Objectives

- Compare and contrast different cases of protein provision in CRRT
- Review types of CRRT and nutritional management
- Evaluate literature surrounding protein requirements in CRRT in childhood
- Discuss potential reasons to consider changing the protein dose in CRRT
Continuous Renal Replacement Therapy (CRRT)

CRRT is used to treat acute kidney injury (AKI) and correct electrolytes/fluids.

CRRT

- Mimics the function of the kidney (24h dialysis)

Indications

A: Acidosis
E: Electrolyte abnormalities
I: Intoxication of medications
O: Overload of fluids
U: Uremia

Ash J, Worrall C. PSAP 6th edition
Protein Requirements Change in CRRT

- Protein requirements significantly change for multiple reasons
  - Essential and non-essential amino acids removed in effluent
  - Hypermetabolic, hypercatabolic:
    - Protein Energy Wasting (PEW)
      - Higher in infants
      - Higher in more critical conditions
Amino Acid Losses in CRRT

- Mostly unpredictable, changes with type of CRRT and condition

Greatest losses in:
- Glutamine (most abundant, low molecular weight) Not supplemented in US
- Proline
- Alanine

Other AAs reported to be conditionally essential in CRRT: Tyrosine, arginine, cysteine, serine, ornithine, citrulline

Amino acid products:
- Trophamine & Travasol

<table>
<thead>
<tr>
<th>Isoleucine</th>
<th>Leucine</th>
<th>Lysine</th>
<th>Methionine</th>
<th>Phenylalanine</th>
<th>Threonine</th>
<th>Tryptophan</th>
<th>Valine</th>
<th>Alanine</th>
<th>Argine</th>
<th>Histidine</th>
<th>Proline</th>
<th>Serine</th>
<th>Taurine</th>
<th>Tyrosine</th>
<th>Glycine</th>
<th>Glutamic Acid</th>
<th>Aspartic acid</th>
<th>Cysteine</th>
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<tbody>
<tr>
<td>820</td>
<td>1400</td>
<td>820</td>
<td>340</td>
<td>480</td>
<td>420</td>
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<td>380</td>
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<td>240</td>
<td>360</td>
<td>500</td>
<td>320</td>
<td>&lt;16</td>
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<tr>
<td>600</td>
<td>730</td>
<td>580</td>
<td>400</td>
<td>560</td>
<td>420</td>
<td>180</td>
<td>580</td>
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<td>1150</td>
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<td>0</td>
<td>40</td>
<td>1030</td>
<td>0</td>
<td>0</td>
<td>0</td>
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</tbody>
</table>
Renal Replacement: Convection, Diffusion, or Both

**Convection:** High-rate diffusion of solutes across a semipermeable membrane

**Diffusion:** Low-rate countercurrent to blood, maximizing solute removal
### Types of CRRT: (CAVH, CVVH, CAVHD, CVVHDF)

<table>
<thead>
<tr>
<th>Type</th>
<th>Description</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>AV</td>
<td>Arteriovenous</td>
<td>Systemic anticoagulation required in CAVH: <em>Citrate</em> calorie intake can be calculated*</td>
</tr>
<tr>
<td>VV</td>
<td>Venovenous</td>
<td>Proven loss is higher in the convection methods. Many non-essential amino acids become conditionally essential, particularly large amounts of <em>glutamine</em> lost in effluent</td>
</tr>
<tr>
<td>HF</td>
<td>Hemofiltration</td>
<td>Slower fluid removal in HD, fluid replacement not needed (less fluid allowed)</td>
</tr>
<tr>
<td>HD</td>
<td>Hemodialysis</td>
<td></td>
</tr>
<tr>
<td>HDF</td>
<td>Hemodiafiltration</td>
<td></td>
</tr>
</tbody>
</table>
Citrate Anticoagulation

Citrate feeds directly into Krebs Cycle, glycolysis, etc.

Citrate anticoagulants include sodium or dextrose.

→ May result in altered calorie needs, insulin resistance.

