MODALITIES of Renal Replacement Therapy in AKI

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In AKI, RRT is a multidimensional task
The components

- MODALITY
  - Diffusion, Convection or both
  - MEMBRANES/FILTERS
  - SOLUTIONS
  - BUFFERS
  - PRESCRIBED DOSE
  - MEASURED DOSE

- MACHINES

- ENVIRONMENT

- NURSING
  - TECHS
  - EDUCATION
  - QUALITY MEASURES
  - INSTITUTIONAL SUPPORT
  - COST
  - TEAM WORK

- OUTCOMES
  - MOF
  - AKI
  - COMORBIDITIES
  - RENAL OR NON RENAL INDICATIONS
  - FLUID STATUS
  - HEMODYNAMICS
  - ACID BASE
  - DYSELECTROLYTEMIAS
  - CATABOLISM
  - DRUGS
  - NUTRITION

- PATIENT

- TEAM WORK

- INSTITUTIONAL SUPPORT

- COST

- QUALITY MEASURES

- NURSING TECHS

- EDUCATION

- MEASURES
A multi-component system

MODALITY
Diffusion, Convection or both
MEMBRANES/FILTERS
SOLUTIONS
BUFFERS
PRESCRIBED DOSE
MEASURED DOSE

RECOVERY FUNCTION
SURVIVAL
HEMODYNAMIC STABILITY
TIMING
DELIVERED DOSE

NURSING
TECHS
EDUCATION
QUALITY MEASURES
INSTITUTIONAL SUPPORT
COST
TEAM WORK

MOF
AKI
COMORBIDITIES
RENAL OR NON RENAL
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CATABOLISM
DRUGS
NUTRITION
Objectives

• Establish the basic components of the CRRT prescription
• Know your CRRT Machines
• Know your Solutions
• What Modality should you use?
• What Dose should you use?
• Writing Prescriptions
• Troubleshooting
What are the characteristics of the “ideal” AKI treatment modality in the ICU?

- Preserves homeostasis
- Does not increase co-morbidity
- Does not worsen patient’s underlying condition
- Is inexpensive
- Is simple to manage
- Is not burdensome for the ICU staff

N. Lameire et al, NDT 1999;14:2570-2573
## Considerations in Renal Replacement Therapy for AKI

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<th>Components</th>
<th>Varieties</th>
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<td>Intermittent Hemodialysis</td>
<td>Daily, Every other day, SLED</td>
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<td>Continuous renal replacement therapies</td>
<td>AV, VV</td>
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<td>Adequacy of dialysis</td>
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</tr>
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</table>
How Do We Choose a Specific RRT Modality?

<table>
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<tr>
<th>Therapeutic Goal</th>
<th>Hemodynamics</th>
<th>Preferred Modality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fluid Removal</td>
<td>Stable</td>
<td>Intermittent Isolated UF</td>
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<td>Unstable</td>
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<tr>
<td>Urea Clearance</td>
<td>Stable</td>
<td>Intermittent Hemodialysis</td>
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<td></td>
<td>Unstable</td>
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<td>Severe Hyperkalemia</td>
<td>Stable/Unstable</td>
<td>Intermittent Hemodialysis</td>
</tr>
<tr>
<td>Severe Metabolic Acidosis</td>
<td>Stable</td>
<td>CRRT</td>
</tr>
<tr>
<td></td>
<td>Unstable</td>
<td>CRRT</td>
</tr>
<tr>
<td>Severe Hyperphosphoremia</td>
<td>Stable/Unstable</td>
<td>CRRT</td>
</tr>
<tr>
<td>Brain Edema</td>
<td>Unstable</td>
<td>CRRT</td>
</tr>
</tbody>
</table>

Cerdá and Ronco Semin Dialysis 2008
MODALITIES OF CRRT

- **SCUF**
  -blood inflow (Blood In)
  -ultrafiltration (UFC)
  -blood out (V)
  -Qb = 100 ml/min
  -Qf = 2-8 ml/min

- **CVVH**
  -blood inflow (Blood In)
  -ultrafiltration (Uf)
  -blood out (V)
  -Qb = 100-200 ml/min
  -Qf = 10-30 ml/min
  -K = 15-45 L/24 h

