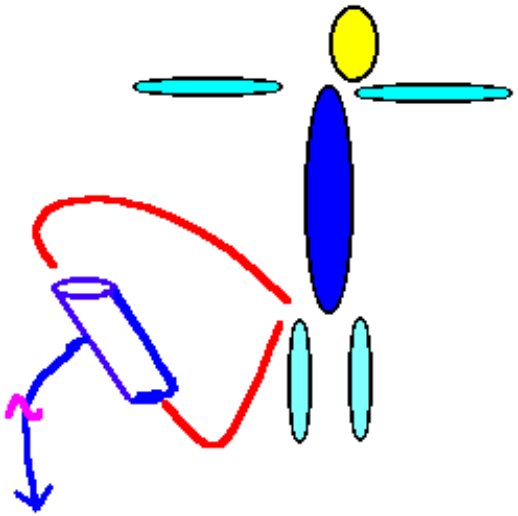
renal replacement therapy in the PICU

by

Joseph DiCarlo MD
Steven Alexander MD
Stanford University

Catherine Headrick RN
Children's Medical Center Dallas



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three modalities

CVVH

peritoneal dialysis

hemodialysis

The selection of renal replacement modality will often reflect the experience and expertise of the individual center, rather than an objective criteria in the individual patient.

Comparisons follow.

hemodialysis

advantages

- maximum solute clearance
- best tx for severe hyper-K+
- ready availability
- limited anti-coagulation time
- bedside vascular access

disadvantages

- hemodynamic instability
- hypoxemia
- rapid fluid + solute shifts
- complex equipment
- specialized personnel
- difficult in small infants

peritoneal dialysis

advantages

- simple to set up + perform
- easy to use in infants
- hemodynamic stability
- no anti-coagulation
- bedside peritoneal access

disadvantages

- unreliable ultrafiltration
- slow fluid + solute removal
- drainage failure, leakage
- catheter obstruction
- respiratory compromise
- hyperglycemia
- peritonitis

CVVH

advantages

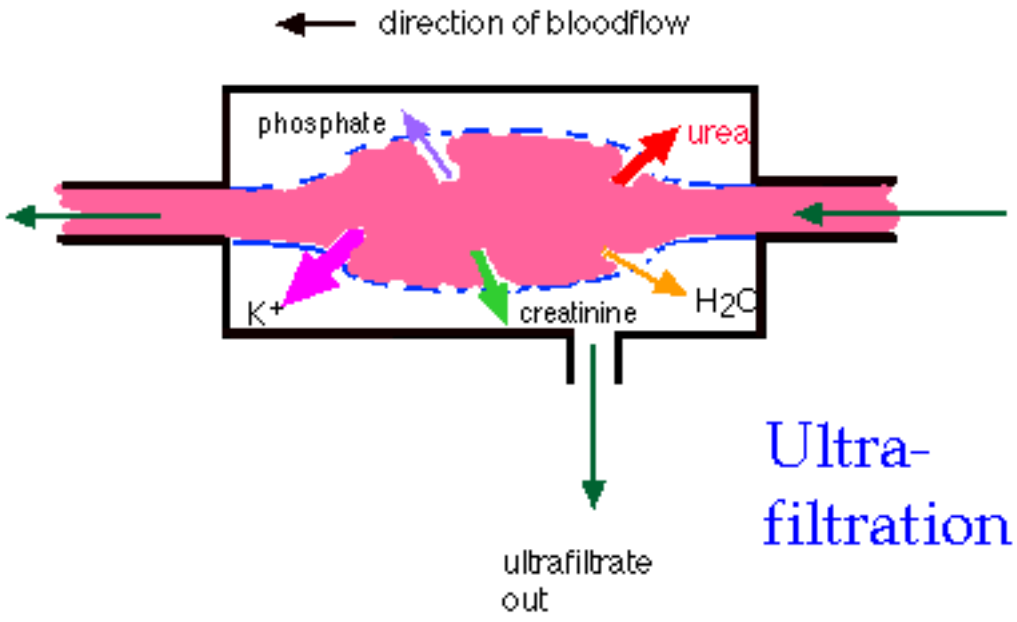
- easy to use in PICU
- rapid electrolyte correction
- excellent solute clearances
- rapid acid/base correction
- controllable fluid balance
- tolerated by unstable patients
- early use of TPN
- bedside vascular access routine

disadvantages

- systemic anticoagulation *
- citrate anticoagulation new
- frequent filter clotting
- hypotension in small infants
- vascular access in infants

introduction

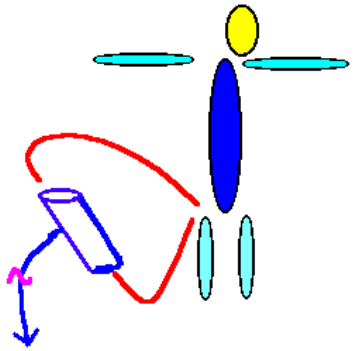
Continuous veno-venous hemofiltration (CVVH) allows removal of solutes and modification of the volume and composition of the extracellular fluid to occur evenly over time.



hemofiltration

A small filter that is highly permeable to water and small solutes, but impermeable to plasma proteins and the formed elements of the blood, is placed in an extracorporeal circuit.

