CRRT in Pediatrics: Indications, Techniques & Outcome

Timothy E. Bunchman
Pediatric Nephrology & Transplantation
Grand Rapids, MI

Overview
(Please interrupt me at any time)

- Access
- Solutions
- Anticoagulation
- Prescription
- Nutrition and Drug Clearance
- Outcome
Convective Clearance
To increase clearance by convection, increase ultrafiltration rate (will require more replacement fluids)

Diffusive Clearance
To increase clearance by diffusion, increase dialysate flow rate
### Sieving Coefficients

<table>
<thead>
<tr>
<th>Solute (MW)</th>
<th>Convective Coefficient</th>
<th>Diffusion Coefficient</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urea (60)</td>
<td>1.01 ± 0.05</td>
<td>1.01 ± 0.07</td>
</tr>
<tr>
<td>Creatinine (113)</td>
<td>1.00 ± 0.09</td>
<td>1.01 ± 0.06</td>
</tr>
<tr>
<td>Uric Acid (168)</td>
<td>1.01 ± 0.04</td>
<td>0.97 ± 0.04*</td>
</tr>
<tr>
<td>Vancomycin (1448)</td>
<td>0.84 ± 0.10</td>
<td>0.74 ± 0.04**</td>
</tr>
<tr>
<td>Calcium (protein bound)</td>
<td>0.67 ± 0.1</td>
<td>0.61 ± 0.07</td>
</tr>
<tr>
<td>Cytokines (large)</td>
<td>adsorbed</td>
<td>minimal clearance</td>
</tr>
</tbody>
</table>

*P<0.05  **P<0.01

---

### Comparison of Urea Clearance: CVVH vs CVVHD

(Maxvold et al, Crit Care med. 2000 Apr;28(4):1161-5)

<table>
<thead>
<tr>
<th>Urea Clearance (mls/min/1.73 m²)</th>
<th>CVVH</th>
<th>CVVHD</th>
<th>p = NS</th>
</tr>
</thead>
</table>

[BFR = 4 mls/kg/min](#)  
[FRF/Dx FR = 2 l/1.73 m²/hr](#)  
[SAM = 0.3 m²](#)
Vascular Access

Figure 2: Mean Patient Weight vs Catheter Size


<table>
<thead>
<tr>
<th>Catheter Size*</th>
<th>Number of Patients</th>
<th>% Survival at 60 hours *</th>
</tr>
</thead>
<tbody>
<tr>
<td>5</td>
<td>6</td>
<td>0 (p &lt;0.0000)</td>
</tr>
<tr>
<td>7</td>
<td>57</td>
<td>43 (p &lt; 0.002)</td>
</tr>
<tr>
<td>8</td>
<td>65</td>
<td>55 (NS)</td>
</tr>
<tr>
<td>9</td>
<td>35</td>
<td>51 (p &lt; 0.002)</td>
</tr>
<tr>
<td>10</td>
<td>46</td>
<td>53 (NS)</td>
</tr>
<tr>
<td>11.5</td>
<td>71</td>
<td>57 (NS)</td>
</tr>
<tr>
<td>12.5</td>
<td>64</td>
<td>60 (NS)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Insertion Site†</th>
<th>Number of Patients</th>
<th>% Survival at 60 hours *</th>
</tr>
</thead>
<tbody>
<tr>
<td>Internal Jugular</td>
<td>58</td>
<td>60 (p &lt; 0.05)</td>
</tr>
<tr>
<td>Subclavian</td>
<td>31</td>
<td>51 (NS)</td>
</tr>
<tr>
<td>Femoral</td>
<td>260</td>
<td>52 (NS)</td>
</tr>
</tbody>
</table>

Vascular Access

Survival favors IJ Location (p< 0.05)

Catheter proximity

- Inadvertent removal of infusions
- Circuit clotting with platelet transfusions
- Entraining calcium into the circuit
Vascular Access

Note the relationship of the line tips.

