# CVVH: An Overview

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# Primary Therapeutic Goals in ARF

- Optimize hemodynamic and volume status
- Minimize further renal injury
- Correct metabolic abnormalities
- Removal of Uremic toxins
- Permit adequate nutrition

Lauchy VA Semin Dial. 2004;17(1):30-6

# Limitations on Dialysis Delivery in ARF

- Hypercatabolic state
- Hemodynamic instability
- Control of Volume status

# Continuous Renal Replacement Therapy (CRRT)

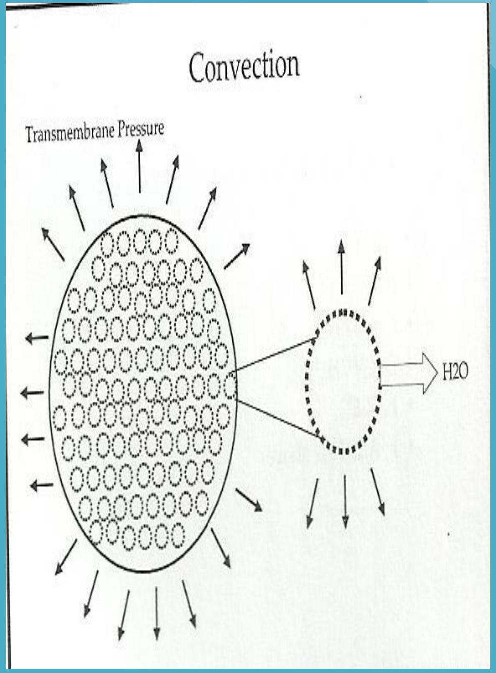
| | |
|---|---|
| **CVVH** | Continuous Veno-Venous Hemofiltration |
| **CVVHD** | Continuous Veno-Venous Hemodialysis |
| **CVVHDF** | Continuous Veno-Venous Hemodiafiltration |
| **SCUF** | Slow Continuous Ultra-Filtration |
| **SLED** | Slow Low Efficiency Dialysis |

# Primary Therapeutic Goals in CRRT

- Solute Removal
  - Diffusion and Convection
- Solute Addition
  - Replacement Fluid
- Fluid Removal
  - Convection
- Detoxification

# Basic CRRT Concepts

- Convection
  - Ultrafiltration coefficient
  - Sieving coefficient (Sc)
  - Solvent Drag
- Diffusion
  - Solvent gradient
- Effluent
- Secondary Membrane Formation
- Replacement Solution
- Clearance

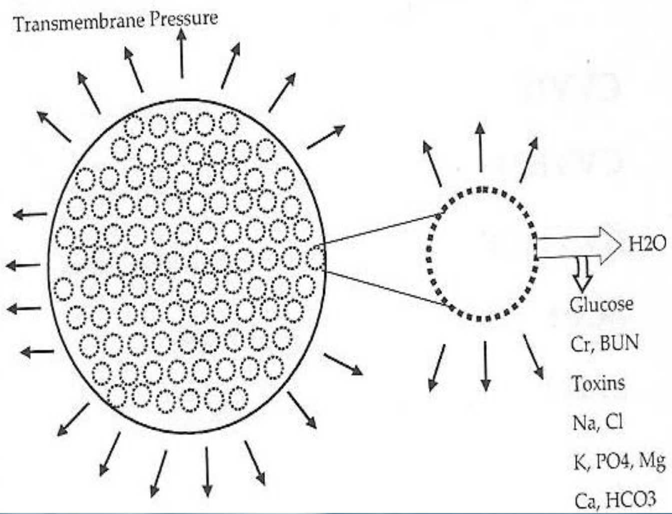



# Convection

- Fluid Removal and Solute Removal
- Movement of fluid across the membrane via transmembrane pressure
- Water moves across the membrane and carries dissolved solutes with it via solvent drag
  - Ultrafiltration is fluid removal
  - Hemofiltration involves partial or total replacement of fluid removed