As the blood perfuses the 'hemofilter' an ultrafiltrate of plasma is removed in a manner analogous to glomerular filtration.



history: kramer 1979 (germany)

Inadvertent cannulation of the femoral artery led to a spontaneous experiment with C-arterio-VH:

- patient's cardiac function alone capable of driving the system
- large volumes of ultrafiltrate were produced through the highly permeable hemofilter
- 'continuous arterio-venous hemofiltration' system could provide complete renal replacement therapy in an anuric adult

history: pediatrics

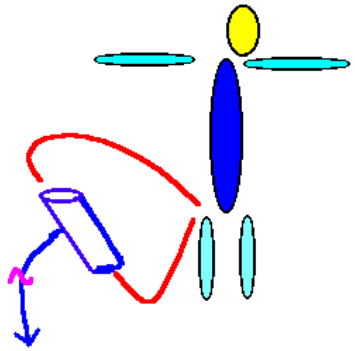
- Lieberman 1985 (USA): slow continuous ultrafiltration ('SCUF') to successfully support an anuric neonate with fluid overload
- Ronco 1986 (Italy): CAVH in neonates
- Leone 1986 (USA): CAVH in older kids
- 1993: general acceptance of pump-driven CVVH as less problematic than CAVH

CVVH

1. near-complete control of the rate of fluid removal (i.e. the ultrafiltration rate)

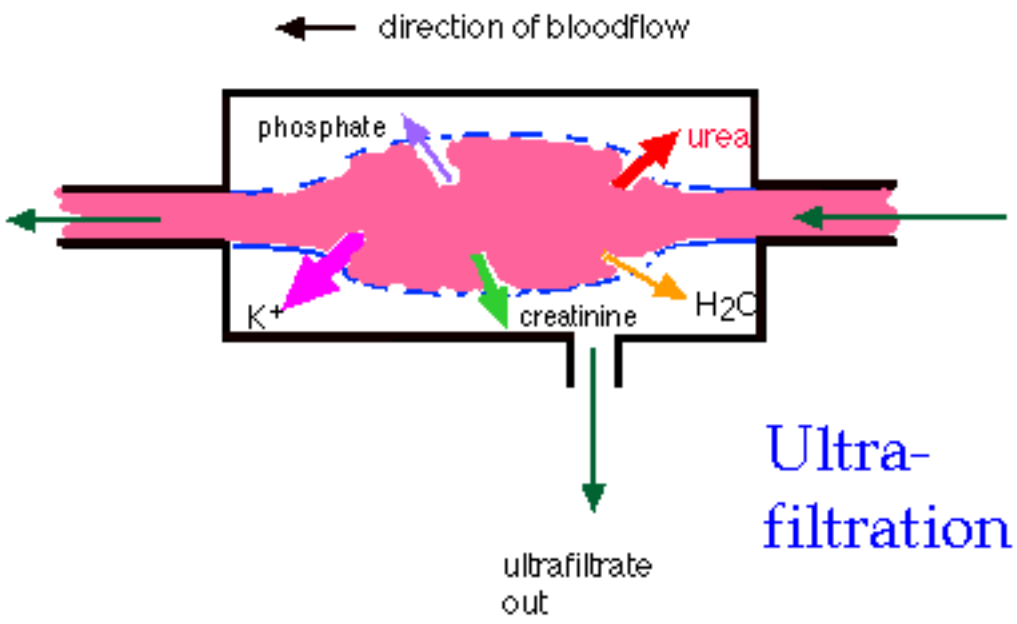
2. precision and stability

3. electrolytes or any formed element of the circulation, including platelets or red or white blood cells, can be removed or added independent of changes in the volume of total body water



ultrafiltration

Filtration across an ultrafiltration membrane is convective, similar to that found in the glomerulus of the kidney.



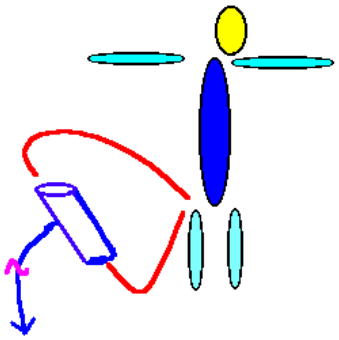
convection

convection

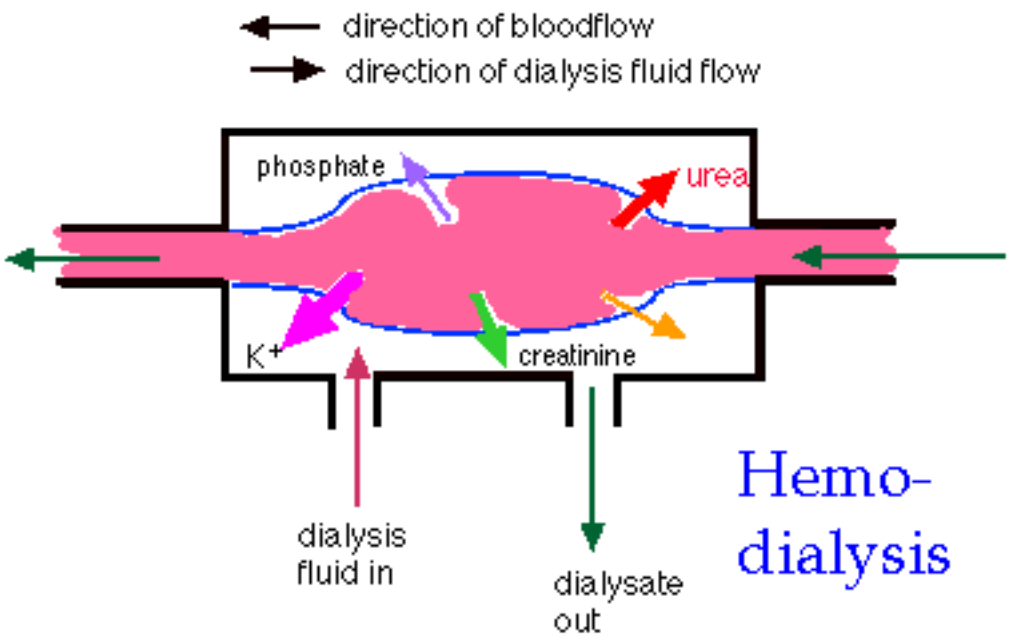
a solute molecule is swept through a membrane by a moving stream of ultrafiltrate, a process that is also called 'solvent drag.'

hemofiltration

during hemofiltration no dialysate is used, and diffusive transport cannot occur. Solute transfer is entirely dependent on convective transport, making hemofiltration relatively inefficient at solute removal.