<table>
<thead>
<tr>
<th>PATIENT SIZE</th>
<th>CATHETER SIZE &amp; SOURCE</th>
<th>SITE OF INSERTION</th>
</tr>
</thead>
<tbody>
<tr>
<td>NEONATE</td>
<td>Dual-Lumen 7.0 French</td>
<td>Femoral vein</td>
</tr>
<tr>
<td></td>
<td>(COOK/MEDCOMP)</td>
<td></td>
</tr>
<tr>
<td>3-6 KG</td>
<td>Dual-Lumen 7.0 French</td>
<td>Internal/External-Jugular,</td>
</tr>
<tr>
<td></td>
<td>(COOK/MEDCOMP)</td>
<td>Subclavian or Femoral vein</td>
</tr>
<tr>
<td>6-30 KG</td>
<td>Dual-Lumen 8.0 French</td>
<td>Internal/External-Jugular,</td>
</tr>
<tr>
<td></td>
<td>(KENDALL/ARROW)</td>
<td>Subclavian or Femoral vein</td>
</tr>
<tr>
<td>&gt;15-KG</td>
<td>Dual-Lumen 9.0 French</td>
<td>Internal/External-Jugular,</td>
</tr>
<tr>
<td></td>
<td>(MEDCOMP)</td>
<td>Subclavian or Femoral vein</td>
</tr>
<tr>
<td>&gt;30 KG</td>
<td>Dual-Lumen 10.0 French</td>
<td>Internal/External-Jugular,</td>
</tr>
<tr>
<td></td>
<td>(KENDALL, ARROW)</td>
<td>Subclavian or Femoral vein</td>
</tr>
<tr>
<td>&gt;30 KG</td>
<td>Triple-Lumen 12 French</td>
<td>Internal/External-Jugular,</td>
</tr>
<tr>
<td></td>
<td>(KENDALL/ARROW)</td>
<td>Subclavian or Femoral vein</td>
</tr>
</tbody>
</table>
**Triple vs Dual in Peds RRT**

- 5 year experience with Pediatric CRRT using the “pigtail” as the CaCl replacement
- If not for citrate CRRT also serves as an added central line for other med/TPN infusion
What staff at bedside has sufficient central access?

..I’ll tell you where to stick this next drug...

Options for CRRT Solutions

- Peritoneal dialysate: **NO**
- Pre-made IV solutions: **MAYBE**
  - Saline, Lactated Ringers
- Multi-bag systems: **UNNECESSARY**
- Custom-made solutions: **NO**
  - Local pharmacy; outsource
- Commercially available CRRT solutions
Commercial Solutions for CRRT: Several Companies, Multiple Options

- **Previously**: limited options
  - No bicarbonate-based solutions
  - US regulations re: “drug” vs. “device”

- **Currently**: multiple manufacturers each offering a variety of formulations
  - Bicarbonate as primary or only base

- **The Choice**: may depend on local policy, vendors, economic pressures

---

### CVVH: Bicarbonate vs Lactate


<table>
<thead>
<tr>
<th></th>
<th>Bicarbonate (n = 61)</th>
<th>Lactate (n = 56)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Plasma Bicarbonate (mmol/l)</td>
<td>23.7 ± 0.4</td>
<td>21.8 ± 0.5</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>Blood Lactate (mg/dl)</td>
<td>17.4 ± 8.5</td>
<td>28.7 ± 10.4</td>
<td>&lt; 0.05</td>
</tr>
<tr>
<td>IV Bicarb given over 24 hrs</td>
<td>13 ± 7</td>
<td>68 ± 39</td>
<td>&lt; 0.01</td>
</tr>
</tbody>
</table>
Evaluation of Errors in Preparation of CRRT Solutions

- Survey of 3 Pediatric Listserves:
  - Pediatric Critical Care, Nephrology, CRRT
- 16/31 programs reported solution compounding errors
- Consequences of improper solutions
  - 2 deaths
  - 1 non-lethal cardiac arrest
  - 6 seizures (hypo/hypernatremia)
  - 7 without complications

Barletta et al, Pediatr Nephrol. 21(6):842-5, 2006 Jun
Normocarb HF (DSI)

- Bicarbonate buffered
- Concentrate must be compounded
- Final volume 3.24 liters (240ml concentrate added to 3 L bag)
- 2 ionic formulations
  - Normocarb HF 25
  - Normocarb HF 35