Luciano A. Pedrini J Nephrol 2003; 16 (suppl 7): S57-S63

## Convection




## Convection

- Ultrafiltration plasma water
  - **Ultrafiltration coefficient** of the membrane
  - Potential to remove water adjusted for the transmembrane pressure
- Solute removal from plasma
  - **Sieving coefficient** for that solute
  - Ratio between the solute concentration in the ultrafiltrate and its average plasma concentration within the dialyzer
  - Inversely related to the solute molecular weight
  - ~1.0 with small solute and highly permeable membranes

Luciano A. Pedrini J Nephrol 2003; 16 (suppl 7): S57-S63

Chelamcharla M, Semin Nephrol. 2005;25(2):81-9

# Diffusion

- Movement of solutes down a concentration gradient across a semipermeable membrane.
- Solutes cross the membrane from the blood to the dialysis fluid compartment.
- Fluid in the dialysis compartment moves in a counter-current direction, thereby maintaining a concentration gradient.

Luciano A. Pedrini J Nephrol 2003; 16 (suppl 7): S57-S63

# Diffusion

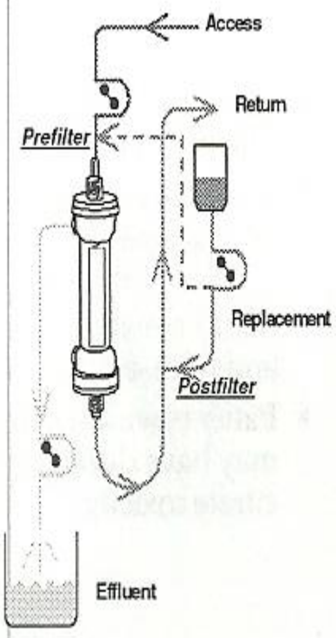
- Diffusive clearance is determined by
  - Molecular weight of the solute
  - Concentration gradient across the membrane
  - Membrane surface area
  - Thickness and pore size

# Effluent

- Represents the end product of the filtration process
- CVVH: Ultrafiltrate
- CVVHD: Dialysate plus variable ultrafiltrate
- CVVHDF: Dialysate plus ultrafiltrate