hemodialysis



Hemodialysis allows the removal of water and solutes by diffusion across a concentration gradient.

diffusion

diffusion

solute molecules are transferred across the membrane in the direction of the lower solute concentration at a rate inversely proportional to molecular weight.

hemodialysis

during hemodialysis, solute movement across the dialysis membrane from blood to dialysate is primarily the result of diffusive transport.

mechanisms + tolerance

modality	solute clearance	uremic control	tolerance by unstable patients
hemodialysis	D / C	excellent	poor
peritoneal dialysis	D / C	good	good
CAVH / CVVH	C	good with hi-flow replacement	excellent
CAVHD / CVVHD	D / C	excellent	excellent

D: diffusion C: convection

	CAVH	CVVH
catheters	(2) 4-6 Fr single lumen	double lumen hemodialysis 7 - 11 Fr
input line	arterial	proximal lumen venous
output line	venous	distal lumen venous
pump	heart	roller

biocompatibility

Various synthetic materials are used in hemofiltration membranes:

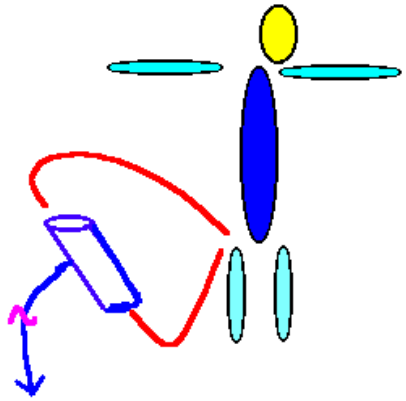
- polysulfone
- polyacrylonitrile
- polyamide

all of which are extremely biocompatible. Consequently, complement activation and leukopenia, both of which are common in hemodialysis, occur infrequently during hemofiltration.

hemofiltration membrane

Hemodialysis membranes contain long, tortuous inter-connecting channels that result in high resistance to fluid flow.

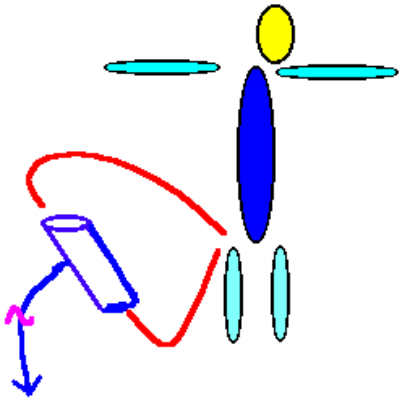
The hemofiltration membrane consists of relatively straight channels of ever-increasing diameter that offer little resistance to fluid flow.



phosphate
bicarbonate
interleukin-1
interleukin-6
endotoxin
vancomycin
heparin
pesticides
ammonia

hemofiltration membrane

Hemofilters allow easy transfer of solutes of less than 100 daltons (e.g. urea, creatinine, uric acid, sodium, potassium, ionized calcium and almost all drugs not bound to plasma proteins). All CVVH hemofilters are impermeable to albumin and other solutes of greater than 50,000 daltons.



phosphate
bicarbonate
ionized Ca++
interleukin-6
endotoxin
vancomycin
heparin
pesticides
ammonia

- ♂♂
- albumin
- protein-bound medications
- platelets

filtration fraction

The degree of blood dehydration can be estimated by determining the filtration fraction (FF), which is the fraction of plasma water removed by ultrafiltration:

$$FF(\%) = (UFR \times 100) / Q_P$$

where Q_P is the filter plasma flow rate in ml/min.

$$Q_P = BFR^* \times (1\text{-}Hct)$$

*BFR: blood flow rate

ultrafiltrate rate

$$FF(\%) = (UFR \times 100) / Q_P$$

$$Q_P = BFR^* \times (1-Hct)$$

For example, when BFR = 100 ml/min and Hct = 0.30 (i.e. 30%), Q_P = 70 ml/min. A filtration fraction > 30% promotes filter clotting. In the example above, when the maximum allowable FF is set at 30%, a BFR of 100 ml/min yields a UFR = 21 ml/min.

QP: the filter plasma flow rate in ml/min.

blood flow rate & clearance

For a child with body surface area = 1.0 m^2, BFR = 100 ml/min and FF = 30%, small solute clearance is 36.3 ml/min/1.73 m^2 (about one third of normal renal small solute clearance).

- target a CVVH clearance of at least 15 ml/min/1.73 m^2
- for small children, blood flow rate > 100 ml/min is usually unnecessary
- high BFR may contribute to increased hemolysis within the CVVH circuit

urea clearance

Urea clearance (C urea) in hemofiltration, adjusted for the patient's body surface area (BSA), can be calculated as follows:

$$C_{urea} = \frac{\text{UF urea conc.}}{\text{BUN}} \times \text{UFR} \times \frac{1.73}{\text{pt's BSA}}$$

Curea: (ml/min/1.73 m^2 BSA)

urea clearance

In CVVH, ultrafiltrate urea concentration and BUN are the same, canceling out of the equation, which becomes:

$$C_{urea} = UFR \times \frac{1.73}{\text{pt's BSA}}$$

C_{urea}: (ml/min/1.73 m^2 BSA)

urea clearance

When target urea clearance (C_{urea}) is set at 15 ml/min/1.73 m^2, the equation can be solved for UFR:

$$15 = UFR \times 1.73 / pt's\ BSA$$

$$UFR = 15 / 1.73 = 8.7\ ml/min$$

C_{urea}: (ml/min/1.73 m^2 BSA)