Chemical Content of Normocarb HF

<table>
<thead>
<tr>
<th>Ion (mEq/L)</th>
<th>HF 25</th>
<th>HF 35</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sodium</td>
<td>140</td>
<td>140</td>
</tr>
<tr>
<td>Potassium</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Chloride</td>
<td>116.5</td>
<td>106.5</td>
</tr>
<tr>
<td>Bicarbonate</td>
<td>25</td>
<td>35</td>
</tr>
<tr>
<td>Calcium</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Magnesium</td>
<td>1.5</td>
<td>1.5</td>
</tr>
</tbody>
</table>
PrismaSate (Gambro)

- Bicarbonate buffered
- Small amount of lactate
- 5 liter bag
- 2 compartments to prevent precipitation
- Six ionic formulations

### Chemical Content of PrismaSate

<table>
<thead>
<tr>
<th>Ion (mEq/L)</th>
<th>BK0/3.5</th>
<th>BGK2/0</th>
<th>BGK4/0/1.2</th>
<th>BGK4/2.5</th>
<th>B22GK4/0</th>
<th>BK2/0</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sodium</td>
<td>140</td>
<td>140</td>
<td>140</td>
<td>140</td>
<td>140</td>
<td>140</td>
</tr>
<tr>
<td>Potassium</td>
<td>0</td>
<td>2</td>
<td>4</td>
<td>4</td>
<td>4</td>
<td>2</td>
</tr>
<tr>
<td>Chloride</td>
<td>109.5</td>
<td>108</td>
<td>110.2</td>
<td>113</td>
<td>120.5</td>
<td>108</td>
</tr>
<tr>
<td>Bicarb</td>
<td>32</td>
<td>32</td>
<td>32</td>
<td>32</td>
<td>22</td>
<td>32</td>
</tr>
<tr>
<td>Lactate</td>
<td>3</td>
<td>3</td>
<td>3</td>
<td>3</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Calcium</td>
<td>3.5</td>
<td>0</td>
<td>0</td>
<td>2.5</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Magnesium</td>
<td>1</td>
<td>1</td>
<td>1.2</td>
<td>1.5</td>
<td>1.5</td>
<td>1</td>
</tr>
<tr>
<td>Gluc(mg/dL)</td>
<td>0</td>
<td>110</td>
<td>110</td>
<td>110</td>
<td>110</td>
<td>0</td>
</tr>
</tbody>
</table>
PrismaSol (Gambro)

- Bicarbonate buffered
- Small amount of lactate
- 5 liter bag
- 2 compartments to prevent precipitation
- Seven ionic formulations

Chemical Content of PrismaSol

<table>
<thead>
<tr>
<th>Ion (mEq/L)</th>
<th>BK 0/3.5</th>
<th>BGK 2/0</th>
<th>BGK 2/3.5</th>
<th>BGK 4/2.5</th>
<th>BGK 4/0</th>
<th>BGK 0/2.5</th>
<th>BK 0/0</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sodium</td>
<td>140</td>
<td>140</td>
<td>140</td>
<td>140</td>
<td>140</td>
<td>140</td>
<td>140</td>
</tr>
<tr>
<td>Potassium</td>
<td>0</td>
<td>2</td>
<td>2</td>
<td>4</td>
<td>4</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Chloride</td>
<td>109.5</td>
<td>108</td>
<td>111.5</td>
<td>113</td>
<td>110.5</td>
<td>109</td>
<td>106.5</td>
</tr>
<tr>
<td>Bicarb</td>
<td>32</td>
<td>32</td>
<td>32</td>
<td>32</td>
<td>32</td>
<td>32</td>
<td>32</td>
</tr>
<tr>
<td>Lactate</td>
<td>3</td>
<td>3</td>
<td>3</td>
<td>3</td>
<td>3</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Calcium</td>
<td>3.5</td>
<td>3.5</td>
<td>2.5</td>
<td>2.5</td>
<td>0</td>
<td>2.5</td>
<td>0</td>
</tr>
<tr>
<td>Magnesium</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1.5</td>
<td>1.5</td>
<td>1.5</td>
<td>1.5</td>
</tr>
<tr>
<td>Gluc(mg/dL)</td>
<td>0</td>
<td>100</td>
<td>100</td>
<td>100</td>
<td>100</td>
<td>100</td>
<td>0</td>
</tr>
</tbody>
</table>
Anticoagulation and Solutions