- **CVVHD**
  -blood inflow (Blood In)
  -blood out (V)
  -Qb = 100-200 ml/min
  -Qf = 2-4 ml/min
  -K = 15-45 L/24 h

- **CVVHDF**
  -blood inflow (Blood In)
  -ultrafiltration (UFC)
  -blood out (V)
  -Qb = 100-200 ml/min
  -Qf = 10-30 ml/min
  -Qd = 10-30 ml/min
  -K = 20-50 L/24 h

- **CVVHDF-SLED**
  -blood inflow (Blood In)
  -ultrafiltration (UFC)
  -blood out (V)
  -Qb = 100-200 ml/min
  -Qf = 2-8 ml/min
  -Qd = 50-200 ml/min
  -K = 40-60 L/24 h
  -Diffusion-Convection (Back Filtration)

- **CPF-PE**
  -blood inflow (Blood In)
  -plasma filter (Plasmafilter)
  -blood out (V)
  -Qb = 100-200 ml/min
  -QF = 20-30 ml/min
  -Can be coupled with CVVH or CVVHDF

- **CHP**
  -blood inflow (Blood In)
  -adsorbent
  -blood out (V)
  -Qb = 100-200 ml/min
  -Can be coupled with CVVH or CVVHDF

- **CPEA**
  -blood inflow (Blood In)
  -plasma filter
  -adsorbent
  -Qb = 100-200 ml/min
  -QF = 20-30 ml/min
  -Can be coupled with CVVH or CVVHDF

- **HVHF**
  -blood inflow (Blood In)
  -ultrafiltration (Uf)
  -blood out (V)
  -Qb = 200-300 ml/min
  -QF = 50-100 ml/min
  -K = 60-120 L/24 h

_Cerdá and Ronco Semin Dialysis 2008_
Components of the RRT prescription

- **Treatment Modality:** SCUF, CVVHDF, CVVH, CVVHD
- **Blood flow rate**
- **Ultrafiltration rate**
- **Replacement fluid:** Type of fluid, Rate, Type of dilution
- **Dialysate fluid:** Type of fluid, Rate
- **Labs**
- **Type of anticoagulation:** Citrate, Heparin, None
Anticoagulation

• Is Anticoagulation required?
  • *Almost always!*

• Systemic, or regional citrate anticoagulation?

• Why would anyone use anything but Citrate regional anticoagulation?
  • Does not affect patient’s coagulation
  • Safe if protocols are in place
  • Helps manage acid base disorders
  • May have a positive impact on recovery
CRRT Machines

NexStage

B.Braun

Fresenius

Prismaflex
CRRT Modalities
Molecular Transport Mechanisms

- Ultrafiltration
- Diffusion
- Convection
- Adsorption

Fluid Transport

Solute Transport
Ultrafiltration

- The movement of fluid through a membrane caused by a pressure gradient.
Diffusion vs. Convection

**Diffusion**

- Diffusion is solute transport across a semi-permeable membrane - molecules move from an area of higher to an area of lower concentration.

**Convection**

- Convection is a process where solutes pass across the semi-permeable membrane along with the solvent ("solvent drag") in response to a positive transmembrane pressure.

*Best for small molecule clearance*

*Effectiveness less dependent on molecular size*
Diffusion

• The movement of solutes from an area of higher concentration to an area of lower solute concentration.
Diffusion

- Random movement of molecules across a semi-permeable membrane

- *Fick’s Law of Diffusion* \( J_d = -D \cdot \left( \frac{dc}{dx} \right) \)

- Where diffusivity coefficient \( D \):
  
  \[ D = \frac{k_B T}{6\pi \mu R} \]

- Effective radius of molecule
Convection

- The movement of membrane-permeable solutes with a water-flow, ultrafiltered water.
Membrane Sieving Coefficient

• Ratio of a specific solute concentration in the ultrafiltrate (removed by convection) to pre- and post-filter solute concentration:

\[ SC = 2 \cdot \frac{C_{UF}}{C_{Pi} + C_{Po}} \]

• Convective flow \( J_c \) of a solute depends on:

\[ J_c = \frac{Q_{UF}}{A} \cdot C_{Pi} \cdot SC \]

QUF – magnitude of UF
A – membrane surface area
Cpi – solute concentration plasma water
SC – solute sieving coefficient
Adsorption

- Molecular adherence to the surface or interior of the membrane.