urea clearance

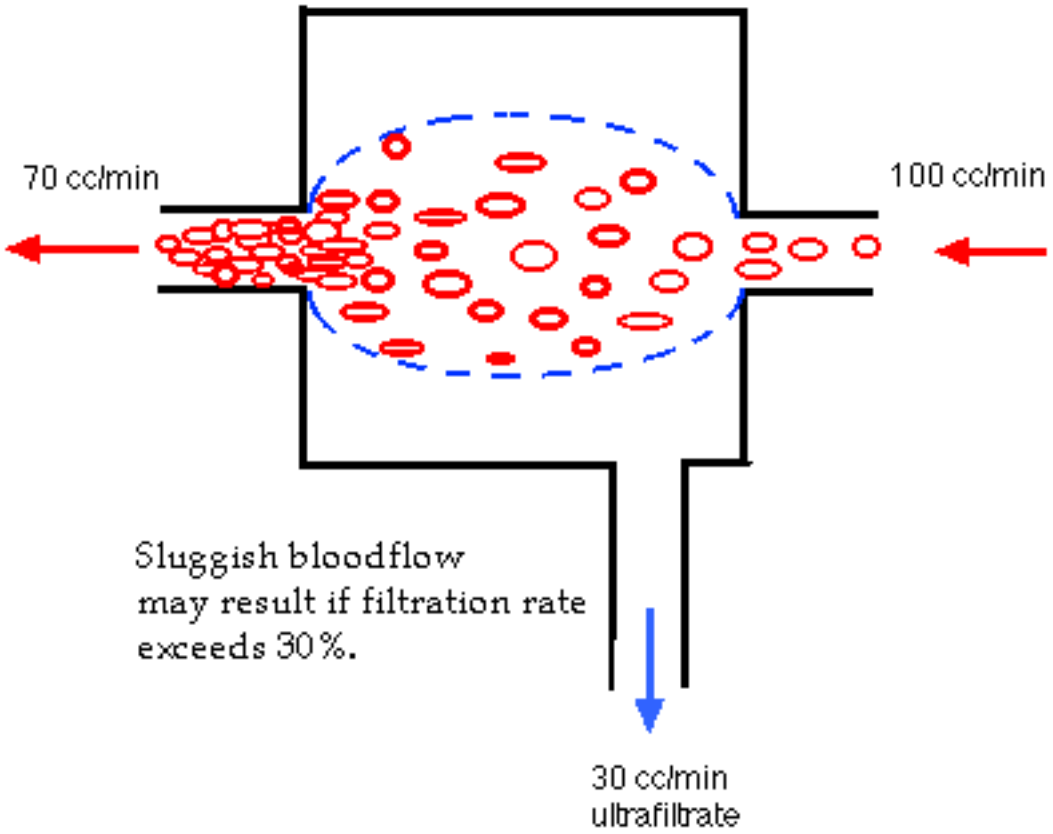
$$C_{urea} = UFR \times \frac{1.73}{\text{pt's BSA}}$$

Thus, in a child with body surface area = 1.0 m^2, a C_{urea} of about 15 ml/min/1.73 m^2 is obtained when UFR = 8.7 ml/min or 520 ml/hr.

This same clearance can be achieved in the 1.73 m^2 adolescent with a UFR = 900 ml/hr.

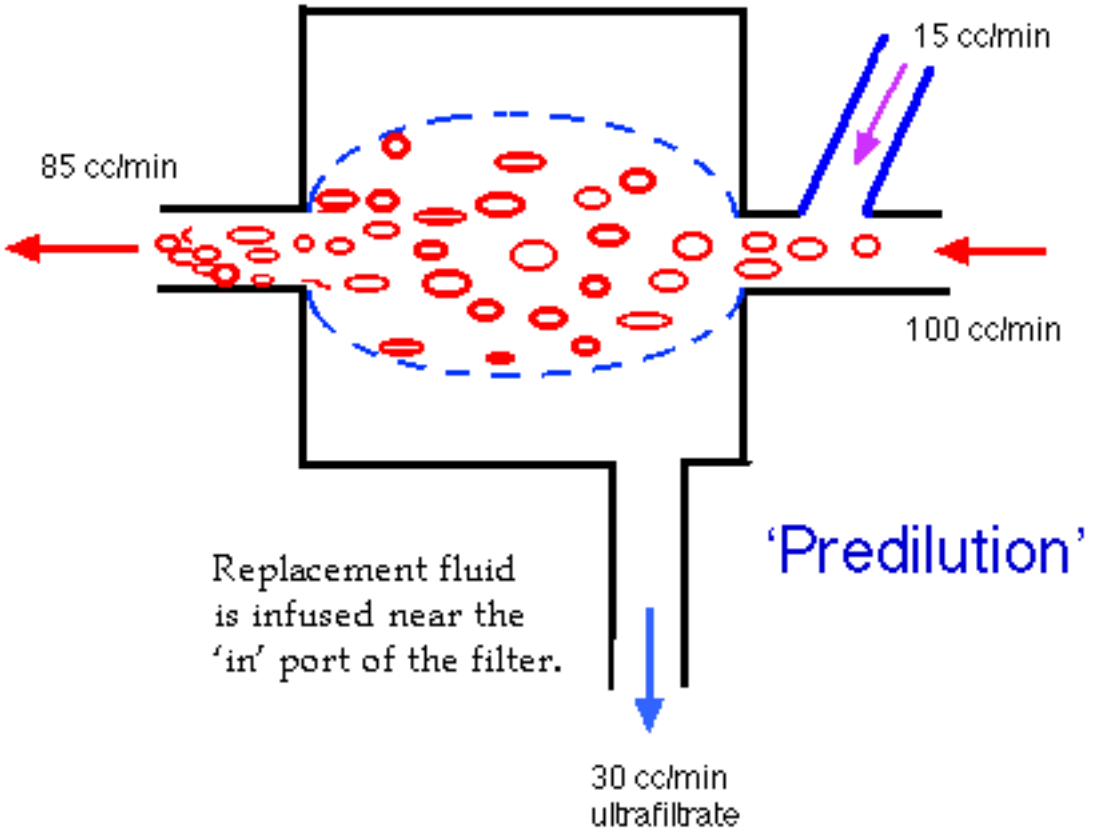
C_{urea}: (ml/min/1.73 m^2 BSA)

sluggishness



A filtration fraction of more than 25 - 30% greatly increases blood viscosity within the circuit, risking clot and malfunction.

pre-dilution

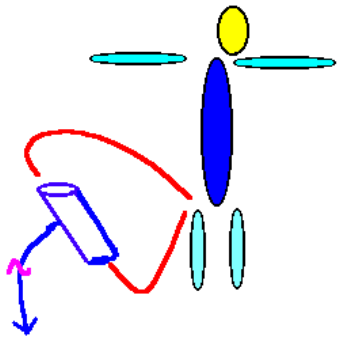


By infusing replacement fluid pre-filter, sludging problems are reduced, but the efficiency of ultrafiltration is compromised, as the ultrafiltrate now contains a portion of the replacement fluid.

fluid balance

Precise fluid balance is one of the most useful features of CVVH. Each hour, the volume of filtration replacement fluid (FRF) is adjusted to yield the desired fluid balance.