May need to consider Ca\textsuperscript{++} content if using citrate for anticoagulation

<table>
<thead>
<tr>
<th>Solution</th>
<th>Calcium?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normocarb HF</td>
<td>No</td>
</tr>
<tr>
<td>Accusol</td>
<td>4 Yes; 1 No</td>
</tr>
<tr>
<td>PrismaSate</td>
<td>2 Yes; 4 No</td>
</tr>
<tr>
<td>PrismaSol</td>
<td>4 Yes; 3 No</td>
</tr>
<tr>
<td>Duosol</td>
<td>2 Yes; 1 No</td>
</tr>
<tr>
<td>NxStage PureFlow</td>
<td>6 Yes; 2 No</td>
</tr>
</tbody>
</table>

FDA Approval Status of CRRT Solutions

<table>
<thead>
<tr>
<th>Solution</th>
<th>FDA Label</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normocarb HF</td>
<td>Replacement</td>
</tr>
<tr>
<td>PrismaSate</td>
<td>Dialysate</td>
</tr>
<tr>
<td>PrismaSol</td>
<td>Replacement</td>
</tr>
<tr>
<td>Accusol</td>
<td>Dialysate</td>
</tr>
<tr>
<td>Duosol</td>
<td>Dialysate</td>
</tr>
<tr>
<td>NxStage PureFlow</td>
<td>Dialysate</td>
</tr>
</tbody>
</table>
Once you have the solutions what do you do with them?

- Prescriptions
  - May depend upon anticoagulation protocols
    - Citrate
    - Heparin
    - None (don’t do this)
- **Is there a optimal rate of replacement fluid?**
- **Is that an optimal rate of dialysate fluid?**

Sites of Thrombus Formation

- Any blood surface interface
  - Hemofilter
  - Bubble trap
  - Catheter
  - Areas of turbulence resistance
    - Luer lock connections / 3 way stopcocks
Sites of Action of Heparin

- **Contact Phase (intrinsic)**
  - XII activation
  - XI IX

- **Tissue Factor (extrinsic)**
  - TF:VIIa
  - platelets / monocytes / macrophages

- **UF HEPARIN**
  - LMWH
  - prothrombin
  - thrombin
  - fibrinogen
  - clot

Heparin Protocols
Benefit and Risks

- **Benefits**
  - Heparin infusion prior to filter with post filter ACT measurement
  - Bolus with 10-20 units/kg Infuse at 10-20 units/kg/hr
  - Adjust post filter ACT 180-200 secs

- **Risks**
  - Patient Bleeding
  - Unable to inhibit clot bound thrombin
  - Ongoing thrombin generation
  - Activates - damages platelets / thrombocytopenia
Effect of anticoagulation on blood-membrane interactions


Sites of Action of Citrate

Contact Phase (intrinsic)
XII activation
XI IX Ca^{++}

Tissue Factor (extrinsic)
TF:VIIa
platelets / monocytes / macrophages

X

Xa

prothrombin

THROMBIN Ca^{++}

fibrinogen

CLOT

CITRATE

Citrate

VIIIa

Ca^{++}

platelets
Solutions needed for Citrate Protocol
(Pediatric Nephrology 2002 17:150-154)

- ACD-A (Baxter, Deerfield, IL)
  - 1000 cc bag, industry standard
- CaCl 8 gms/1 liter of NS
  - pharmacy made
- Normocarb Dialysis/Replacement Soln
  (Dialysis Soln Inc)
  - Can be prepared at bedside or pharmacy
- Normal Saline

Preprinted Orders

**Pharmacy Orders**

1. Normocarb-Replacement Dialysate
   - KCl ________ mEq/L (0-2 mEq/L)
   - KPO4 ________ mEq/L (0-2 mEq/L)
   - (total K not to exceed 5 meq/l)