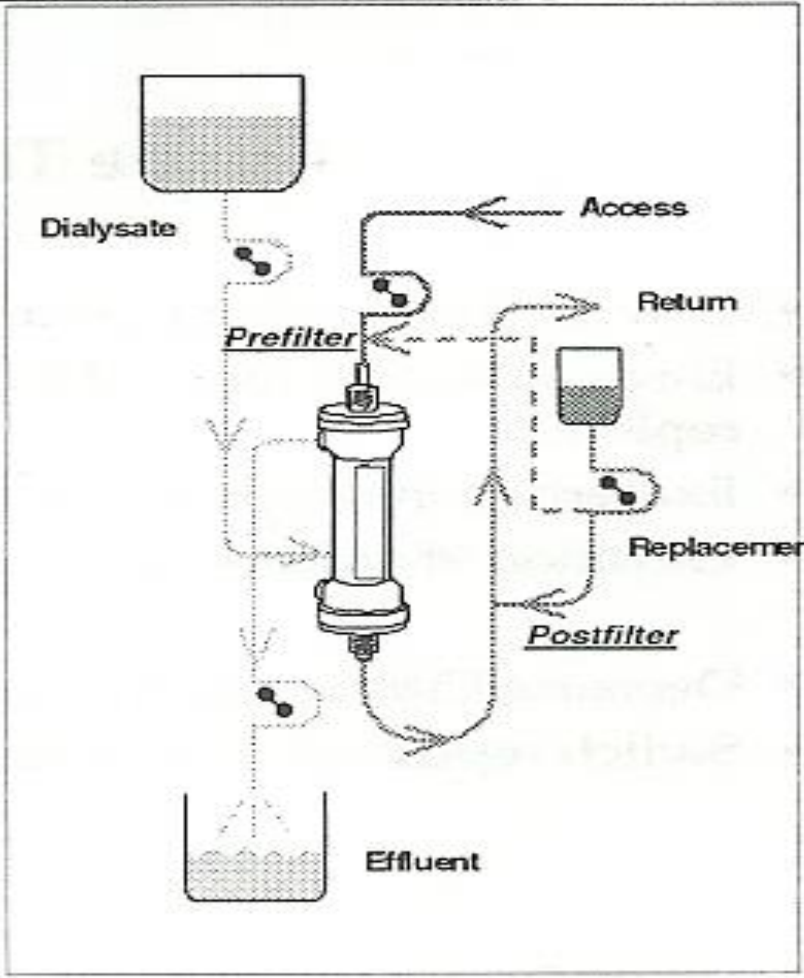
# CVVH

Continuous
Veno-Venous
Hemofiltration



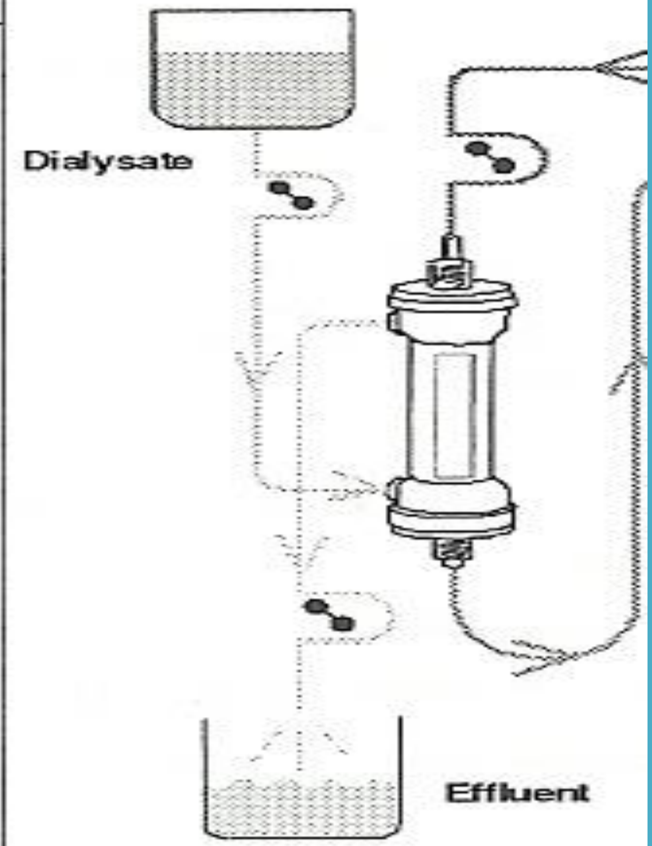
# CVVHDF

Continuous
Veno-Venous
HemoDiaFiltration



# CVVHD

**Continuous
Veno-Venous
HemoDialysis**



# Technical Aspects

| | SCUF | CVVH Hemofiltration | CVVHD HemoDialysis | CVVHDF HemoDiaFiltration |
|---|---|---|---|---|
| Blood filter | High Permeability | High Permeability | Low Permeability | High Permeability |
| Middle Molecule Clearance | + | +++ | - | +++ |
| Replacement Fluid | None | RF | None | RF |
| Dialysate | None | None | D | D |

Adapted from Johnson RJ, Feehally J, Comprehensive Clinical Nephrology 2nd Edition

# Replacement Solution

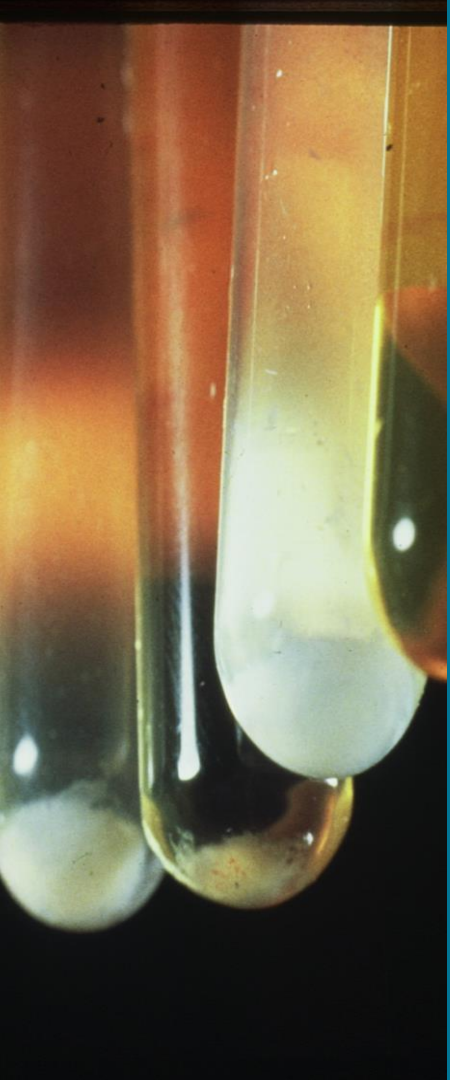
- Replaces the ultrafiltrate removed by hemofiltration and hemodiafiltration.
- Buffers: Lactate, bicarbonate or citrate
- Lactate and Citrate metabolized by liver and muscle to bicarbonate.
- Bicarbonate is most easily tolerated
  - can be unstable in solution
- Lactate is more stable
  - may contribute to an existing lactic acidosis in septic or liver failure patients
- Citrate
  - Regional anticoagulation