FRF	=	total fluid out	-	total fluid in	-	desired
to be given in next hour		in the previous hour		excluding FRF		fluid balance

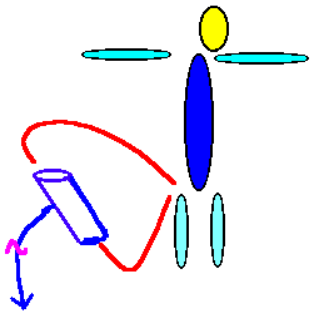


replacement

Ultrafiltrate is concurrently replaced with a combination of:

- custom physiologic solutions
- ringer's lactate
- total parenteral nutrition solutions

In patients with fluid overload, a portion of the ultrafiltrate volume is simply not replaced, resulting in predictable and controllable negative fluid balance.



physiologic replacement fluid

bag #1	7.5 ml CaCl 10% 1000 ml NaCl 0.9%
bag #2	1.6 ml MgSO4 50% (6.4 mEq Mg) 1000 ml NaCl 0.9%
bag #3	1000 ml NaCl 0.9%
bag #4	100 ml NaHCO3 (100 mEq NaHCO3) 10 ml D50W (5gm dextrose) 900 ml NaCl 0.9%

replacement fluid: final conc.

sodium	140	mEq/L
chloride	120	mEq/L
bicarbonate	25	mEq/L
calcium	2.6	mEq/L
magnesium	1.6	mEq/L
dextrose	124	mg/dL
potassium	0	

replacement fluid: commercial

standardized replacement fluid for CVVH*

component	mmol/liter	notes
sodium	140	
potassium	0[3]	
calcium	1.6	mEq/L = mmol/L divided by 0.25
magnesium	0.75	mEq/L = mmol/L divided by 0.5
chloride	101	
lactate	45	
glucose	11	mg/dL = mmol/L divided by 0.556

* Gambro Hemofiltrasol 22.

[3] Potassium is added if needed, up to 4 mmol/liter

replacement fluid: potassium

Potassium is usually excluded from the initial FRF formula in patients with renal failure. Eventually, most patients need some potassium (and phosphate) supplementation.

- a physiologic concentration of potassium must be added to each of the four FRF bags

- if instead 16 mEq of KCl were added to a single bag, serious hyperkalemia could develop quickly

replacement fluid: Ringer's

Many adults are successfully treated with CVVH using Lactated Ringer's solution as the FRF. Ringer's is:

- convenient
- cheaper
- eliminates risk of pharmacy error in formulation of the Michigan bags

Michigan FRF may be preferable in critically ill children, especially infants, but we have not compared the two solutions systematically.

drug clearance & dosing

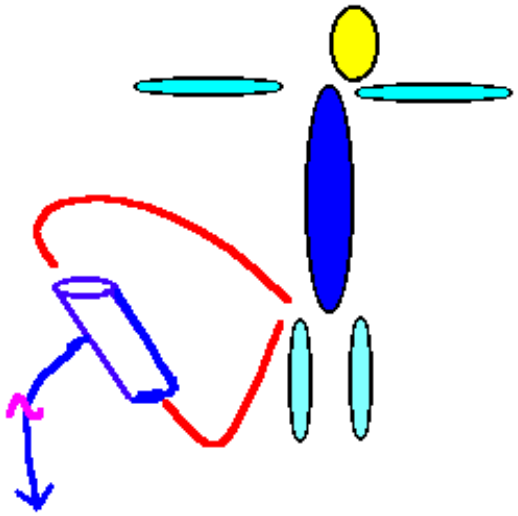
Drug therapy should be adjusted using frequent blood level determinations, or by using tables that provide dosage adjustments in patients with reduced renal function:

- Bennett's tables require an approximation of patient's GFR
- the CVVH 'GFR' is approximated by the ultrafiltrate rate (UFR), plus any residual renal clearance
- using Bennett's tables, in most CVVH patients, drug dosing can be adjusted for a 'GFR' in the range of 10 to 50 ml/min.

anti-coagulation

To prevent clotting within and shutdown of the CVVH circuit, active anti-coagulation is often needed.

- heparin
- citrate
- 'local' vs. systemic

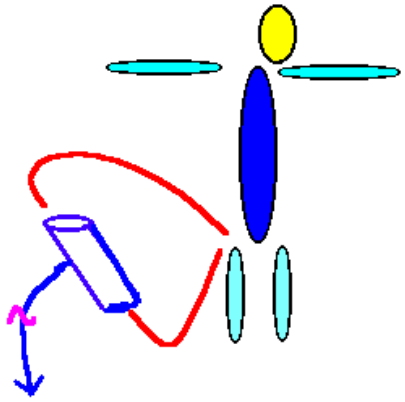


anti-coagulation

Patients with coagulopathies may not need any heparin.

