Renal Development and Function

Acute Kidney Injury in the Newborn

Renate D. Savich, M.D.
Renal Development and Acute Kidney Injury

- Physiology of the Developing Kidney
- Background and Epidemiology of AKI
- Pathophysiology
- Causes and Differential Diagnosis
- Presentation/Assessment
- Treatment
- Outcome
Physiology of the Developing Kidney

- Renal Development
- Renal Blood Flow
- Glomerular Filtration
- Concentration and Dilution of Urine
Renal Development

- Formation of new nephrons start during 5\textsuperscript{th} week and not complete until 34 weeks (800,000-2.7 million units)
- No new nephron development after term birth
- Nephron development can continue in premature infant postnatally
- HOWEVER, nephron development postnatally in very preterm infants is likely abnormal
  - Decreased nephron number
  - Increased risk of future chronic kidney disease

Carmody Pediatrics 2013;131:11698-1179
Nephron Development

(a) Proximal nephric duct
(b) Branching morphogenesis
(c) Collecting duct
(d) Urinary space

Proximal ureter
Metanephric mesenchyme
Commissure
S-shaped body
Collecting duct
Nephron
Alveolar
arteriole
Glomerulus
Proximal tubule
Distal tubule
Collecting duct
Bowman’s capsule
Glomerular capillaries
Glomerular basement membrane
Podocyte
Mesangial cells
Foot processes
Urinary space
Podocytes
Physiology of the Developing Kidney

• During intrauterine life:
  - Kidneys play minor role in regulating fetal salt and water balance
  - Placenta has primary function to regulate fetal salt and water in utero

• The most important functions of the prenatal kidneys are the formation and excretion of urine to maintain an adequate amount of amniotic fluid.
After Birth

• **Postnatally**- newborn dependent upon kidney to maintain sodium and water balance

• Preterm immature kidneys must take over role that placenta had in utero

• Thus, preterm has higher risk for abnormalities in water and electrolyte homeostasis
Renal Blood Flow

- Absolute renal blood flow (RBF) and the percentage of cardiac output directed to the kidneys increase steadily with advancing gestational age.

- Renal blood flow (% of Cardiac Output)
  - Fetal/Preterm: 2-4
  - Term: 2.5 (birth)- 18 (6 weeks)
  - Adult: 25
Renal Blood Flow Increase Over Lifetime

<table>
<thead>
<tr>
<th>AGE</th>
<th>RBF (mL/min/1.73 m²)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Newborn</strong></td>
<td></td>
</tr>
<tr>
<td>Premature (30-34 weeks)</td>
<td>40 ± 6</td>
</tr>
<tr>
<td>Term</td>
<td>88 ± 4</td>
</tr>
<tr>
<td>1-2 weeks</td>
<td>220 ± 40</td>
</tr>
<tr>
<td>6 months-1 year</td>
<td>352 ± 73</td>
</tr>
<tr>
<td>1-3 years</td>
<td>540 ± 118</td>
</tr>
<tr>
<td>Adult</td>
<td>620 ± 92</td>
</tr>
</tbody>
</table>
Renal Blood Flow

- Low RBF of the fetus due to high renovascular resistance caused by the increased activity of the renin-angiotensin-aldosterone and sympathetic nervous systems.

- Increase in postnatal renal blood flow caused by:
  - Decreasing renal vascular resistance
  - Increasing cardiac output
  - Increasing renal perfusion pressure
Glomerular Filtration Rate

- The glomerular filtration rate (GFR) in the fetal kidney increases steadily with advancing gestational age.

<table>
<thead>
<tr>
<th>AGE</th>
<th>GFR (mL/min/1.73 m²)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Newborn</td>
<td>14 ± 3</td>
</tr>
<tr>
<td>Premature (30-34 weeks)</td>
<td>21 ± 4</td>
</tr>
<tr>
<td>Term</td>
<td>50 ± 10</td>
</tr>
<tr>
<td>1-2 weeks</td>
<td>77 ± 14</td>
</tr>
<tr>
<td>6 months-1 year</td>
<td>96 ± 22</td>
</tr>
<tr>
<td>1-3 years</td>
<td>118 ± 18</td>
</tr>
</tbody>
</table>
Glomerular Filtration

- The achievement of adult GFR may be delayed in preterm infants, especially those with very low birthweights and those with nephrocalcinosis.