The interaction membrane-molecule is driven by individual molecule and membrane characteristics.
Solute Classes by Molecular Weight

Daltons

- **0 - 5**: Urea (60)
- **5 - 50**: Potassium (35), Phosphorus (31), Sodium (23)
- **50 - 100**: Glucose (180), Uric Acid (168), Creatinine (115), Phosphate (80)
- **100 - 500**: Aluminium/Desferoxamine Complex (700)
- **500 - 5,000**: Glucose (180), Uric Acid (168), Creatinine (115), Phosphate (80)
- **5,000 - 50,000**: Inulin (5,200)
- **50,000 - 100,000**: Myoglobin (17,500), Beta 2 Microglobulin (11,800)
- **100,000 - 1,000,000**: Albumin (55,000 - 60,000)
- **1,000,000 - 10,000,000**: Inflammatory Mediators (1,200-40,000)
- **10,000,000 - 100,000,000**: Protein (100,000 - 200,000)

**Categories**

- “small”
- “middle”
- “large”
Clearance Profiles by Modality

INDEXED TOXIN CLEARANCE

Hemodialysis

HEMOFILTRATION

Natural Kidney

CUTOFF POINT:
The MW of the smallest solute retained by the membrane:
The MW of a solute with a sieving coefficient of 0.1

MOLECULAR SIZE

Urea (small molecule)

β₂-m (Middle molecule)

Albumin (large molecule)
Ultrafiltration

Blood In
(from patient)

Blood Out
(to patient)

Fluid Volume Reduction

LOW PRESS → HIGH PRESS

to waste

SCUF: Slow Continuous Ultrafiltration

- Primary therapeutic goal:
  - Safe management of fluid removal
- Fluid removal rate dictated by patient tolerance
- Blood Flow: variable (not critical)
- Dialysate: Not required
- Replacement: Not required
Membrane Performance Characteristics

• Membrane Ultrafiltration Coefficient $K_{UF}$ (ml/h/mmHg/m2)

\[ K_{UF} = \frac{Q_{UF}}{TMP} \cdot \frac{1}{A} \]

• Filter Ultrafiltration Coefficient ($DK_{UF}$) (ml/h/mmHg)

\[ DK_{UF} = K_{UF} \cdot A \]

• Ultrafiltration Rate

\[ Q_{UF} = DK_{UF} \cdot TMP \]

DEFINES MEMBRANES:

LOW FLUX $K_{UF}<10$
HIGH FLUX $K_{UF}>25$
Transmembrane Pressure (TMP)

\[ \text{TMP} (l) = P_B (l) - P_D (l) - \pi_B (l) \]

\[ \text{TMP}^* = \frac{P_{Bi} + P_{Bo}}{2} - \frac{P_{Di} + P_{Do}}{2} - \frac{\pi_{Bi} + \pi_{Bo}}{2} \]

\[ \text{TMP}^* = \frac{P_{PRE} + P_{OUT}}{2} - P_{EFF} \]
Hemofiltration

Blood In *(from patient)*

Blood Out *(to patient)*

to waste

Repl. Solution
CVVH: Continuous Venovenous Hemofiltration

• Primary therapeutic goal:
  • **Convective** solute removal

• Blood Flow: variable

• Replacement (for convection):
  ~35 - 70 mL/min (~2 – 4 L/hr)
  • Solute clearance determined primarily by replacement fluid rate and dilution mode

• Dialysate: Not required
Hemodialysis

**INTERMITTENT HEMODIALYSIS:**
DIALYSATE FLOW
500-800 ml/min

**CONTINUOUS V-V HEMODIALYSIS:**
DIALYSATE FLOW
17 TO 33 ml/min
CVVHD: Continuous Venovenous Hemodialysis

• Primary therapeutic goal:
  • Solute removal by diffusion

• Blood Flow rate: variable

• Dialysate (for diffusion): ~35-70 ml/min (~2-4 L/hr)
  • Solute removal determined primarily by dialysate flow rate