- if patient's ACT is > 200 seconds before treatment, we do not use heparin

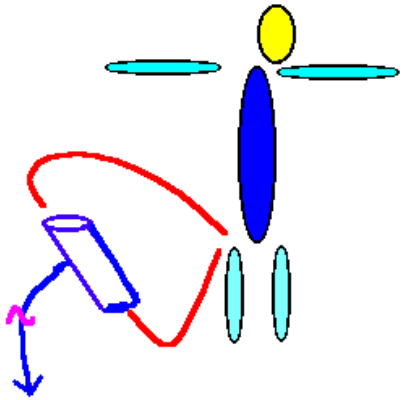
- coagulopathies spontaneously improve, often signaled by filter clotting…



anti-coagulation: heparin

Patients with coagulopathies may not need any heparin.

- when the ACT is <200 seconds, a loading dose of heparin @ 5-20 units/kg is given
- heparin as a continuous infusion (initial rate 5 units/kg/hr) into 'prefilter' limb of circuit
- adjust heparin rate to keep ACT from the venous limb ('postfilter') 160 to 200 seconds



anti-coagulation: citrate

Citrate regional anticoagulation of the CVVH circuit may be employed when systemic (i.e., patient) anticoagulation is contraindicated for any reason (usually, when a severe coagulopathy pre-exists).

- CVVH-D mode has countercurrent dialysis across the filter cartridge

- CVVH-D helps prevent inducing hypernatremia with the trisodium citrate solution

anti-coagulation: citrate

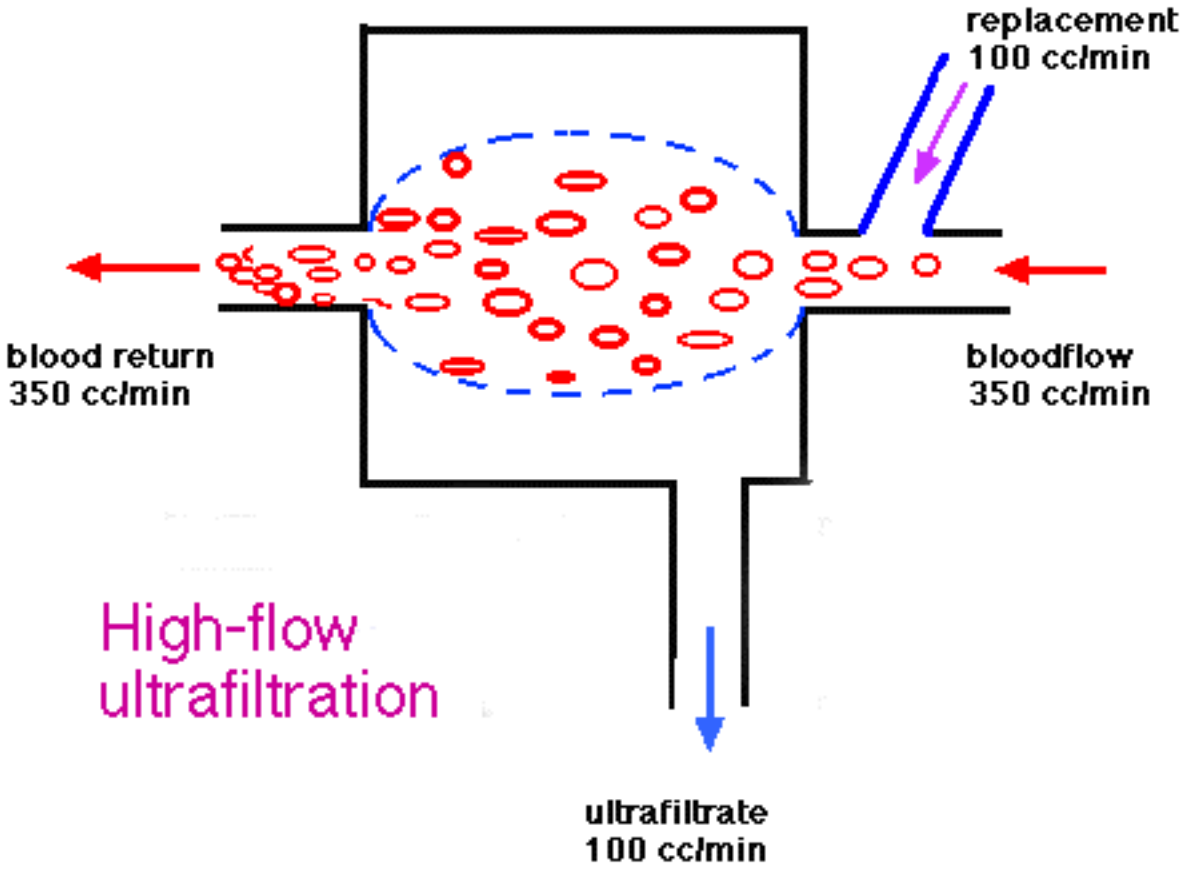
Citrate regional anticoagulation of the CVVH circuit :

- 4% trisodium citrate 'prefilter'
- citrate infusion rate = filtration rate (ml/min) x 60 min. x 0.03
- replacement fluid: normal saline
- calcium infusion: 8% CaCl in NS through a distal site
- dialysate: Na 117 . glucose 100-200 . K 4 . HCO_3 22 . Cl 100 . Mg 1.5

Ionized calcium in the circuit will drop to $\leq$ 0.3, while the systemic calcium concentration is maintained by the infusion.

Sramek et al: Intensive Care Med. 1998; 24(3): 262-264.