- The progressive increase in GFR during the initial weeks of postnatal life primarily results from an increase in glomerular perfusion pressure.
Increase in GFR in Preterm Infants

Vieux Pediatrics 2010;125:e1186-1192
Tubular Reabsorption

- The kidney must REABSORB 99+% of what is filtered through glomerulus
  - Water
  - Na
  - Cl
  - Bicarb
  - K (about 90%)
  - Urea (about 40-50)

- Premature kidneys have trouble with this!
  - Lower GFR and Immature tubules
Urine Production

- Urine production begins at 10 to 12 weeks gestation. A total of 5 mL/hour of urine is produced by 20 weeks’ gestation, which comprises 90% of the amniotic fluid volume by this gestational age.
- The urine production rate continues to increase with gestational age, reaching 50 mL/hour by 40 weeks of gestation.
- Fetal oliguria during the second trimester can lead to pulmonary hypoplasia and oligohydramnios sequence.
Dilution of Urine

- Term newborn infant has full ability to maximally dilute urine in response to a water load, achieving adult values of 50 mOsm/kg.

- Preterm infants are unable to fully dilute their urine, but can achieve urine osmolalities of 70 mOsm/kg.
Dilution of Urine in Preterm Infant

• Response of premature infants to acute water load is limited:
  - low GFR
  - decreased activity of sodium transporters in the diluting segment of the nephron

• The excessive administration of water may place the newborn infant at a high risk for dilutional hyponatremia and hypervolemia.
Urine Concentrating Ability and Tubular Reabsorption of Water and Na

- Water reabsorption and urine concentrating ability are impaired at birth/preterm
  - Leads to (needed) diuresis that typically occurs during the first week after birth
- Tubular resorption of sodium inefficient in very preterm infants
Concentration of Urine

Impaired in Infants-Esp PRETERM

<table>
<thead>
<tr>
<th>AGE</th>
<th>Maximum Urine Osm (mOsm/kg)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Newborn</strong></td>
<td></td>
</tr>
<tr>
<td>Premature (30-34 weeks)</td>
<td>480</td>
</tr>
<tr>
<td>Term</td>
<td>800</td>
</tr>
<tr>
<td>1-2 weeks</td>
<td>900</td>
</tr>
<tr>
<td>6 months-1 year</td>
<td>1200</td>
</tr>
<tr>
<td>1-3 years</td>
<td>1400</td>
</tr>
<tr>
<td>Adult</td>
<td>1400</td>
</tr>
</tbody>
</table>
Sodium Homeostasis in Fetus and Neonate

- $\text{FE}_{\text{Na}}$, is greater in the fetus than in the newborn.
  - 0.75 gestation: 14-15%
  - 0.9 gestation: 11%
  - 145d, near term: 5%

Sodium Excretion Following Birth at 24-40 hrs

Segar, Seminars in Fetal & Neonatal Medicine 22 (2017) 76-82
Na Excretion Differences Persist at Two Weeks

Daily urine sodium excretion

Daily urine sodium losses

Segar, Seminars in Fetal & Neonatal Medicine 22 (2017) 76-82
Creatinine

- Widely used marker for GFR-secreted by tubular epithelium
- In newborn is a reflection of maternal creatinine
- In preterm infants, the creatinine level rises during the first days after birth, is dependent on gestational age, with neonates less than 27 weeks’ gestation having the largest increase in serum creatinine during the first 4 days after birth before gradually decreasing
Term infant-rises first 24-36 hours, decreases and stabilizes about 5 days of age.

Preterm infant-peak at about 2-3 days, stabilizes at about 6 days of age.

<table>
<thead>
<tr>
<th>Gestational Age (wk)</th>
<th>Creatinine (mg/dL) (mcmol/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>23 to 26</td>
<td>0.77 to 1.05 (68.1 to 92.8)</td>
</tr>
<tr>
<td>27 to 29</td>
<td>0.76 to 1.02 (67.2 to 90.2)</td>
</tr>
<tr>
<td>30 to 32</td>
<td>0.70 to 0.80 (61.9 to 70.7)</td>
</tr>
<tr>
<td>33 to 45</td>
<td>0.77 to 0.90 (68.1 to 79.6)</td>
</tr>
</tbody>
</table>
Serum Creatinine Level

- Dependent on maternal renal function, clinical presentation, gestational age
- Usually considered abnormal when serum creatinine is 1.5 mg/dL (132.6 mcmol/L) or greater
- Suspect AKI when plasma creatinine increases in preterm and term newborns or fails to decrease in term newborns in the first week of life
- Can take 48-72 hrs for creatinine to rise after acute insult
Acute Kidney Injury (AKI)

- Very common problem
- Incidence
  - 3-8% among NBICU admissions
  - 12-40% of VLBW/ELBW Infants
- More common in newborns
  - After surgery-(after cardiac surgery 52%)
  - Post asphyxia-( 9% moderate, 56% severe)
  - Sepsis, feeding problems (dehydration)
  - ECMO-(64%)

AKI Definition

- Sudden decrease in kidney function as measured by a decline in glomerular filtration rate (GFR) and that results in the progressive retention of creatinine and nitrogenous waste products and the inability to regulate fluid and electrolyte homeostasis.