2. CaCl2 8000mg in 1000ml of 0.9 NaCl
   (infuse in central line other than Hemofiltration access)

3. ACD-A
   - (This needs to be administered on the prefiltter access of the hemofiltration access.)

4. If Replacement fluids are needed:
   - _______Normocarb
   - _______Normal Saline
   - Add to NS/Normocarb:
     - KCl ________ mEq/l
     - KPO4 ________ mEq/l

**Hemofiltration Orders**

- Blood Flow Rate (BFR) ________ ml/min
- Replacement Rate ________ ml/hr
- Net ultrafiltration rate ________ ml/hr
- ACD-A Rate ________ ml/hr
- CaCl2 Rate ________ ml/hr
- Dialysate Rate ________ ml/hr

**Recommendations**

- Blood Flow Rate (BFR) ________ ml/min
- Replacement Rate ________ ml/hr
- Net ultrafiltration rate ________ ml/hr
- ACD-A Rate ________ ml/hr
- CaCl2 Rate ________ ml/hr
- Dialysate Rate ________ ml/hr

2-5ml/kg/min
2000ml/1.73m2/hr
Patient net loss 1-2ml/kg/hr
Start 1.5 x BFR
Start at 0.4 x ACD-A Rate
**Citrate: Technical Considerations**

- Measure patient and system iCa in 2 hours then at 6 hr increments
- Standing protocol on nursing flow sheet adjusted by bedside ICU nurse
- Pre-filter infusion of Citrate
  - Aim for system iCa of 0.25-0.4 mmol/l
    - Adjust for levels
- Systemic calcium infusion
  - Aim for patient iCa of 1.1-1.3 mmol/l
    - Adjust for levels

ACD-A/Normocarb Wt range 2.8 kg – 115 kg
- Average life of circuit on citrate 72 hrs (range 24-143 hrs)
Orders for citrate and Ca rates
(adapted for N Gibney)

<table>
<thead>
<tr>
<th>CITRATE INFUSION SLIDING SCALE</th>
<th>CALCIUM INFUSION SLIDING SCALE</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>PRISMA iCa++</strong></td>
<td><strong>INFUSION ADJUSTMENT</strong></td>
</tr>
<tr>
<td>&gt; 20 kg</td>
<td>&lt; 20 kg</td>
</tr>
<tr>
<td>&lt; 0.25</td>
<td>↓ by 10 ml/hr</td>
</tr>
<tr>
<td>0.25 – 0.4 (Optimum range)</td>
<td>No adjustment</td>
</tr>
<tr>
<td>&gt; 0.5</td>
<td>↑ by 20 ml/hr</td>
</tr>
</tbody>
</table>

**NOTIFY MD IF CITRATE INF. RATE > 200 ML/HR**

**NOTIFY MD IF CALCIUM INF. RATE > 200 ML/HR**

Complications of Citrate:
Metabolic alkalosis

- Metabolic alkalosis due to
  - 1 mmol of citrate converts to 3 mmol of HCO3
  - Normocarb 35 meq/l HCO3
  - NG losses
  - TPN with acetate component
Complications of Citrate: Rx of Metabolic alkalosis

- Rx Metabolic alkalosis by
  - Normocarb 35 meq/l HCO3
    - Decrease bicarbonate dialysis rate and replace at the same rate with NS (pH 5) to allow for the total solution exposure to be identical (ie no change in solute clearance) yet this will give less HCO3 exposure and an acid replacement
  - NG losses
    - Replace with ½-2/3 NS
  - TPN with acetate component
    - Use high Cl ratio

Metabolic Alkalosis resolved

- Since we have change to Normocarb 25 (less bicarbonate) we no longer see metabolic alkalosis
Complications of Citrate: “Citrate Lock”

- Seen with rising total calcium with dropping patient ionized calcium
  - Essentially delivery of citrate exceeds hepatic metabolism and CRRT clearance
- Rx of “citrate lock”
  - Decrease or stop citrate for 15-30 mins then restart at 70% of prior rate

Metabolic alkalosis

- No longer a clinical issue
- Since we moved to Normocarb HF 25 we no longer have this issue
Complications

