality	Urea Clearance, mL/min	Creatinine Clearance, mL/min
CVVHpre	9.8 ± 0.46	9.0 ± 0.74
CVVHpost	11.3 ± 0.51[a]	10.7 ± 0.62[b]
CVVHD	11.3 ± 0.67[a]	10.0 ± 0.65

CVVHpre, predilution continuous venovenous hemofiltration; CVVHpost, postdilution continuous venovenous hemofiltration; CVVHD, continuous venovenous hemodialysis.

[a]Statistically significant when compared with CVVHpre; [b]statistically significant when compared with CVVHpre.

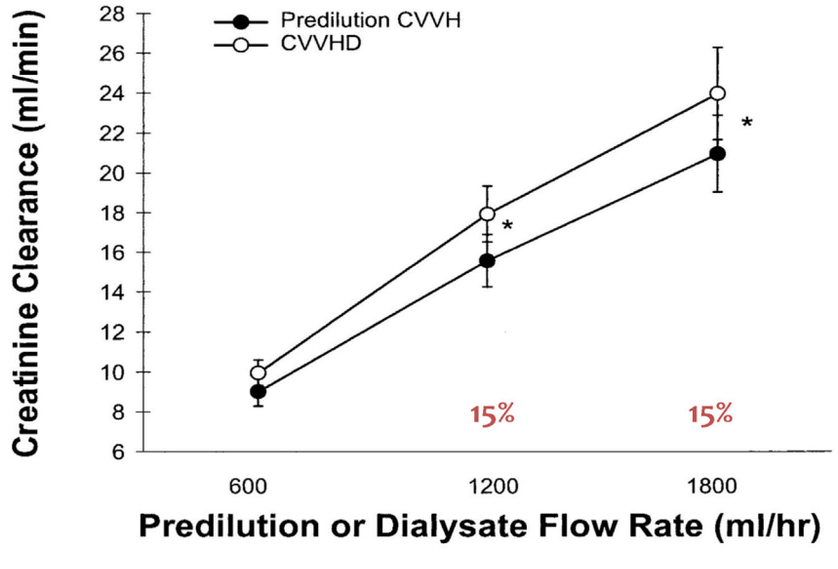
Parakininkas D et al. Pediatr Crit Car Med (2004)

CVVHpre vs. CVVHD



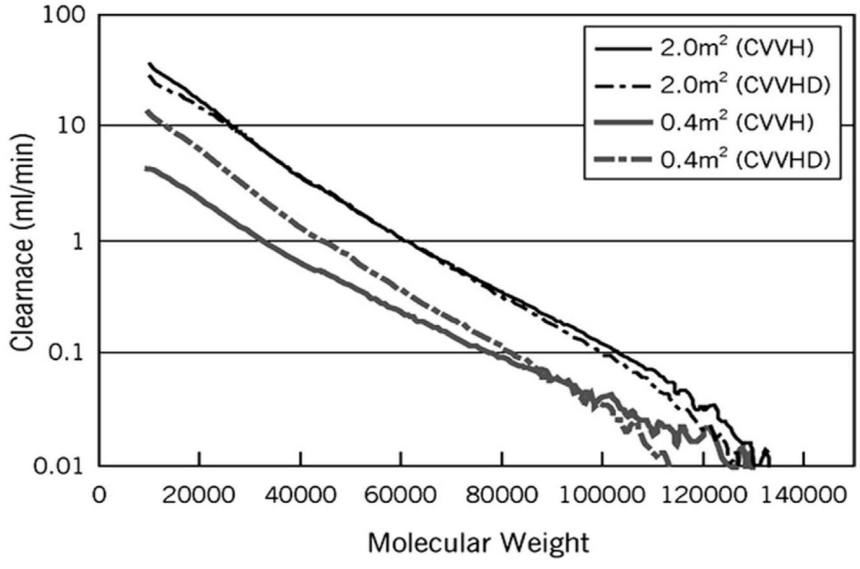
Parakininkas D et al. Pediatr Crit Car Med (2004)

