Acute Kidney Injury and Continuous Renal Replacement Therapy: The Basics

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AKI: Definition and Diagnosis

• Abrupt reduction in glomerular filtration rate (GFR)

• Differential diagnosis includes:
  – Pre-renal
    • Volume depletion; cardiac dysfunction
  – Renal
    • Vascular; glomerular; tubular; interstitial
  – Post-renal
    • Obstruction
Acute Tubular Necrosis: A Common Cause of AKI

- Ischemic injury
  - Medullary hypoxic gradient
  - High ATP utilization

- Toxic Injury
  - Exogenous
    - Drugs (gentamicin, amphotericin, cisplatin, etc.)
    - Toxins (heavy metals, herbs, radiocontrast, etc.)
  - Endogenous
    - Heme pigments (rhabdomyolysis)
    - Uric acid (tumor lysis syndrome)
Clinical Issues in AKI

• Oliguria
  – Volume overload and hypertension
  – Inability to provide nutrition, therapy

• Diminished renal clearance
  – Electrolyte imbalance
  – Acidosis
  – Uremia
Conservative Management of AKI: Traditional Methods

• Limit fluid intake
  – Can reduce volume overload problems
  – Can’t address issues of nutrition, etc
• Limit input of retained substances
  – Can reduce risks for hyperkalemia, etc
  – Can’t address imbalances from metabolism
• Try not to mess up
• Wait and Hope
Goals of Renal Replacement Therapy (RRT)

- Restore fluid, electrolyte and metabolic balance
- Remove endogenous or exogenous toxins as rapidly as possible
- Permit needed therapy and nutrition
- Limit complications
RRT Options in AKI

- Hemodialysis, Peritoneal Dialysis, CRRT
  - Each has advantages & disadvantages

- Modality choice guided by
  - Patient Characteristics
    - Disease/Symptoms
    - Hemodynamic stability
  - Goals of therapy
    - Fluid removal, electrolyte correction, or both
  - Availability, expertise and cost

CRRT: What is it?

Continuous Renal Replacement Therapy

- **Strict definition:** any form of kidney dialysis therapy that operates continuously, rather than intermittently.
- **More common definition:** continuous hemofiltration technique, often used for hemodynamically unstable patients.
**Diffusion**

- Small molecules diffuse easily
- Larger molecules diffuse slowly
- *Dialysate* required
  - Concentration gradient
  - Faster dialysate flow increases mass transfer
**Convection**

- Small/large molecules move equally
  - Limit is cut-off size of membrane
  - Higher UF rate yields higher convection *but* risk of hypotension
  - May need to *Replace* excess UF volume
Clearance: Convection vs. Diffusion
Advantages of CRRT

• SLOW: Hemodynamically unstable patients may not tolerate rapid ultrafiltration with intermittent hemodialysis

• CONTINUOUS: Can help to preserve metabolic stability in critically ill patients; can maintain fluid balance for oliguric patients who require high daily input (IV medications, parenteral nutrition)
<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
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<tbody>
<tr>
<td>SCUF</td>
<td>Slow Continuous Ultrafiltration</td>
</tr>
<tr>
<td>CVVH</td>
<td>Continuous Veno-Venous Hemofiltration</td>
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<tr>
<td>CVVHD</td>
<td>Continuous Veno-Venous Hemodialysis</td>
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<tr>
<td>CVVHDF</td>
<td>Continuous Veno-Venous Hemodiafiltration</td>
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CRRT Schematic

- SCUF
- CVVH
- CVVHD
- CVVVHDF
Indications for CRRT

Consider CRRT in those patients with oligoanuria and volume overload who also have:

- Sepsis
- Hemodynamic instability or hypotension
- Cardiac dysfunction
- Vascular leak syndrome
- Large daily fluid requirement
- Unusable peritoneal membrane
- Any condition that makes IHD very difficult
Prescribing Pediatric CRRT

- Vascular access
- Hemofilter
- Prime
- Blood pump speed ($Q_B$)
- Anticoagulation
- Ultrafiltration rate
- Infused fluids
  - CVVH: Pre- and/or post-dilutional replacement
  - CVVHD: Counter-current dialysate
  - CVVHDF: Dialysate and replacement fluid
Vascular Access for Pediatric CRRT

- Usually hemodialysis catheter
- Internal jugular, subclavian, femoral positions
- Choose shortest, fattest catheter possible (highest flows with least resistance)
- Consider surgical help for line placement
- Neonates: umbilical lines can be used but are suboptimal
  - Will new neonatal-specific devices allow us to use smaller lines?
Hemofilter for CRRT