- Hemodynamic
- Thermal
  - < 25 kg may mask fever
- Nutritional

Factors effecting hemodynamics-1

- Volume status of patient
  - Excessive Ultrafiltration
    - over aggressive ultrafiltration prescription
    - error of ultrafiltration monitoring
  - Inadequate replacement
  - Accidental disconnect
RESULTS
(Kudelka et al, CRRT 1997)

Trilogy Pump: Accuracy over Range of Flow Rates

Ultrafiltration accuracy
2.8 kg infant on PRISMA

Ultrafiltration accuracy
2.8 kg infant on PRISMA

Prescription
BFR 30 mls/min
Dx FR 300 mls/hr

Hour of Therapy
Factors effecting hemodynamics-2

- Vasopressor Enhancement
  - Enhancement of vasopressor effectiveness will occur with improvement of acidosis
  - Other agents (e.g. atracurium) is metabolism is pH dependent therefore drug clearance in general is effected with pH change

Factors effecting hemodynamics-3

- Vasopressor clearance
  - Due to proximity of infusion
    - recirculation effecting delivery and clearance
    - be aware of infusing vasopressor agents in immediate proximity to the "arterial" port of the hemofiltration machine
Factors effecting hemodynamics

- Vasopressor clearance
  - Vasopressor agents all have in common a small molecular weight and minimal protein binding
    - Epinephrine
    - Norepinephrine
    - Dopamine
    - Dobutamine

Factors effecting hemodynamics-4

- Circuit reaction
  - Circuit compliance
  - Circuit extracorporeal volume
    - more or a problem in pediatrics

- Membrane reaction
  - Bradykinin release syndrome
Membranes Compatibility

- Complement activated reaction to blood/hemodialysis membrane interaction that causes
  - leukopenia
  - thrombocytopenia
  - increased Alveolar-Arterial gradient to pulmonary sequestration resulting in hypoxia

- Use of more biocompatible membranes (eg AN-69 polyacrylonitrile) results in less complement activation

- Hemodialysis data has shown that biocompatible membranes (eg AN69 membrane) improve survival in ARF, have a shorter time to recovery of renal function, and is less associated with oliguria
Membranes Compatibility

- AN-69 membranes have been associated with “Bradykinin Release Syndrome” in patients on ACE inhibitors
- This “Bradykinin Release Syndrome” may be pH dependent
- But what about its use in CRRT?
Bradykinin Release Syndrome  
(Brophy et al, AM J Kid Dis, June 2001)

- What is the link
  - Blood bank blood has
    - ICa of 0.04 mmol/l
    - K+ of 40-60 mEq/l
    - pH of 6.4
  - Therefore we hypothesize that if this is a pH blood reaction either we buffer the blood or bypass the membrane

---

Bradykinin Release Syndrome  
(Lacour et al, Nephrologie 13:135-6, 1992)

- Pts all on ACE inhibitors on AN69 membrane for chronic hemodialysis
- 19 pt events rinse with physiologic soln (pH < 5) prior to HD vs 10 pt events rinsed with HCO3 (pH > 5) based solutions prior to HD
- Less BRS noted with HCO3 pre-rinse
Comparison of Total Amino Acid losses: CVVH vs CVVHD

(Maxvold et al, Crit Care Med 2000 Apr;28(4):1161-5)

Amino Acid Losses (g/day/1.73 m²)

<table>
<thead>
<tr>
<th></th>
<th>CVVH</th>
<th>CVVHD</th>
</tr>
</thead>
<tbody>
<tr>
<td>12.4</td>
<td>11.6</td>
<td>NS</td>
</tr>
</tbody>
</table>

Nutritional losses Replacement fluid vs dialysate


- **Study design**
  - Fixed blood flow rate-4 mls/kg/min
  - HF-400 (0.3 m² polysulfone)
  - Cross over for 24 hrs each to pre filter replacement or Dx at 2000 mls/hr/1.73 m²
- **Indirect calorimetry to measure REE**
- **TPN source of nutrition @ 120% of REE**
- **10% Aminosyn II**
  - 1.5 gms/kg/day of protein
Nitrogen losses in CRRT