CVVHpre vs. CVVHD



Parakininkas D et al. Pediatr Crit Car Med (2004)

Middle-Molecule Clearance



Messer J et al. ASAIO J (2009)

pCRRT Registry

Table 3. Clinical Variables in Survivors and Nonsurvivors

	Survivors	Nonsurvivors	*P*
Fluid overload (%)	12.5 ± 25.7	23.0 ± 23.0	<0.001
PRISM II score at PICU admission	13.1 ± 8.5	15.9 ± 9.4	0.009
Inotrope no. at CRRT initiation	1.0 ± 1.1	1.5 ± 1.2	<0.001
Weight (kg)	36.4 ± 29.0	31.6 ± 30.4	0.02
Age (y)	9.0 ± 6.5	8.0 ± 7.5	0.2
MODS diagnosis (%)	68.1	92.2	<0.001
Oncologic diagnosis (%)	20.1	28.9	0.08
Sepsis diagnosis (%)	30.2	34.4	0.4
Inborn error of metabolism or intoxication diagnosis (%)	9.5	4.7	0.1
CRRT indications included fluid overload (%)	72.2	84.4	0.01
CRRT modality (%)			0.002
Convective	61.0	43.0	
Diffusive	39.0	57.0	
Sex (%)			0.9
Male	58.6	58.6	
Female	41.1	41.4	
PICU length of stay (d)	20.5 ± 23.3	23.0 ± 32.3	0.5
eGFR (mL/min/1.73 m²)	41.5 ± 39.1	44.5 ± 45.0	0.6

Note: Values expressed as percentage or mean ± standard deviation. Association of demographic and clinical factors with mortality. $P < 0.05$ represents a significant association between increasing fluid overload severity and the respective variable (using analysis of variance for continuous variables and χ^2 for categorical variables).

Abbreviations: CRRT, continuous renal replacement therapy; eGFR, estimated glomerular filtration rate; MODS, multiorgan dysfunction syndrome; PICU, pediatric intensive care unit; PRISM, Pediatric Risk of Mortality.

Sutherland SM et al. Am J Kidney Dis (2010)

Mortality

Table 4. Final Multivariate Logistic Regression Model

Variable[1]	Univariate Odds Ratio (95% confidence interval)	Multivariate Odds Ratio (95% confidence interval)
Percentage of fluid overload	1.02 (1.01-1.03)[a]	1.03 (1.01-1.05)[a]
Oncologic diagnosis	1.61 (0.94-2.76)[b]	3.16 (1.64-6.07)[c]
Diagnosis of MODS	5.54 (2.69-11.41)[d]	4.66 (2.04-10.65)[d]
Convective CRRT modality	0.48 (0.30-0.77)[a]	0.80 (0.41-1.55)
PRISM II score at PICU admission	1.04 (1.01-1.06)[a]	1.02 (0.99-1.05)
Inotrope no.	1.50 (1.22-1.85)[d]	1.26 (0.99-1.60)[b]
Fluid overload × convective CRRT modality	NA	0.98 (0.95-0.99)[a]

Note: Multivariate logistic regression model includes variables with univariate and multivariate odds ratios and 95% confidence intervals. Odds ratios for each variable included in the multivariate model. Percentage of fluid overload remained independently associated with mortality; the odds ratio of 1.03 suggests a 3% increase in mortality for each 1% increase in amount of fluid overload present at CRRT initiation.

Abbreviations: CRRT, continuous renal replacement therapy; MODS, multiorgan dysfunction syndrome; NA, not applicable; PICU, pediatric intensive care unit; PRISM, Pediatric Risk of Mortality.

[a] $P < 0.05$.
[b] $P < 0.1$.
[c] $P < 0.01$.
[d] $P < 0.001$.