P Heering Intensive Care Med 1999, 25:1244-1251

Tan HK Int J Artif Organs. 2003 Jun;26(6):477-83.

# Citrate Regional Anticoagulation

- Citrate causes anticoagulation by chelation of calcium in the extracorporeal system
- Systemic anticoagulation does not occur
  - as ionized calcium level is restored when blood returning from the extracorporeal system is mixed with venous blood
- Rapid metabolism of citrate restores bicarbonate level and releases calcium
- Patients with severe liver failure and lactic acidosis may have difficulty metabolizing citrate and develop citrate toxicity



# Citrate Toxicity

- Low ionized Calcium despite repletion
- Elevated total serum Calcium in response to repletion
- Exacerbation of serum acidosis
- Elevation of anion gap

- Decrease Citrate replacement solution rate
- Switch replacement solutions

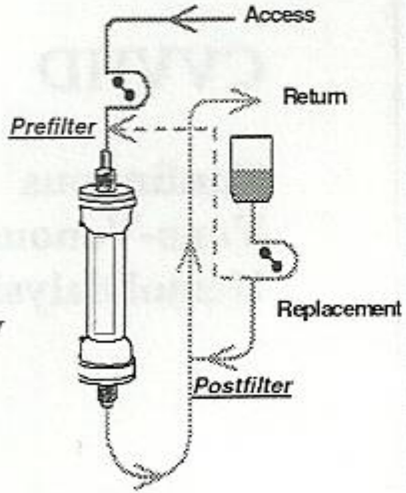
# Citrate Replacement solution

- **Sodium Citrate = 40 mEq/Liter,**
- **Dextrose = 2 gm/Liter,**
- **Sodium Chloride = 105 mEq/Liter,**
- **Magnesium Sulfate = 1.5 mEq/Liter.**

- CVVH with maximum replacement of 2000 cc citrate/hour.
- CVVHDF add dialysate to improve clearance.
- Calcium replacement scales adjusted depending on clearance

# Pre- vs. post-dilution

- Post-dilution:
  - High small solute clearance/ml
  - UF rate limited by
    - Hematocrit
    - QB
  - Maximal UF is 25% plasma flow
- Pre-dilution:
  - Less clearance/ml (diluted)
  - Reduced efficiency by 10-15%
  - UF rate is **not** limited



# Pre-Dilution

- Replacement fluid infused at the proximal side
- Relatively low viscosity of the blood within the filter
- Efficiency of ultrafiltration is compromised
- Reduces net filtration fraction
- Minimizes concentration of clotting factors
- Prolongs filter lifespan

# Post-Dilution

- Replacement fluid infused via distal side
- Most efficient technique
- Maximum clearances
- Maximally dehydrates the blood in the hemofilter
- Higher viscosity of the blood within the filter
- Clotting of filter

# Ultrafiltration Membranes

- Hemofilters allow the passage of molecules with a molecular weight of less than 50,000 Daltons.
- Small molecules freely filtered
  - sodium, potassium, bicarbonate, glucose and ammonia.
- Larger soluble substances filtered
  - myoglobin, insulin, and interleukins
  - medications (vancomycin, heparin)
- Protein bound molecules are not filtered effectively