- 7 adults with MOSF on CVVHDF
- 2.5 gms/kg/day of TPN AA delivered
- 24 hr nitrogen balance, AA clearance, protein catabolism performed

Nitrogen losses in CRRT

- BUNs maintained at 26.6 mmol/l
- Protein catabolic rate avg 235 gms/day
  - (range 107-355 gms)
- Median nitrogen losses 24.3 gms/day
  - (range 21.1-65.5 gms)
- Median nitrogen balance -1.8 gms/day
  - (range -21 to + 17.9 g/day)
D. “Known drug characteristics”

- These recommendations made by panel of nephrologists and pharmacists
- Based on:
  - Protein Binding Information
  - Volume of Distribution
  - Molecular Weight

When in doubt, start here...

- Blood flow, filter type are not very important.
- Find out
  - In CVVHD: Dialysate flow rate (ml/hr)
    - Usually 2 L/1.73m²/hr (33 mL/1.73m²/min)
  - In CVVH: Substitution Fluid rate (ml/hr)
    - Usually 2L/1.73m²/hr (33 mL/1.73m²/min)
  - Add this to patient’s native Cr Cl (ml/1.73m²/min)
  - This is patient’s new Cr Cl → dose accordingly
  - Works in most cases...is good enough for initial estimates. Follow up with drug level monitoring.
### Sieving Coefficient & Protein Binding

<table>
<thead>
<tr>
<th>Drug</th>
<th>Reported SC</th>
<th>Free Fraction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amikacin</td>
<td>0.93</td>
<td>0.95</td>
</tr>
<tr>
<td>Imipenem</td>
<td>0.78</td>
<td>0.80</td>
</tr>
<tr>
<td>Metronidazole</td>
<td>0.84</td>
<td>0.80</td>
</tr>
<tr>
<td>Penicillin</td>
<td>0.68</td>
<td>0.50</td>
</tr>
<tr>
<td>Ranitidine</td>
<td>0.78</td>
<td>0.85</td>
</tr>
<tr>
<td>Vancomycin</td>
<td>0.80</td>
<td>0.90</td>
</tr>
<tr>
<td>Valproic Acid</td>
<td>0.22</td>
<td>0.10</td>
</tr>
</tbody>
</table>

### Drug Prescribing in Renal Failure

- Commonly carried text by pharmacists
- [http://www.kdp-baptist.louisville.edu/renalbook/](http://www.kdp-baptist.louisville.edu/renalbook/)
- New edition to come out soon
- Recommendations for new drugs
- IHD and CRRT recommendations
- Pediatric recommendations
Conclusions:
- Minimum UF rates should be ~ 35 ml/kg/hr
- Survivors had lower BUNs than non-survivors prior to commencement of hemofiltration
Renal Replacement Therapy in the PICU: Pediatric Outcome Literature

- Few pediatric studies (all single center) use a severity of illness measure to evaluate outcomes in pCRRT:
  - Lane noted that mortality was greater after bone marrow transplant who had > 10% fluid overload at the time of HD initiation
  - Faragson\(^3\) found PRISM to be a poor outcome predictor in patients treated with HD
  - Zobel\(^4\) demonstrated that children who received CRRT with worse illness severity by PRISM score had increased mortality

1. Bone Marrow Transplant 13:613-7, 1994
Renal Replacement Therapy in the PICU Pediatric Outcome Literature

- 122 children studied
- No PRISM scores
- Most common diagnosis
  - IHD: primary renal failure
  - CRRT: sepsis
    - 31% survival
- Conclusion: patients who receive CRRT are more ill


Pediatric ARF: Modality and Survival

Ped Neph 16:1067-1071, 2001
Pediatric ARF: Modality and Survival

- Patient survival on pressors (35%) lower than without pressors (89%) (p<0.01)
- Lower survival seen in CRRT than in patients who received HD for all disease states

Ped Neph 16:1067-1071, 2001

Renal Replacement Therapy in the PICU Pediatric Literature

- Lesser % FO at CVVH (D) initiation was associated with improved outcome (p=0.03)
- Lesser % FO at CVVH (D) initiation was also associated with improved outcome when sample was adjusted for severity of illness (p=0.03; multiple regression analysis)