Chua, NeoReviews 2005:e369
AKI in Neonates

- However, applying this definition to neonates remains challenging
- Serum creatinine levels are expected to increase in the first days after birth before gradually decreasing, and impaired sodium reabsorption and concentrating ability mean that many neonates may not become oliguric despite a decrease in GFR.
- Premature infants at increased risk of AKI
AKI Definition

- KDIGO defines AKI as any of the following being present:
  - increase in serum creatinine by 0.3 mg/dL (27 mmol/L)
  - increase in serum creatinine by 1.5 times the previous baseline
  - urine volume less than 0.5 mL/kg/h for 6 hours.
Proposed Classification of Neonatal Acute Kidney Injury

<table>
<thead>
<tr>
<th>Stage</th>
<th>Creatinine</th>
<th>Urine Output</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Creatinine increase ≥0.3 mg/dL (&gt;27 μmol/L) within 48 hours or creatinine increase &gt;1.5–1.9 times previous lowest value</td>
<td>&lt;0.5 mL/kg/h for 6–12 hours</td>
</tr>
<tr>
<td>2</td>
<td>Creatinine increase ≥2.0–2.9 times previous lowest value</td>
<td>&lt;0.5 mL/kg/h for &gt;12 hours</td>
</tr>
<tr>
<td>3</td>
<td>Creatinine level ≥2.5 mg/dL (≥221 μmol/L), creatinine increase ≥3 times previous lowest value, or dialysis</td>
<td>&lt;0.3 mL/kg/h for &gt;24 hours or anuric for &gt;12 hours</td>
</tr>
</tbody>
</table>

Selweski PEDIATRICS 2015; 136, e464
Acute Kidney Injury

- Generally due to decreased plasma flow rate
- To maintain this renal autoregulation occurs through:
  - Dilation of afferent arteriole
  - Constriction of efferent arteriole

![Diagram showing the nephron with labeled parts: Afferent Arteriole, Glomerulus, Efferent Arteriole, Proximal Tubule. Diagram also lists factors affecting glomerular filtration: A. Flow in the afferent arteriole (1), B. Transcapillary hydraulic pressure [difference between (2) and (4)], C. Colloid osmotic pressure (1, 2, 3), D. Permeability of glomerular capillaries (2).]
Renal Autoregulation

Mediated by increase in catecholamine secretion that is triggered by decreased renal perfusion

- Results in generation of vasodilator prostaglandins and prostacyclin
  - PG lead to afferent arteriole dilatation

- Catecholamines activate renin-angiotensin system
  - Mediates efferent vasoconstriction
  - Premature infants have less ability to vasoconstrict
Acute Kidney Injury

• Also involves abnormal tubular function
  - Reduced sodium resorption
  - Increased loss of bicarbonate
  - Diminished excretion of water
Acute Kidney Injury

• Can be anuric/oliguric
  - Urine output < 1.0 (or 0.5) mL/kg/hr or lack of urine output by 48 hours

• Nonoliguric
  - May have normal volume of urine with increasing creatinine

• Dependent on type of renal injury
Urine output after AKI in Asphyxia

- Due to severe asphyxia
  - Non oliguric - 60%
  - Oliguric - 25%
  - Anuric - 15%

Andreoli, Current Opin Pediatr 2002
Classification of AKI—Underlying Causes—Can be Multifactorial

- **Prerenal** - 85%
  - Due to inadequate renal perfusion
- **Renal** - 11%
  - Due to intrinsic renal disease including vascular insults
- **Postrenal** - 4%
  - Due to obstruction to the flow of urine
Causes/Timing of AKI

The injury to the kidney may have occurred during development, perinatally, or postnatally:

- Prenatal Injury/Vascular Damage
- Congenital Renal Diseases
- Postnatal Renal Diseases
Classification of AKI - Underlying Causes

- **Prerenal - 85%**
  - Due to inadequate renal perfusion
- **Renal - 11%**
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Prerenal Causes of AKI

- Hypovolemia/Dehydration
- Hemorrhage
- Hypotension
- Hypoxia-ischemia
- Sepsis/Necrotizing enterocolitis
- Cardiac/Congestive Heart Failure
- Drugs
- Hyperviscosity
Prerenal Causes of AKI

- Decreased true intravascular volume
  - Dehydration (insensible)/poor feeding
  - Third space losses (sepsis, shock, NEC)
  - Gastrointestinal losses
    - Vomiting or diarrhea
  - Hypoalbuminemia
  - Increased urinary losses
Prerenal Causes of AKI