• Replacement: Not required
CVVHDF: Continuous Venovenous Hemodiafiltration

- **Primary therapeutic goal:**
  - Solute removal by **diffusion and convection**
  - Combines CVVH and CVVHD therapies

- **Blood Flow:** variable

- **Dialysate:** typically ~15 – 50 mL/min (~1 – 3 L/hr)

- **Replacement:** typically ~15 – 50 mL/min (~1 – 3 L/hr)

- **Total (dialysate + replacement):** typically ~2 – 4 L/hr
Blood Flow Rate \((Q_b)\)

- 200 ml/min is the usual blood flow rate
  - When using heparin, a low flow rate promotes coagulation of the system
  - When using citrate, a low flow rate is convenient
  - It allows to keep a low ionized calcium (bound to citrate) within the filter
Ultrafiltration (UFR)

• Rate of fluid removal from the patient (ml/hr)
• UF orders can mean different things in different protocols:
  – Net 24 hour net fluid balance + desired patient fluid removal
    – Patients are too variable to predict 24 hour goals
  – Hourly desired patient fluid management
    – The nurse measures patient I and O every hour, and sets the difference as the fluid to be removed during the next hour PLUS the ordered NET fluid removal rate.
How is UF ordered in different protocols?

- Total input: 5.2 L/day (pressors, TPN, antibiotics, etc)
- Urine output: 200 ml/day
- Desired negative balance in the next 24 hrs: Negative 1 L

- **24 hour protocols**
  - \( \frac{(5.2-0.2+1)}{24} = 250 \text{ ml/hour} \)
  - \( \frac{1000}{24} = 50 \text{ ml/hr} \)

- **Hourly protocol: CRRT as a continuous volume regulation device**
  - Input during last hour: 216 ml
  - Output during last hour: 8 ml
  - Desired hourly loss: -100 ml/hour
  - Calculated necessary NET fluid removal next hour: \( (216+100)-8 = 308 \text{ ml} \)
Filtration Fraction (FF)

- Measures how much the plasma entering the filter is concentrated by ultrafiltration

\[ \text{FF} = \frac{1 - \text{Prot}_\text{IN}}{\text{Prot}_\text{OUT}} \]

- Estimated as

\[ \text{FF} = \frac{Q_{\text{UF}}}{Q_P} = \frac{Q_{\text{UF}}}{Q_B(1-HCT) + Q_{\text{PRE}}} \]

- Practically,

\[ \text{CR} = \frac{Q_{\text{POST}} + Q_{\text{UF}}^{\text{NET}}}{Q_B} \]

SHOULD BE KEPT BELOW 25% TO REDUCE HEMOCONCENTRATION AND PROTEIN-MEMBRANE INTERACTION
Let’s use what we just learned...

- 44 yr. old male baseline Cr 1.2 mg/dl, with a history of B-cell lymphoma is started on chemotherapy and develops tumor-lysis syndrome, septic shock and AKI. Admission weight: 100 Kg

<table>
<thead>
<tr>
<th>TIME</th>
<th>Sodium (mEq/L)</th>
<th>Potassium (mEq/L)</th>
<th>Chloride (mEq/L)</th>
<th>Bicarbonate (mEq/L)</th>
<th>Blood Urea N (mg/dl)</th>
<th>Creatinine (mg/dl)</th>
<th>Glucose (mg/dl)</th>
<th>Htc (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>23:00</td>
<td>132</td>
<td>6.4</td>
<td>98</td>
<td>14</td>
<td>54</td>
<td>5.6</td>
<td>122</td>
<td>30</td>
</tr>
</tbody>
</table>

- Liver function normal
- Last night, the fellow on call started the patient on CRRT.
## Components of the prescription