# TMP TransMembrane Pressure

- Pressure exerted on the membrane during operation
- Primary factor determining filtration rate
- Pressure difference between blood and fluid compartment
- Usual range 100 - 500 mmHg
- Increased TMP associated with increased UF rate

- TMP= [(Filter Pressure + Return Pressure)/2] – Effluent Pressure

# Clearance

- Clearance is the rate at which solutes are cleared
  - excretion rate of solute / blood concentration of solute
- Solute clearance in CVVH depends on UF Rate
- Clearance in Predilution 10-15% < Postdilution
- Predilution mode Clearance improved
  - large hemofilters
  - high UF Rate

## Strategies to Increase Solute Clearance

- Increase Transmembrane pressure
- Increase filter permeability to water
- Increase filter surface area
- Increase blood flow

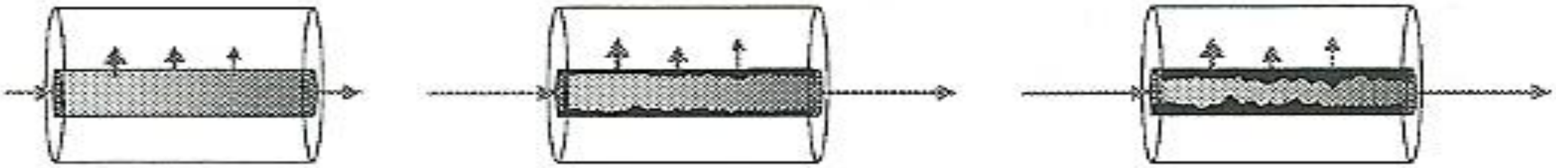
- CVVHDF
  - Add dialysis to convection

Johnson RJ, Feehally J, Comprehensive Clinical Nephrology 2nd Edition

# Secondary Membrane Formation

"gel layer" or "protein cake"

- Protein layer formed over surface of dialyzer membrane with transmembrane pressure
- Reduces the effective solute and water permeability.
- Adsorption occurs in all membranes
- Magnified in CRRT



- Pre-pump increases filter life
  - Dilute blood going into the filter
  - Dilute protein and red cell concentration

Ronco C, Contrib Nephrol. 1991;93:175-8

Mehta R, Atlas of Diseases of the Kidney 1999

# Indications for CRRT

- Patients with/ at risk for hypotension:
  - severe hemodynamic instability
  - hepatic failure
  - CHF
  - sepsis or multiple organ failure
- Patients at risk of cerebral complications:
  - hepatic failure, stroke or head trauma
  - high risk for cerebral edema

# Indications for CRRT

- Increased metabolic needs
  - massive burns
  - sepsis
  - multiple organ failure
- Volume overload
  - massive volume overload
  - Patients receiving large amounts of fluids or blood products
  - When volume management is critical

# Non-renal Indications for CRRT

- Lactic acidosis
  - Ongoing production
- Crush injury
  - Myoglobin Removal
- Tumor lysis syndrome
- Temperature control
  - Relative hyper or relative hypothermia*
- Massive volume overload without ARF
- High $NH_3$

*Kopcke J. Anaesthesiol Reanim. 1996;21(6):159-62.

# Potential Advantages of CRRT

- Increased total solute clearance
- Gradual clearance may be better tolerated
  - Decreases frequency of hypotension
  - Decreases risk of cerebral edema
- Continuous clearance may help in removal of toxins with high intracellular concentrations
- Increased clearance of middle molecules

- <u>**Precise adaptable volume control**</u>

# Potential disadvantages of CRRT

- Anticoagulation requirement
- Lack of rapid fluid and solute removal
- Limited role in overdose setting
- Relative Hypothermia
- Electrolyte Depletion
  - K, $PO_4$, Ca

# Technical Complications of CRRT

- Vascular access malfunction
- Blood flow reduction and circuit clotting
- Loss of filter efficiency
- Line disconnection
- Air embolism
- Fluid and Electrolyte balance errors