Fluid Overload as a Risk Factor

Foland et al, CCM 2004; 32:1771-1776

N=113

*p=0.02; **p=0.01

Kaplan-Meier survival estimates, by percentage fluid overload category

Foland et al, CCM 2004; 32:1771-1776


Kaplan-Meier survival estimates, by percentage fluid overload category

**BASELINE DEMOGRAPHICS**

- 157 patients entered (1/1/2001 to 5/31/04)
- 116 with MODS (2+ organs involved)
  - Mean age $8.5 \pm 6.8$ years (2 days to 25.1 years)
  - Mean weight $33.7 \pm 25.1$ kg (1.9 to 160 kg)
  - Median 3 ICU days prior to CRRT initiation
    - Range 0 to 103 days
    - 67% less than 7 days

Goldstein SL et al: *Kidney International* 2005

**ppCRRT MODS Data: 116 children**

(From *ppCRRT Ki 2005 Feb;67(2):653-8*)

<table>
<thead>
<tr>
<th>Variable (values mean +/- SD)</th>
<th>Survivors</th>
<th>Non-Survivors</th>
<th>p-value (t-test)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>$8.5 \pm 6.7$</td>
<td>$8.5 \pm 7.2$</td>
<td>NS</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>$34.2 \pm 25.4$</td>
<td>$31.7 \pm 25.8$</td>
<td>NS</td>
</tr>
<tr>
<td>PRISM at ICU Admit</td>
<td>$14.3 \pm 8.2$</td>
<td>$16.2 \pm 9.7$</td>
<td>NS</td>
</tr>
<tr>
<td>PRISM at CRRT Initiation</td>
<td>$13.9 \pm 8.2$</td>
<td>$18.6 \pm 7.2$</td>
<td>$&lt; 0.003$</td>
</tr>
<tr>
<td>CVP at CRRT Initiation</td>
<td>$16.5 \pm 6.1$</td>
<td>$21.2 \pm 6.6$</td>
<td>$&lt; 0.003$</td>
</tr>
<tr>
<td>BUN at CRRT Initiation</td>
<td>$61.1 \pm 41.8$</td>
<td>$67.8 \pm 45.7$</td>
<td>NS</td>
</tr>
<tr>
<td>% FO at CRRT Initiation</td>
<td>$14.2 \pm 15.9$</td>
<td>$25.4 \pm 32.9$</td>
<td>$&lt; 0.03$</td>
</tr>
<tr>
<td>No. of Pressors</td>
<td>$1.4 \pm 1.1$</td>
<td>$1.7 \pm 1.1$</td>
<td>NS</td>
</tr>
</tbody>
</table>
**ARF recovery: Long-term Followup**

- ~ 9% of those who survived RRT progressed on to ESRD
- Markers in a separate 29 children shows evidence of hyperfiltration
  - Increase in microalbuminuria, increase in GFR, evidence of hypertension
  - Askenzai DJ et al, Kid Int 2006, 69:17-19

**Typical Prescription-1**

- Hemofiltration circuit and membrane proportional to the BSA of the child
- BFR 2-8 mls/kg/min (access dependent)
- Replacement or Dialysate flow rate 2000-3000 mls/hr/1.73m²
- Net Fluid removal per hour 1-2 mls/kg/hr based upon hemodynamics of the child
  - DO NOT TAKE MORE THEN THE CHILD WILL GIVE!
Typical Prescription-2

- Maximize nutrition early preferably enteral with protein delivery 2-3 gms/kg/day (we target our BUN ~ 40 mg/dl)
- Monitor medication closely
  - Consider Meds that can be monitored
    - Eg vancomycin, tobramycin
- Anticipate as patient gets better transition to PD or HD
Conclusion

- CRRT in Pediatrics has markedly improved in the past 15 years due to
  - Improved access
  - Improved machinery
  - Improved cooperation between Intensivists and Nephrologist
- Outcome data shows a moderate but true increase in survival

The 6th International Conference on Pediatric Renal Replacement Therapy will be held Rome, Italy April 8-10, 2010

www.pcrrt.com
Timothy.bunchman@devoschildrens.org