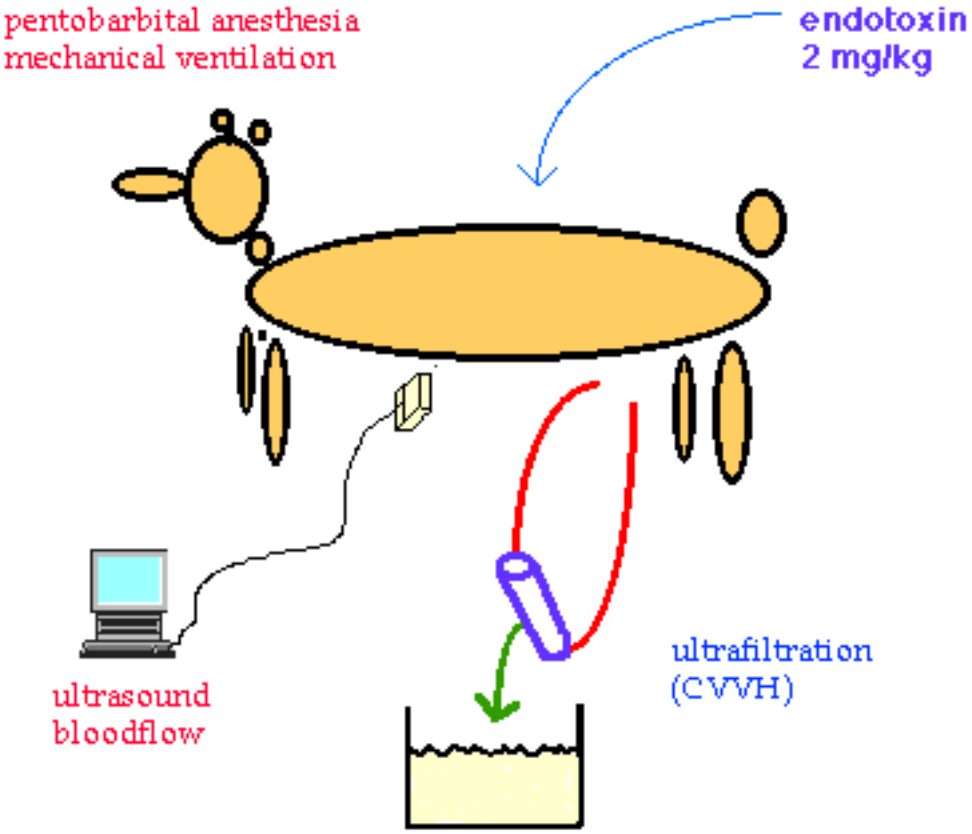
experimental: high flow



High-volume CVVH might improve hemodynamics, increase organ blood flow, and decreased blood lactate and nitrite/nitrate concentrations.

experimental: septic shock

Zero balance veno-venous hemofiltration was performed with removal of 3L ultrafiltrate/h for 150 min.
Thereafter the ultrafiltration rate increased to 6 L/h for an additional 150 min.



Rogiers et al: Effects of CVVH on regional blood flow and nitric oxide production in canine endotoxic shock.

experimental: septic shock

	UF @ 6 L/min	no UF	
mean art. BP (mmHg)	77 ± 19	40 ± 15	p < .05
cardiac index (mL/min.kg)	0.17 ± .04	0.06 ± .04	p < .05
stroke index (mL/kg)	1.0 ± 0.4	0.4 ± 0.3	p < .05
LV strokework index (g/m.kg)	1.0 ± 0.6	0.2 ± 0.2	p < .05
hepatic blood flow (% baseline)	+226 ± 68	+70 ± 34	

Rogiers et al: Effects of CVVH on regional blood flow and nitric oxide production in canine endotoxic shock.

scenario I

Septic shock, day #3 of hospitalization. Ultrafiltrate production is tightly controlled by a flow regulator on the outflow port of the filter.

- dry weight: 20 kg
- today's weight: 24 kg
- bloodflow through filter: 75 cc / min
- ultrafiltrate production: 0.5 cc / min

scenario I

fluids IN

	(hourly)		(daily)
i.v. fluids:	100	X 24	2,400
TOTAL:	100	X 24	**2,400**

fluids OUT

	(hourly)		(daily)
urine:	10	X 24	240
ultrafiltrate:	30	X 24	720
TOTAL:	40	X 24	**960**

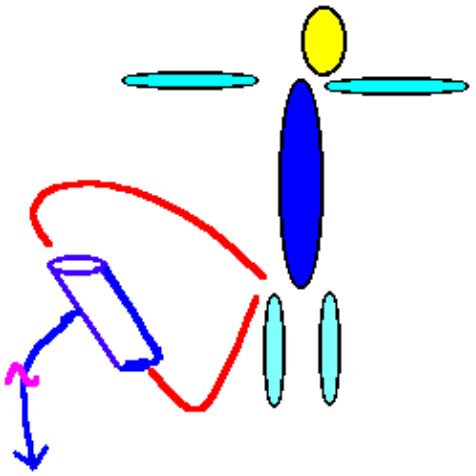
net balance (cc/day): 1,440

With this low level of ultrafiltrate production, fluids IN / OUT are still not balanced [the child's intake is 100 cc/hr IV, and output is (30 cc UF+ 10 cc urine) = 40 cc/hour]. Ultrafiltrate production should be increased to achieve total fluid balance.

scenario II

Septic shock, day #4 of hospitalization. Ultrafiltrate production is increased to 90 cc/hour, tightly controlled by a flow regulator on the outflow port of the filter.

- dry weight: 20 kg
- today's weight: 24 kg
- bloodflow through filter: 75 cc / min
- ultrafiltrate production: 1.5 cc / min



scenario II

Fluids IN / OUT are balanced [the child's intake is 100 cc/hr IV, and output is (90 UF+ 10 cc urine) = 100 cc/hour].

fluids IN

	(hourly)		(daily)
i.v. fluids:	100	X 24	2,400
TOTAL:	100	X 24	**2,400**

fluids OUT

	(hourly)		(daily)
urine:	10	X 24	240
ultrafiltrate:	90	X 24	2,160
TOTAL:	100	X 24	**2,400**

net balance (cc/day): 0

But the system is still not used efficiently --- only 2% of the blood volume passing through the filter is being converted to ultrafiltrate; this does not provide much solute clearance.

scenario III

Septic shock, day #2 of hospitalization. CVVH is initiated, and ultrafiltrate is produced at a rate of 1440 cc/hour, tightly controlled by a flow regulator on the outflow port of the filter.