# Clinical Complications of CRRT

- Bleeding
- Thrombosis
- Line Infection and sepsis
- Relative Hypothermia masking low grade fever
- Nutrient losses
- Inadequate blood purification due to down time
  - median 3 h per day down time[1]
- Thrombocytopenia
  - destruction or retention of platelets passing through hemofilter.[2]

1. Uchino S,Intensive Care Med. 2003 Apr;29(4):575-8.

2. Mulder J, Int J Artif Organs. 2003;26(10):906-12.,

# Contraindications of CRRT

- Life-threatening hyperkalemia

# Drug Dosage in CRRT

- Minimal removal of protein bound drugs
- Some may be removed via membrane adsorption

- Drug clearances increased with CVVHDF
- Higher doses may be needed with higher UF rates

- GFR = 10 ml/min Low UF rate
- GFR = 30 ml/min Medium UF rate
- GFR = 50 ml/min High UF rate

Mehta R, Atlas of Diseases of the Kidney 1999

Bugge JF.Acta Anaesthesiol Scand. 2001;45(8):929-34.

# Nutrition and CRRT

- Increased azotemia induced by protein or amino acids in TPN[1]
- Fluid overload caused by the administration of TPN[1]
- Negative balances of selenium, copper, thiamine[2],
- Loss of Magnesium and calcium[3]
- High-protein diet safe for patients with ARF on CRRT[4]
- Protein intake of 2.5 g/kg/day
  - increases the likelihood of positive nitrogen balance[5]
  - corrects amino acid deficiencies.[6]

1. Bellomo R. Blood Purif. 2002;20(3):296-303. 2. Berger MM. Am J Clin Nutr. 2004;80(2):410-6.
3. Klein CJJPEN J Parenter Enteral Nutr. 2002;26(2):77-92 4. Bellomo R. Ren Fail. 1997;19(1):111-20.
5. Scheinkestel CD Nutrition. 2003;19(11-12):909-16. 6. Scheinkestel CD. Nutrition. 2003;19(9):733-40.

# Estimate GFR in CRRT

- eGFR = $\frac{\text{Replacement Solution ml per hour}}{\text{Ideal body weight}}$
- eGFR = $\frac{\text{3000 ml/hr}}{\text{70 kg}}$
- eGFR= 42

# CRRT and Sepsis

- Many immune mediators are water soluble and fall into the middle-molecular-weight category
  - Theoretically removed via hemofiltration.
  - adsorption to the filter membrane
- CRRT in animal models of sepsis and have demonstrated some beneficial effects.
  - CVVH reduces plasma TNF, but not IL-6, IL-10.
- Early isovolemic CVVH at 2 l/hour in established sepsis
  - No reduction of several cytokines and anaphylatoxins
  - Organ dysfunction not improved.
- CVVH has not been shown to benefit SIRS/Sepsis in the absence of ARF

Venkataraman R. Critical Care 2003, 7:139-145

# High Volume HemoFiltration and Sepsis

- HVHF: ultrafiltration of more than > 35 ml/kg/hour
- 'sepsis doses' of ultrafiltration 3.8–6 l/hour
  - increased survival
  - decreased vasopressor requirements
- animal studies
  - significant hemodynamic benefit
  - improvement in immune cell responsiveness
  - reduced mortality
- More studies are needed to clarify the role of HVHF
  - hyperdynamic septic shock
    - with or without acute renal failure
  - sepsis and SIRS.


Cole L. Intensive Care Med 2001, 27:978-986

Oudemans-van Straaten HM, Intensive Care Med 1999, 25:814-821.

Honore PM Int J Artif Organs. 2004, 27(12):1077-82.

# CRRT vs Hemodialysis

- No consistent statistically significant difference in survival
  - Vinsonneau et al. Lancet 2006; 368: 379-85
- Both methods are complementary
- IHD
  - Faster Potassium elimination
  - Faster Drug/ Toxin elimination
  - Better for overdose
- CRRT
  - Regulation of higher calories requirements
  - Hemodynamically unstable patients
  - Precise adaptable volume control