Sutherland SM et al. Am J Kidney Dis (2010)

Survival by Diagnosis

Table 5. Survival by Diagnosis for All Patients and by Weight Group

	All Patients		Patients > 3 kg		Patients ≤ 3 kg	
Diagnosis	No. of Patients	Survivors	No. of Patients	Survivors	No. of Patients	Survivors
Congenital heart disease	14	5 (36)	11	4 (36)	3	1 (33)
Metabolic disorder	14	10 (71)	14	10 (71)		
Multiorgan dysfunction	13	2 (15)	9	1 (11)	4	1 (25)
Sepsis syndrome	12	5 (42)	12	5 (42)		
Liver failure	9	2 (22)	9	2 (22)		
Malignancy	5	0	4	0	1	0
Congenital nephrotic syndrome	4	2 (50)	2	2 (100)	2	0
Congenital diaphragmatic hernia	3	0	1	0	2	0
Hemolytic uremic syndrome	2	1 (50)	2	1 (50)		
Heart failure	2	1 (50)	2	1 (50)		
Obstructive uropathy	1	1 (100)	1	1 (100)		
Renal dysplasia	1	0			1	0
Other	5	3 (60)	2	1 (50)	3	2 (67)
Total	85	32 (38)	69	28 (41)	16	4 (25)

Symons JM et al. Am J Kidney Dis (2003)

CRRT in children up to 10kg

Table 5. Survival by Diagnosis for All Patients and by Weight Group

	All Patients		Patients > 3 kg		Patients ≤ 3 kg	
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Sepsis syndrome	12	5 (42)	12	5 (42)		
Liver failure	9	2 (22)	9	2 (22)		
Malignancy	5	0	4	0	1	0
Congenital nephrotic syndrome	4	2 (50)	2	2 (100)	2	0
Congenital diaphragmatic hernia	3	0	1	0	2	0
Hemolytic uremic syndrome	2	1 (50)	2	1 (50)		
Heart failure	2	1 (50)	2	1 (50)		
Obstructive uropathy	1	1 (100)	1	1 (100)		
Renal dysplasia	1	0			1	0
Other	5	3 (60)	2	1 (50)	3	2 (67)
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Symons JM et al. Am J Kidney Dis (2003)

THE JOURNAL OF PEDIATRICS • www.jpeds.com ORIGINAL ARTICLES

Continuous Renal Replacement Therapy for Children ≤10 kg: A Report from the Prospective Pediatric Continuous Renal Replacement Therapy Registry

David J. Askenazi, MD, MSPH[1], Stuart L. Goldstein, MD[2], Rajesh Koralkar, MBBS, MPH[1], James Fortenberry, MD[3], Michelle Baum, MD[4], Richard Hackbarth, MD[5], Doug Blowey, MD[6], Timothy E. Bunchman, MD[7], Patrick D. Brophy, MD[8], Jordan Symons, MD[9], Annabelle Chua, MD[10], Francisco Flores, MD[11], and Michael J. G. Somers, MD[4]

Objective To report circuit characteristics and survival analysis in children weighing ≤10 kg enrolled in the Prospective Pediatric Continuous Renal Replacement Therapy (ppCRRT) Registry.

Study design We conducted prospective cohort analysis of the ppCRRT Registry to: (1) evaluate survival differences in children ≤10 kg compared with other children; (2) determine demographic and clinical differences between surviving and non-surviving children ≤10 kg; and (3) describe continuous renal replacement therapy (CRRT) circuit characteristics differences in children ≤5 kg versus 5-10 kg.

Results The ppCRRT enrolled 84 children ≤10 kg between January 2001 and August 2005 from 13 US tertiary centers. Children ≤10 kg had lower survival rates than children >10 kg (36/84 [43%] versus 166/260 [64%]; $P < .001$). In children ≤10 kg, survivors were more likely to have fewer days in intensive care unit prior to CRRT, lower Pediatric Risk of Mortality 2 scores at intensive care unit admission and lower mean airway pressure (P_{aw}), higher urine output, and lower percent fluid overload (FO) at CRRT initiation. Adjusted regression analysis revealed that Pediatric Risk of Mortality 2 scores, FO, and decreased urine output were associated with mortality. Compared with circuits from children 5-10 kg at CRRT initiation, circuits from children ≤5 kg more commonly used blood priming for initiation, heparin anticoagulation, and higher blood flows/effluent flows for body weight.