<table>
<thead>
<tr>
<th>COMPONENT</th>
<th>23:00 pm</th>
<th>07:00 am</th>
</tr>
</thead>
<tbody>
<tr>
<td>MODALITY</td>
<td>CVVH</td>
<td></td>
</tr>
<tr>
<td>BLOOD FLOW RATE $Q_B$</td>
<td>200 ml/min</td>
<td></td>
</tr>
<tr>
<td>ULTRAFILTRATION RATE $Q_{UF}$</td>
<td>Zero</td>
<td></td>
</tr>
<tr>
<td>REPLACEMENT FLUID $Q_{RF}$</td>
<td>BGK 4/0 2200 ml/hour</td>
<td></td>
</tr>
<tr>
<td>TYPE OF DILUTION</td>
<td>2000 pre- and 200 post-filter</td>
<td></td>
</tr>
<tr>
<td>ANTICOAGULATION</td>
<td>Citrate</td>
<td></td>
</tr>
</tbody>
</table>
Is this a good prescription?

• Strengths:
  • Used a protocol
  • Anticoagulation to prevent clotting
Next morning

• The patient has been on CRRT for the last 12 hrs. You see the patient in the morning.

<table>
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<tr>
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<th>Sodium (mEq/L)</th>
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<td>30</td>
</tr>
<tr>
<td>07:00</td>
<td>132</td>
<td>6.8</td>
<td>98</td>
<td>16</td>
<td>56</td>
<td>4.8</td>
<td>96</td>
<td>29</td>
</tr>
</tbody>
</table>

• What is happening with the patient?

• **Make the needed adjustments to the treatment.**
Learning Points

• Was there treatment downtime?
• What is the prescribed dose?
• What is the delivered dose?
• What is the composition of the replacement and dialysate fluid?

• What changes would you like to make?
Dose of therapy

• **Prescribed dose**: Approximates the effluent rate normalized to the patient’s weight

• Prescribed dose =
  - **CVVH**: Effluent flow rate = $Q_{rf} + \text{Ultrafiltration}$
  - **CVVHDF**: Effluent flow rate + Dialysis flow rate + Ultrafiltration ($Q_{rf} + Q_{d} + \text{patient fluid removed}$) in ml/h/Kg BW
KDIGO Guidelines

• Recommended dose: 20-25 ml/Kg/h

• To achieve this delivered dose, it is generally necessary to prescribe in the range of 25–30 ml/kg/h, and to minimize interruptions in CRRT.
Dose Calculations

**CVVH**

**POST-DILUTION**

Dose = \( Q_e \times SC \)

Where \( SC = \frac{C_e}{C_b} = 1 \) and \( Q_e = Q_{rf} + UF \)

**PRE-DILUTION**

Dose = \( Q_e \times \left( \frac{Q_{bw}}{Q_{bw} + Q_{preRF}} \right) \)

**CVVHD**

Dose = \( Q_d \times SC \)

**CVVHDF**

**POST-DILUTION**

Dose = \( Q_e \times SC \)

Where \( Q_e = Q_d + Q_{rf} + UF \)

**PRE-DILUTION**

Dose = \( (Q_d + [(Q_{rf} + UF) \times \left( \frac{Q_{bw}}{Q_{bw} + Q_{preRF}} \right)]) \)
Estimated delivered dose:
Predilution systems are a bit more complicated

• Prescribed dose * dilution factor.
• Dilution factor = \( \frac{Q_{bw}}{Q_{bw} + Q_{preRF}} \)
  
  • \( Q_{bw} \): Rate of blood water flow. \( Q_{b}(1-Hct) \)
  • \( Q_{preRF} \): Rate of prefilter replacement fluid

• Dilution factor = \( \frac{[Q_{b}(1-Htc)]}{[Q_{b}(1-Htc)] + Q_{preRF}} \)
Back to our patient

• Was there treatment downtime?
  • Ask the nurse or look at the run sheet; TOUCH THE SCREEN!!!

• What is the prescribed dose?
  • Calculate: 2200/100= 22 ml/kg/hr
  • Where can you find in on the machine?

• What is the \textit{delivered} dose?
  • 22 * (0.8)= 17.6ml/kg/h

• What is the composition of the replacement and dialysate fluid?
  • K concentration: 4 meq/l
You change the prescription from this one...