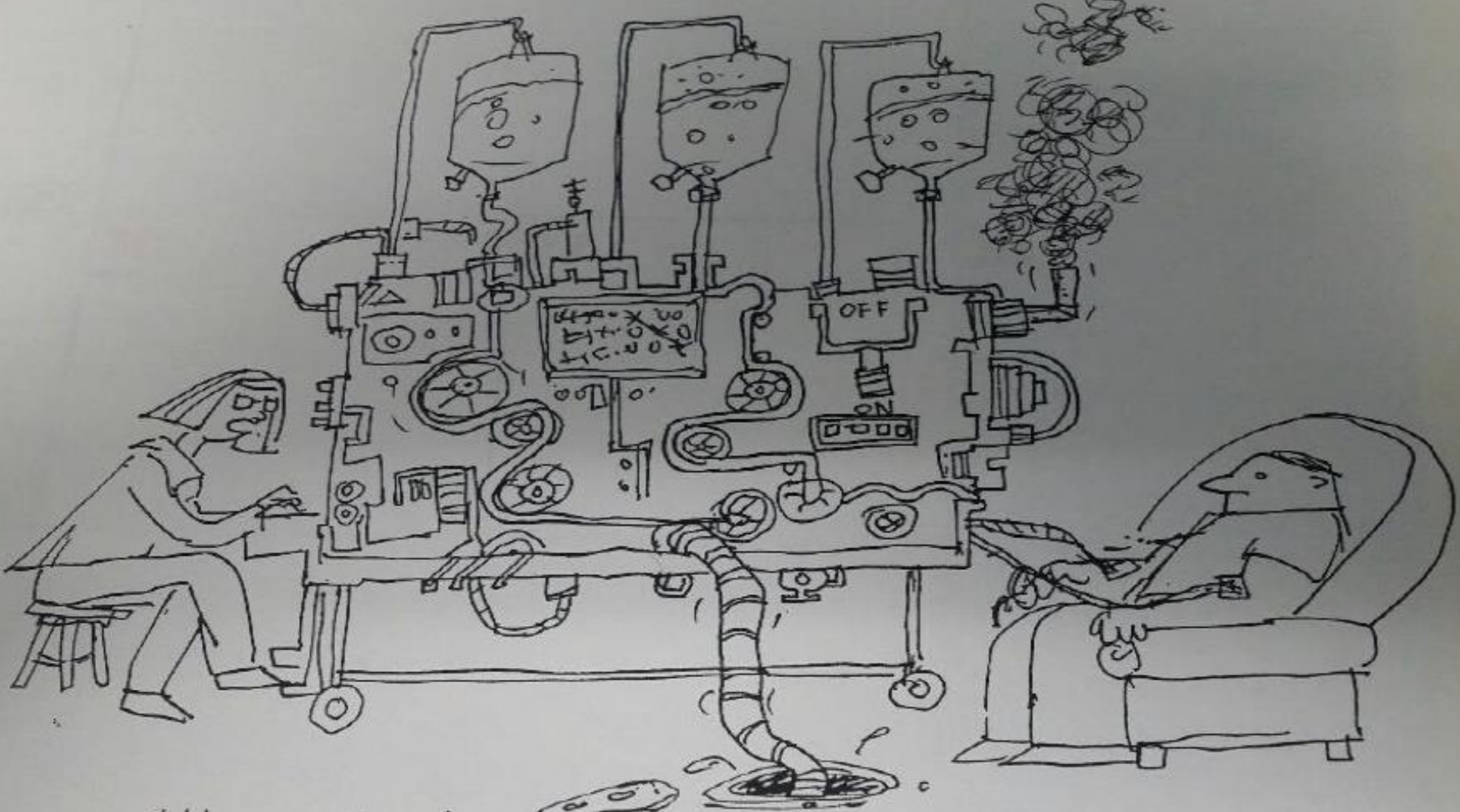
# Cessation of CRRT

- All criteria for initiating CRRT are absent
- Urine output averages 1ml/kg/hr over a 24hr period
- Fluid balance can be kept approximately neutral with current urine output
- There is a complication related to CRRT

- When criteria are fulfilled begin a 12-24 hour period without CRRT
- Reevaluate for indications for CRRT

- CRRT should be initiated early and ceased late

Bellomo R, Ronco C. Intensive Care Med 1999;25:781-9




"How about a tune, this thing is also a piano!"


QUESTIONS ????