Conclusion Mortality is more common in children who are ≤10 kg at the time of CRRT initiation. Like other CRRT populations, urine output and FO at CRRT initiation are independently associated with mortality. CRRT prescription differs in small children. *(J Pediatr 2013;162:587-92)*.

CRRT in Neonates <3kg

- 8 neonatal patients at SMC, 2007-2010
- CRRT time 7.8 days (1-37), circuit survival 13.9±8.6 hrs

Table 1. Clinical and Laboratory Findings at CRRT Initiation

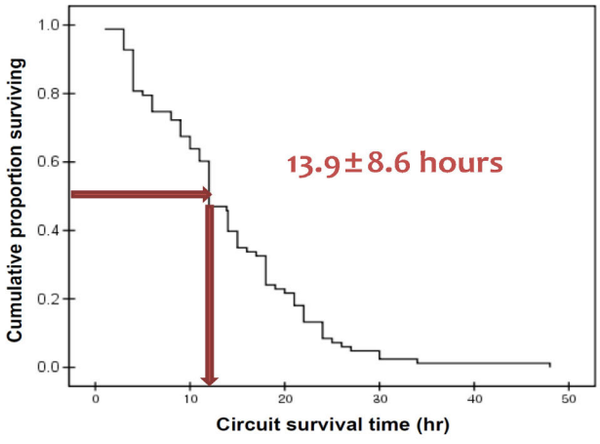
Pt. no.	Sex	GA (wk)	Birth wt (g)	Age (day)	Wt (kg)	BUN (mg/dL)	Cr (mg/dL)	Ammonia (umol/L)	Underlying disease	Outcome	PRISM III score
1	M	36^{+2}	2,823	3	2.71	14.3	2.36	-	Subgaleal hemorrhage, DIC, MODS	Death	22
2	M	38^{+2}	3,310	23	2.83	51.8	1.72	-	NEC, sepsis, MODS	Death	14
3	F	30^{+3}	990	38^{+2} wk*	2.63	80.1	2.92	-	Sepsis, MODS	Death	15
4	F	25	830	5*	2.98	81.3	0.82	-	Sepsis, MODS	Death	14
5	F	38^{+6}	2,580	17	2.74	70.1	3.11	-	Atypical HUS	Survival	9
6	M	36^{+4}	2,600	5	2.6	52.4	2.30	358	LCHAD deficiency or TFP deficiency	Survival	14
7	F	39	2,920	9	2.65	19.0	0.93	986	Propionic academia	Survival	9
8	M	38^{+3}	3,300	4	2.92	2.7	0.44	373	Citrullinemia	Survival	2

Sohn YB et al. Korean J Pediatr (2012)

CRRT in Neonates <3kg

Table 2. Adverse Events during CRRT

Adverse event	No. of patients (%)
Electrolyte disturbance	7 (87.5)
Hypokalemia	4 (50.0)
Hypophosphatemia	4 (50.0)
Hypocalcemia	1 (12.5)
Catheter related events	4 (50.0)
Catheter malfunction	3 (37.5)
Catheter insertion site bleeding	3 (37.5)
Catheter insertion site infection	1 (12.5)
Hypotension on connection of CRRT	2 (25.0)



Sohn YB et al. Korean J Pediatr (2012)

ECMO and CRRT

JAE IL SHIN

Department of Pediatrics, Severance Children's Hospital,
Yonsei University College of Medicine

Learning objectives

- Role of CRRT in children receiving ECMO
- CRRT filter connection with the ECMO
- Effectiveness of CRRT in the setting of ECMO

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Extracorporeal Membreane Oxygenation (ECMO)