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<td>Zero</td>
<td>Zero</td>
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<tr>
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<td>BGK 4/0 2200 ml/hour</td>
<td>BGK 4/0 2700 ml/hour</td>
</tr>
<tr>
<td>TYPE OF DILUTION</td>
<td>2000 ml/h pre-filter</td>
<td>200 ml/h pre-filter</td>
</tr>
<tr>
<td></td>
<td>200 ml/h post-filter</td>
<td>2500 ml/h post-filter</td>
</tr>
<tr>
<td>ANTICOAGULATION</td>
<td>Citrate</td>
<td>Citrate</td>
</tr>
<tr>
<td>Prescribed Dose</td>
<td>22 ml/Kg/h</td>
<td></td>
</tr>
<tr>
<td>Delivered Dose</td>
<td>17 ml/Kg/h</td>
<td></td>
</tr>
</tbody>
</table>
Components of the new prescription

- Type of anticoagulation: Citrate
- Treatment Modality: CVVH
- Blood flow rate: 200ml/min
- Ultrafiltration rate: 0 ml/hr
- Replacement fluid: BGK 4/0, 2700 ml/hr
- Type of dilution: 200 ml pre-filter, 2500 ml post-filter
- Labs: BMP, systemic and post cell ionized calcium
To this new prescription...

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<tr>
<td>Prescribed Dose</td>
<td>22 ml/Kg/h</td>
<td>27 ml/Kg/h</td>
</tr>
<tr>
<td>Delivered Dose</td>
<td>17 ml/Kg/h</td>
<td>26.9 ml/Kg/h</td>
</tr>
</tbody>
</table>
Is this a good CRRT order?

- Anticoagulation: uses regional citrate anticoagulation
- Modality: CVVH post filter
- Prescribed Dose: 2700/100 = 27 ml/kg/h
- Delivered Dose: 26.9 ml/Kg/h

- Appears to be good CRRT prescription!

- But the nurse is upset: she tells you that the filter clotted 6 hrs. after starting the treatment, and has clotted for the second time in the last 12 hrs.
Filtration Fraction

That mysterious, scary, silly math formula...

\[ \frac{Q_{RF}}{Q_{UF}} \]

**WHAT FRACTION OF THE FLUID THAT ENTERS THE FILTER (PLASMA + REPLACEMENT FLUID) IS LOST BY FILTRATION? \( \rightarrow \) HOW CONCENTRATED DOES PLASMA BECOME?**
Filtration Fraction

\[ FF = \frac{(Q_{\text{eff}} - Q_{d})}{(Q_{bw} + Q_{rf(pre)})} \times 100 \]

- \( Q_{\text{eff}} \): Effluent flow rate
- \( Q_{d} \): Dialysate flow rate
- \( Q_{bw} \): \( Q_{b} \) (1-Hct)
  - \( Q_{b} \): Blood flow per hour
- \( Q_{rf(pre)} \): Pre-filter replacement fluid

**CVVH**

\[ FF = \frac{Q_{e}}{Q_{b} \cdot (1-Htc) + Q_{RFpre}} \]

**CVVHD**

\[ FF = \frac{Q_{e} - Q_{d}}{Q_{b} \cdot (1-Htc)} \]

**CVVHDF**

\[ FF = \frac{Q_{e} - Q_{d}}{Q_{b} \cdot (1-Htc) + Q_{RFpre}} \]
Can I find this on the machine?

- You can find it on the screen on good machines
- Make sure the nurse has entered the Hct for that day
Filtration Fraction

• $\text{FF} = \frac{Q_{\text{eff}}}{Q_{bw} + Q_{rf(\text{pre})}} \times 100$

• $Q_{\text{eff}}$: 2700 ml/h

• $Q_{bw}$: 12000 (0.70) = 8400 ml

• $\text{FF} = \frac{2700}{8400 + 200} \times 100$

• $\text{FF} = 31\%$ !!!

• What are your options?
  - Redistribute the pre and post RF
  - Increase blood flow

• GOAL: FF <25%
Filtration Fraction

• Keep FF below 25%.

• How do I decrease filtration fraction?
  • Increase blood flow rate.
  • Change replacement to pre-filter fluid.
CONCLUSIONS

• Know the basics
• Review the prescription: Do your own calculations
• **Touch** the machine; know where goes what
• Adjust the treatment to the moment-to-moment patient needs
• Be part of the team