- dry weight: 20 kg
- today's weight: 23.6 kg
- bloodflow through filter: 75 cc / min
- ultrafiltrate production: 25 cc / min

scenario III

fluids IN

	(hourly)		(daily)
i.v. fluids:	100	X 24	2,400
replacement:	1,240	X 24	29,760
TOTAL:	1,340	X 24	**32,160**

fluids OUT

	(hourly)		(daily)
urine:	10	X 24	240
ultrafiltrate:	1,440	X 24	34,560
TOTAL:	1,450	X 24	**34,800**

net balance (cc/day): -2,640

A net deficit of 100 cc/hr is desired. A body weight loss of two kilograms or more is expected over the next 24 hours. This is much better use of the filter --- balancing total body fluids, and providing solute clearance by producing over 1 liter of ultrafiltrate per hour.

scenario III: questions

1. ultrafiltration production (25 cc/min) is now equal to 33% of the filter bloodflow (75 cc/min). What mechanical problem might be expected with the filter? How can this problem be avoided?

2. how much fluid volume can be dedicated to nutrition (either parenteral or enteral)?

scenario III: questions (a)

Over 30 liters of ultrafiltrate is being produced per day; this child weighs only twenty kilograms. A 'replacement solution' is infused to offset most of the volume lost. The following scenario can be imagined:

- the heart rate gradually increases, from 100 beats/min up to 140 beats/min. The central venous pressure falls from 8 mmHg to 3 mmHg. How should therapy be adjusted?

After two or three days of aggressive ultrafiltration, total body water may be depleted; either UF production should be decreased or (better) replacement fluid should be increased.

scenario III: questions (b)

Over 30 liters of ultrafiltrate is being produced per day; this child weighs only twenty kilograms. A 'replacement solution' is infused to offset most of the volume lost.

> the child is initially responsive to verbal commands, and moves all extremities spontaneously. Over two days she gradually becomes obtunded, and barely moves. What should be checked?

Electrolyte depletion is always an issue --- particularly phosphate ion, which when severely depleted makes energy production impossible. The child with [PHOS] < 1 will likely be comatose.

scenario III: questions

Over 30 liters of ultrafiltrate is being produced per day; this child weighs only twenty kilograms. A 'replacement solution' is infused to offset most of the volume lost.

- at the onset of high flow CVVH, the child had a moderate metabolic acidosis (base deficit -3 mmol/L). After two days of high flow CVVH, hemodynamics are stable but the base deficit is -8 mmol/L. Is there a problem with the replacement solution?

The source of base in the replacement solution may be the culprit. Is it lactate (e.g., in Ringer's)? A compromised liver might not be able to handle a large lactate load.

scenario IV

Septic shock, day #5 of hospitalization. CVVH was initiated three days previously, and the body weight has been returned to baseline. Ultrafiltrate production is now continued at a rate of 1440 cc/hour, controlled by a flow regulator on the outflow port of the filter.

- dry weight: 20.0 kg
- today's weight: 20.5 kg
- bloodflow through filter: 75 cc / min
- ultrafiltrate production: 25 cc / min

scenario IV

No net deficit is desired. Fluids IN / OUT should be balanced.

fluids IN

	(hourly)		(daily)
i.v. fluids:	100	X 24	2,400
replacement:	1,350	X 24	32,400
TOTAL:	1,450	X 24	**34,800**

fluids OUT

	(hourly)		(daily)
urine:	10	X 24	240
ultrafiltrate:	1,440	X 24	34,560
TOTAL:	1,450	X 24	**34,800**

net balance (cc/day): 0

question:

ultrafiltrate is produced at 1440 cc / hour. What limitations in equipment might prevent such a high rate of production?

PD: preferential indications

- infants < 2500 gm
- severe hypothermia or hyperthermia
- hemolytic - uremic syndrome (+-)

PD: inadequate

- severe hyperammonemia (inborn errors)
- intoxication with dialyzable poisons

PD: percutaneous catheters

- Cook 5-Fr + larger
- 8.5 Fr even for neonates (less obstruction)
- peritonitis risk if >> 6 days

PD: surgical catheters

- Tenckhoff (several manufacturers)
- double-cuff Tenckhoff decreases peritonitis risk

PD: equipment for acute PD

- Y-tubing manual exchange for small volumes
- automatic cycle for XC volumes > 100 cc
- infuse approx. 5 minutes
- dwell 15 - 45 minutes
- drain 5 - 15 minutes

PD: acute prescription

- dialysate dextrose concentration
- dialysate additives
- exchange volume
- inflow, dwell + outflow times

PD: dialysate

- standard dextrose 1.5%, 2.5%, and 4.25%
- higher dextrose () increases UF
- shorter dwell time increases UF
- larger XC volumes increases UF

PD: dialysate buffer

- standard solutions contain lactate as buffer
- infants might not be able to convert lactate
- unconverted lactate worsens acidosis
- custom-made bicarbonate / dextrose solution

PD: regimen

- initial exchange volume 10-15 cc/kg (avoid leak)
- usually 2.5% dextrose
- one-hour cycle (5 - 45 - 10)
- shorter cycle (30 - 45 m) better solute removal
- increase XC to 30 cc/kg within three days
- increase to 40 cc/kg within a week

PD: precautions

- blood pressure tends to decline during drain
- if infant becomes hypotensive during DWELL:
  - do not drain
  - replenish fluids

PD: complications

- one-way obstruction (omentum)
  - allows inflow but not drainage
  - replace catheter
- catheter clotting
  - add 250 - 500 U heparin to initial 2-liter dialysate bag
- peritonitis

PD: peritonitis

- cloudy dialysate drainage
- dialysate > 100 WBC/cc
- > 50% polymorphonuclear leukocytes
- gram positive organisms [PICU: gram (-) also]
- intraperitoneal antibiotics pending culture results
- vancomycin (8 mg/L) + ceftazidime (125 mg/L) --- or ---
- gentamicin (8 mg/liter dialysate)
- add heparin 500 U/L to reduce fibrin formation
- cephalosporin @ catheter placement prophylaxis