Total unintentional calories could add up to 1434 kcal/d (propofol, citrate, lactate)  Jonckheer J et. al 2019

Running thin: implications of a heparin shortage

Heparins are the most widely used parenteral anticoagulants. Although it can be extracted from several animal sources, heparin derived from swine is the most common source and currently the only form of heparin used in the USA. Unfortunately, disruptions in manufacturing and distribution of heparin due to the COVID-19 pandemic have led to a shortage, which has been compounded by direct contact with infected animals and via ticks. The virus has also spread to several countries in Europe and Asia; global shifts in infectious disease burden and vector transmission could reflect, in part, detrimental consequences of climate change. The virus causes a number of clinical manifestations ranging from asymptomatic to severe cases requiring medical intervention. The implications of this shortage for public health will be significant and long-lasting.
Example JP

JP is a 14 year old female with T2DM and AML, TXP pt complicated by MDR Pseudomonas bacteremia and skin lesions, hemmorhagic cystitis with clots, ARDS, candidemia and AKI

→ Acute kidney injury and fluid overload. Tx: CRRT

→ Patient requires nutrition support

  Protein provision: PN - 1.1 g/kg/d   EN - 0.4 g/kg/d
Example KD

KD is a 19 year-old female with relapsed anaplastic large cell lymphoma s/p BMT complicated by bacteremia and mucositis presenting with AMS

→ AMS d/t worsening hyperammonemia. Tx: CRRT

→ Patient requires nutrition support

Protein provision: PN 0.4 g/kg/d [dextrose & lipids inc. to limit catabolism]
Patient Case JV

CC
Acute renal failure following liver txp, later readmitted for chest pain d/t NSTEMI in the setting of hypercalcemia

HPI
ARDS requiring mechanical ventilation
Pulmonary edema
Acute renal failure with fluid overload
Hypertriglyceridemia
Steatohepatitis

PMH
Maple Syrup Urine Disease
Insulin-dependent diabetes
Patient Case JV

Scheduled Medications:

ASA 81 mg NJ daily: \(\uparrow K \uparrow Na\)

atovaquone 1,500 mg NJ daily: \(\downarrow Na\)

cefepime 2,000 mg IV q12hr: \(\rightarrow\text{filtered out}\)

collagenase topical 1 appl TOP daily \(\checkmark\)

darbepoetin alfa 30 mcg SQ weekly: \(\rightarrow\text{hypervolemia}\)

heparin flush 20 unit IV Q8hr \(\checkmark\)

hydrocortisone 16 mg IV Q6hr: \(\uparrow Ca \downarrow K \downarrow N\)

omeprazole 20 mg JT daily: \(\uparrow TG\)

tacrolimus 3.2 mg NJ Q12hr: \(\uparrow TG \downarrow Mg \uparrow K\)

valganciclovir 450 mg NJ Q48hr: \(\uparrow K \downarrow Phos\)

vancomycin 125 mg NG QID \(\checkmark\)

Labs:

\[
\begin{array}{ccc}
136 & 98 & 32 H \\
4.98 H & 23 & 1.76 H \\
\end{array}
\]

\[
\begin{array}{ccc}
Ca 12.5 CH & Mg 1.9 \\
Phos 6.8 H & \\
7.1 L & 198 \\
7.22 & 23.4 L
\end{array}
\]
Patient Case JV

Continuous Medications:
- cisatracurium infusion 0.40 mg/kg/hr
- D40W 500 mL + NaCl IVF 20 mEq IV
- dexmedetomidine 0.90 mcg/kg/hr
- epinephrine 0.05 mcg/kg/min
- fentanyl 2.00 mcg/kg/hr
- heparin 10,000 unit
- insulin regular 0.01 unit/kg/hr
- norepinephrine 0.05 mcg/kg/min
- vasopressin 10.00 munit/kg/hr

Labs:
- Ca 12.5 CH
- Mg 1.9
- Phos 6.8 H
- 7.1 L
- 7.22
- 23.4 L
- 136
- 98
- 32 H
- 4.98 H
- 23
- 1.76 H
- 202 H
Patient Case JV

Assessment & Plan:

- Continue sedation regimen
- Vasopressin infusion, weaning epinephrine, continuing norepinephrine
- Follow calcium levels
- Consult ID: empirically on valganciclovir, vancomycin, cefepime, atovaquone
- Monitor tacrolimus levels

<table>
<thead>
<tr>
<th></th>
<th>9/12/19</th>
<th>11/6/19</th>
<th>11/20/19</th>
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</thead>
<tbody>
<tr>
<td>Protein provision (g/kg/d)</td>
<td>1.0</td>
<td>1.5</td>
<td>EN 1.3</td>
</tr>
<tr>
<td>Ca level</td>
<td>6.7</td>
<td>15.0</td>
<td>12.1</td>
</tr>
</tbody>
</table>
The Role of the Pharmacist

- Medication dosing and adjustments for renal replacement and AKI
- Assist RD in calculating PN osmolarity and fluid provision
- Identify medication vs. disease causes of abnormal electrolytes and labs