- Extracorporeal Membrane Oxygenation (ECMO)
  →Began in 1970's
- Cardiopulmonary support not responding to other conventional therapies in reversible underlying process
- Extracorporeal Life Support Organization (ELSO) Registry
  → database of ECMO support in about 90 US centers
  - Composed of nearly all ECMO cases worldwide over 40,000 cases
  - 2 separate registries – cadiac and noncardiac

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ECMO

- Indications of ECMO
  - Severe acute heart or lung failure
  - Expected mortality risk ≥ 80% despite optimal conventional therapy
- ECMO initiation usually improves hemodynamic status

ELSO Registry General Guidelines. April 2009

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ECMO and AKI

- **ECMO initiation causes AKI through:**

  - Increased inflammatory response
  - Hypercoaguable state
  - Hemolysis/ hemoglobinuria

Toomasian J, et al. Perfusion 2011

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Concomitant ECMO and CRRT

***There are controversies on:**

- Optimal population
- Indication
- Timing of initiation
- Optimal mode and method of therapy
- Optimal dose

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Role of CRRT in ECMO

- Treatment of AKI
- Decrease fluid overload
- Control of electrolyte abnormalities and treatment of AKI
- Management of fluid balance to improve nutritional support
- Removal of inflammatory mediators (adsorption) by ECMO and underlying diseases
- Decreased use of furosemide
- Tx of complication of ECMO (e.g. intravascular hemolysis with kidney impairment)

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AKI in ECMO population

- Incidence of AKI in ECMO population→ 40-80%

Condition	AKI	CRRT
Non-cardiac neonates	25%	
Neonates with CDH	71%	16%
Pediatric cardiac dz	72%	59%
Pediatric respiratory dz	63%	30%

- AKI on ECMO is associated with increased mortality, controlling for confounders (Askenazi 2012)
  - AKI on adult ECMO: OR 12.1 (2.5-59)
  - AKI on pediatric ECMO: OR 24.0 (4.2-137)

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CRRT and mortality in pediatric ECMO

- ELSO Registry (1998-2008)
- Patients with AKI and CRRT had higher mortality when risk factors were adjusted in:
  - Neonates (25% AKI) with AKI (OR 3.2) and RRT (OR 1.9)
  - Children (46% AKI) with AKI (OR 1.7) and RRT (OR 2.5)
- Therapies to prevent/ameliorate AKI and optimize RRT could improve outcomes

Askenazi et al., Pediatr Crit Care Med, 2011

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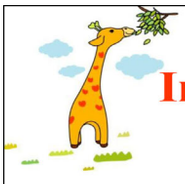
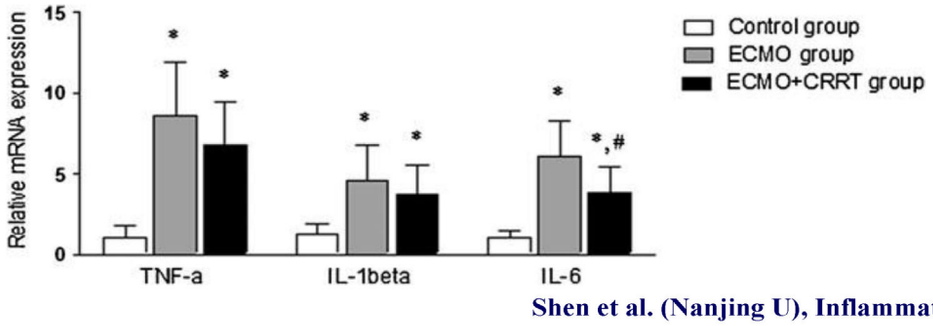


Impact of ECMO on Inflammation in pig model

- Circulation of blood across synthetic surfaces
  → pro-inflammatory response in addition to original disease
- Early elevation of TNF-alpha, IL-1beta, IL-6, IL-8 within 3-4 hours post-ECMO cannulation (Fortenberry et al., J Peds 1996; Massoudy et al., Chest 2001)