- Hemofilter size
  - Volume, porosity
- Membrane material
  - Polysulfone, AN-69, PAES, etc.
- Tubing set – integrated or separate?
- "Open" vs. "closed" systems – do you have a choice?
Priming the Circuit for Pediatric CRRT

- Blood
  - Small patient, large extracorporeal volume

- Albumin
  - Hemodynamic instability
  - Risk of ↓Ca++

- Saline
  - Common default approach

- Self
  - Volume loaded renal failure patient
Choosing $Q_B$ for Pediatric CRRT

Suggested methods to determine blood flow rate ($Q_B$) for CRRT have included:

- Calculation: 3-5 ml/kg min
- Table:
  - 0-10 kg: 25-50ml/min
  - 11-20kg: 80-100ml/min
  - 21-50kg: 100-150ml/min
  - >50kg: 150-180ml/min

The real determinant – **the vascular access**
Anticoagulation for CRRT

- No anticoagulation
- Heparin
- Citrate
- ? other things ?
Heparin Anticoagulation for CRRT

Advantages:
- Long history
- Established protocols
- Intuitive
- It works

Disadvantages:
- Systemic anticoagulation
- Frequent monitoring
- Risk of hemorrhage, HIT
Citrate: A Regional Anticoagulant

![Diagram of citrate and calcium balance](image-url)
Citrate Accumulation Risk with Citrate Anticoagulation

- Excess citrate being delivered to patient
- Exceeds metabolic and filtration rates
- Ionized Ca\(^{++}\) levels may be appropriate
- **Clue**: Patient’s total calcium level rises while ionized Ca\(^{++}\) level stays in range
- **Intervention**: Reduce citrate infusion rate and/or increase removal
Ultrafiltration in Pediatric CRRT

- Choose UF rate to
  - balance input
  - remove excess fluid over time
  - “make room” for IV fluids and nutrition
  - provide solute clearance by convection
- SCUF, CVVHD, post-dilution CVVH: UF rate may be limited by blood flow
- Pre-dilution CVVH: High flow of pre-dilution fluid lessens hemoconcentration, may slow clotting
Infused Fluids for Pediatric CRRT

- SCUF: No infused fluids
- CVVHD: Counter-current dialysate
- CVVH: Pre- and/or post-dilution replacement fluid
- CVVHDF: Dialysate and replacement fluids
Options for CRRT Solutions

- Peritoneal dialysate: ANCIENT HISTORY
- Pre-made IV solutions: MAYBE
  - Saline, Lactated Ringers
- Custom-made solutions: RARELY
- On-line generation: DEVICE-DEPENDENT
- Commercially available CRRT solutions
Rate for Infused Fluid

• Higher rates increase clearance
• Lower rates may simplify electrolyte balance and limit losses
• Equations to help choose rate for fluid:
  – 20-60 ml/kg/hr
  – 2000 – 3000 ml/hr/1.73m²
• May need higher rates to balance citrate delivery
Potential Problems with CRRT

- Bleeding
- Thrombocytopenia
- Thermic loss
- Infection
- Nutritional deficiency
- Electrolyte imbalance
- Bradykinin release syndrome
Bradykinin Release Syndrome

- Mucosal congestion, bronchospasm, hypotension at start of CRRT
- Resolves with discontinuation of CRRT
- Thought to be related to bradykinin release when patient’s blood contacts hemofilter
- Exquisitely pH sensitive
- Associated with AN-69 membrane (negatively charged)
Blood Prime Buffering to Prevent Bradykinin Release Syndrome

- Used in ECMO; can adapt for CRRT
- Add bicarb, calcium to blood prior to priming system
- Addresses pH, hypocalcemia associated with banked PRBCs
Bypass System to Prevent Bradykinin Release Syndrome

Recirculation System to Prevent Bradykinin Release Syndrome

Recirculation Plan:
- \( Q_b = 200 \text{ml/min} \)
- \( Q_d \approx 40 \text{ml/min} \)
- Time 7.5 min

Normalize pH

Normalize \( K^+ \)

Simple Systems to Limit Likelihood of Bradykinin Release Syndrome

- Don’t prime on with blood
- Don’t use the AN-69 membrane
How to Prescribe Pediatric CRRT in 10 Easy Steps

1. Select a machine
2. Choose filter/tubing
3. Determine prime
4. Set $Q_B$
5. Decide on modality
6. Calculate fluid rate
7. Order specific fluids
8. Pick anticoagulation
9. Make fluid balance plan
10. Consider complications
Pediatric CRRT: Things to Remember

• It’s not dialysis
• The “C” stands for “Continuous”
• Lots of things are coming out
• Keep an eye on the balance sheet
• We are providing a service
• There’s a patient in there
• It all starts with the access