Adapted from Ash J, Worrall C. PSAP 6th edition
Famotidine Dosing Changes in CRRT

BCH Formulary:

Dosing for Continuous Renal Replacement Therapy

Famotidine 0.5 mg/kg/dose IV q24hr
Antibiotic Dosing Changes in CRRT

- Sepsis, shock, acute kidney injury alters pharmacokinetic parameters
- Low-protein binding, low volume of distribution leads certain medications to be susceptible to filtration by CRRT

Pharmacokinetics and Pharmacodynamics of Extended-Infusion Cefepime in Critically Ill Patients Receiving Continuous Renal Replacement Therapy: A Prospective, Open-Label Study.

Cefepime dosing regimens in critically ill patients receiving continuous renal replacement therapy

We Underdose Antibiotics in Patients on CRRT

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ABSTRACT

Appropriate antibiotic dosing in critically ill, infected, patients receiving continuous renal replacement therapy (CRRT) is crucial to improve patient outcomes. Severe sepsis and septic shock result in changes in pharmacokinetic parameters, including increased volume of distributions and decreased protein binding leading to increased clearance. Consequently, antibiotic dosing regimens should be adjusted to compensate for these changes. Inadequate dosing may result in subtherapeutic concentrations and increased risk of treatment failure and infection-related mortality. Therefore, careful dosing adjustment is essential.
## Professional Recommendations on Protein in CRRT

<table>
<thead>
<tr>
<th>Source</th>
<th>Protein (g/kg)</th>
</tr>
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<tbody>
<tr>
<td><strong>Adults</strong></td>
<td></td>
</tr>
<tr>
<td>ESPEN 2009</td>
<td>1.0 - 1.7</td>
</tr>
<tr>
<td>KDIGO 2012</td>
<td></td>
</tr>
<tr>
<td>ASPEN/SCCM 2016</td>
<td>Up to 2.5</td>
</tr>
<tr>
<td><strong>Pediatrics</strong></td>
<td></td>
</tr>
<tr>
<td>Wong Vega M et. al 2019</td>
<td>At least 2.5</td>
</tr>
<tr>
<td>Jonckheer J et. al 2019</td>
<td>1.5 - 2.5</td>
</tr>
</tbody>
</table>
Is Nitrogen Balance Useful?

- **Nutritional status (weight)** and **albumin** (by the end of treatment) were the only significant nutritional variables related to mortality
  - Significant nutritional variables of 174 PICU patients, ages ranging 4 mo. - 7 years (Europe)
    - *BMC Nephrol. 2012;13:125*

- Studies cited conclude pediatrics may require minimum of 2.5 grams of protein/kg/d in order to maintain a positive nitrogen balance
  - *BMC Nephrol. 2012;13:125*
Is Nitrogen Balance Useful?

- Albumin is not used as a nutritional marker in practice: "negative acute phase protein"

![Figure 1. Characteristic Patterns of Change in Plasma Concentrations of Some Acute-Phase Proteins after a Moderate Inflammatory Stimulus.](image)
Modifying Nutrition Therapy During CRRT (Review)

- **Indirect calorimetry (IC)** preferred for estimating calories (Strong Recommendation)
  - Schofield equations may be used in absence of IC (Weak Recommendation)
- No recommendation can be made for estimating protein needs
  - N-balance formulas not validated in CRRT, unknown removal rate of AAs/urea
- Calories should be adapted to influx and efflux of nutrients (Strong Recommendation)
  - Recommend increasing protein intake 25-100%
Meeting Protein Needs in ECMO

- Utilizing early CRRT alleviates the need for fluid restriction, allowing for prescribing of higher PN volume and improved protein delivery
  - For neonates requiring ECMO on CVVH/CVVHD, compared to group not receiving early CRRT
  - Group not receiving early CRRT, no CRRT?


- ASPEN 2010 Nutrition Support of Neonates Supported with **Extracorporeal Membrane Oxygenation** [ECMO]:
  - Protein target 3 g/kg/d

Key Points

Variations in practice exist, lack of prospective trials, but a lot of information to go by:

When prescribing protein for children on CRRT, consider

Setting the caloric target using REE measure from *indirect calorimetry*

*Increasing protein 25–100%, not exceeding 2.5 g/kg/d for children > 12 mo.*

*Monitoring improvement in weight, observe normalization of serum albumin*

*Account for calories from citrate. Consider loss of glutamine*

*BMC Nephrol. 2012;13:125
BMC Nephrol. 2012;13:125
Questions?
References