Shen et al. (Nanjing U), Inflammation, 2013

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CRRT in ECMO

- **Survey of ELSO Centers**

- Fluid overload (43%)
- Prevention of fluid overload (16%)
- AKI (35%)
- Electrolyte abnormalities (4%)

Fleming GM, et al. ASAIO J 2012. 58(4):407-14

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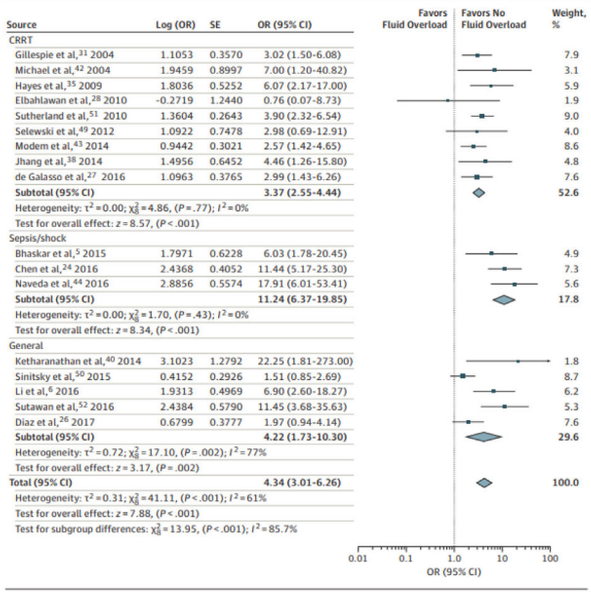
Fluid overload and outcome

- **Fluid overload is associated with:**
  - Acute kidney injury
  - Increased mortality
  - Increased ventilator days
  - Increased ICU LOS
  - In both children and adults



JAMA Pediatr 2018 Mar 1;172(3):257-268.

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Fluid overload in ECMO

Fluid Overload in ECMO Population:

- ECMO Database in Univ of Michigan
- Survival 18/53 (34%) in children on ECMO+CRRT
- FO at initiation of CRRT was less in survivors (24.5%) than in nonsurvivors (38%)

Use of lasix and nutritional support in CRRT+ ECMO Population:
→ Less use of less lasix use and more nutritional support (calories)

Selewski DT, et al Crit Care Med 2012

Hoover et al Intensive Care Med 2008; 34:2241-2247

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ELSO Guidelines

- The goal of fluid management is to return the extracellular fluid volume to normal (dry weight) and maintain it there.
- The hourly fluid balance goal should be set and maintained until normal extracellular fluid volume is reached.
- Spontaneous or pharmacologic diuresis should be instituted until patient is close to dry weight and edema has cleared.
  → This will enhance recovery from heart or lung failure and decrease the time on ECLS.

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ELSO Guidelines

- As with all critically ill patients, full caloric and protein nutritional support is essential.
- RRT use is often performed to enhance fluid removal and to allow adequate nutritional support
- Despite the literature surrounding fluid overload (>10%) as a risk factor for death, review of the ELSO registry also finds that use of RRT is also a risk factor for poor outcome.
  → cautious interpretation is needed!

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CRRT connection to ECMO

- In-line hemofilter: IV pump controlled, decrease ECMO flow by shunt
- Separate CRRT circuit
  - Less complication related to ECMO, but access problem
- CRRT circuit attached on to the ECMO circuit

16

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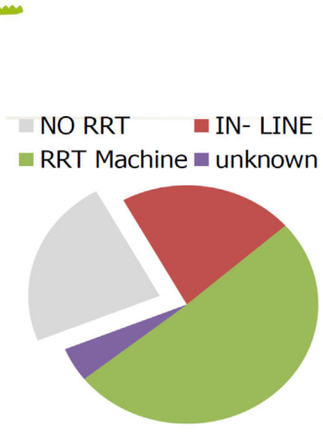
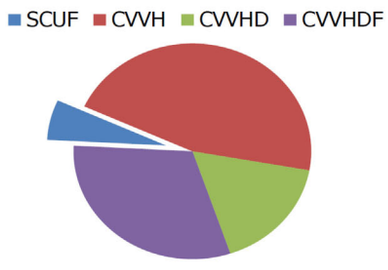
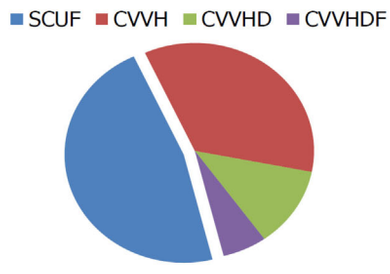
In-line hemofilter/CRRT connection to ECMO





Modality with CRRT



Modality with in-line hemofilter

A Multicenter International Survey of Renal Supportive Therapy During ECMO: The Kidney Intervention During Extracorporeal Membrane Oxygenation (KIDMO) Group

17
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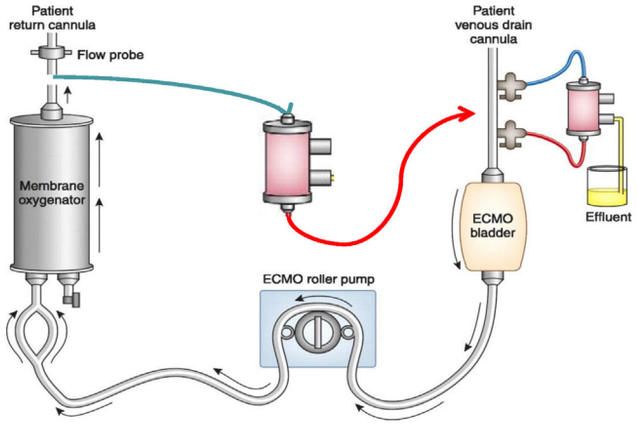
CRRT connection to ECMO



18
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Pressures in ECMO and caution

- Before pump
  - Negative pressure
  - Access pressure on CRRT may be positive !
  - Once leak, air suck into circuit→ air embolism
- Pump to oxygenator
  - Highest positive pressure
  - Once leak, blood out
- After oxygenator
  - Positive pressure
  - Once leak, blood out

19

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CRRT in ECMO

- Extracorporeal Blood Volume= ECMO + CRRT
- Younger infants→ blood priming
- No CRRT device is FDA approved/designed for use with ECMO
- Pressure alarms
  - Too negative/positive drain pressures
  - Too negative/positive return pressures

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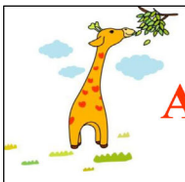

Anticoagulation during ECMO and CRRT

- ECMO and CVVH circuit can last for days without anticoagulation
- ECMO: heparin anticoagulation is common
- Nafamostat mesilate: maintenance dose: 0.1-0.5 mg/kg/hr

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Outcomes of RRT/ECMO (ELSO Registry)

	Survival	
Neonatal respiratory	2696/5319	(51%)
Pediatric respiratory	1010/2498	(40%)
Adult respiratory	815/1781	(46%)
Cardiac 0-30d	527/2198	(24%)
Cardiac 31d – 364d	364/1210	(30%)
Cardiac 1y-16 y	437/1094	(40%)
Cardiac >16 y	366/1386	(26%)

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Summary

- AKI is extremely common in ECMO patients
- CRRT can be connected with ECMO
  - Control fluid overload
  - Meet enough nutritional support
  - Less furosemide exposure
- Success of ECMO and CRRT depends on the primary disease
- Those with AKI and those who receive RRT have worse outcomes – independent of important confounders
- Improved understanding of how best to support ECMO patients with AKI is likely to improve outcomes
- Future works
  - Korean registry
  - Connection methods of CRRT to ECMO

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Pediatric CRRT 2020

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