- Decreased true intravascular volume
  - Perinatal hemorrhage
    - Twin-twin transfusion syndrome
    - Fetal maternal hemorrhage
    - Cord accidents/prolapse avulsion
    - Subgaleal hemorrhage
    - Intraventricular hemorrhage
    - Intracranial hemorrhage
Prerenal Causes of AKI

- Decreased effective intravascular volume
  - Cardiac/Congestive Heart Failure
    - Patent ductus of the arteriosus
    - Coarctation of the aorta
    - Hypoplastic left heart
    - Pericarditis, cardiac tamponade
  - High ventilatory support (increased MAP)
Prerenal Causes of AKI

- In utero drugs that reduce blood flow
  - COX2 inhibitors
  - Nonselective nonsteroidal anti-inflammatory drugs
  - Angiotensin-converting enzyme inhibitors
  - Angiotension receptor antagonists

- Post natal drugs that reduce renal blood flow
  - Indomethacin or Ibuprofen
  - Angiotensin-converting enzyme inhibitors
Prerenal Failure

- Inadequate renal perfusion leads to decreased renal function in an intrinsically normal kidney
- Re-establishing normal renal perfusion results in return of normal renal function
- Can lead to intrinsic renal disease if perfusion is not restored—acute tubular necrosis
Classification of AKI-Underlying Causes

- **Prerenal-85%**
  - Due to inadequate renal perfusion
- **Renal-11%**
  - Due to intrinsic renal disease including vascular insults
- **Postrenal-4%**
  - Due to obstruction to the flow of urine
Renal Anomalies

- Cystic disease/dysplasia
- Polycystic kidney disease
- Congenital nephrotic syndrome
- Renal agenesis

Wide-set eyes
Depressed nasal bridge
Beaked nose
Receding chin
Posteriorly rotated, low-set ears
Small, compressed chest wall
Arthrogryposis
Hip dislocation
Club foot
Respiratory failure
Drugs and AKI

Drug-induced

- Aminoglycosides, Vancomycin
- NSAID (indomethacin)
- Amphotericin B, Acyclovir
- ACE inhibitors (captopril, enlapril)
- IV contrast media

Up to 87% of VLBW infants exposed to at least 1 nephrotoxic drug (avg 14 days)

Intrinsic Renal Failure

• Vascular lesions
  - Renal artery thrombosis
    ▪ May be a complication of umbilical artery catheter (UAC)
    ▪ Associated with hypertension
  - Renal vein thrombosis
    ▪ May present with an abdominal mass, thrombocytopenia and gross hematuria, due to dehydration or DIC
    ▪ Increased in Infants of Diabetic Mothers, hereditary prothrombotic factors
Intrinsic Renal Failure

• Infectious causes
  - Sepsis
  - Pyelonephritis
  - Syphilis
  - Toxoplasmosis
  - Candidiasis
Renal Intrinsic Disease: Causes

- Acute Tubular Necrosis
- Hemoglobin/myoglobin
  - Hemolytic disease
- DIC (Disseminated Intravascular Coagulation)
- Cortical necrosis from ischemia
  - Perinatal asphyxia
  - Cardiac surgery
Classification of AKI-Underlying Causes

- **Prerenal-85%**
  - Due to inadequate renal perfusion
- **Renal-11%**
  - Due to intrinsic renal disease including vascular insults
- **Postrenal-4%**
  - Due to obstruction to the flow of urine
Postrenal/Obstructive

- Urethral obstruction
  - Posterior urethral valves
- Bilateral ureteral obstruction-ureteropelvic, ureterovesical
- Obstruction in a solitary kidney
- Neurogenic bladder due to myelomeningocele
- Extrinsic bilateral ureteral or bladder obstruction
  - Tumor
- Intrinsic bilateral obstruction
  - Calculi
  - Bilateral fungal bezoar/renal candidiasis
Diagnosis of AKI Etiology

- Differentiate between prerenal, intrinsic renal and post renal or MIXED
- Physical Exam, Clinical findings
- Laboratory studies
- Imaging
Presentation

• AKI should be suspected in newborns who have an elevated or rising serum creatinine (and blood urea nitrogen) and/or anuria/oliguria

• Other laboratory abnormalities
  - Hyponatremia
  - Hyperkalemia
  - Metabolic acidosis
  - Hyperphosphatemia
  - Hypocalcemia
Presentation

• Oliguria
• Systemic hypertension
• Cardiac arrhythmia
• Evidence of fluid overload or dehydration
• Decreased activity
• Seizures
• Vomiting
• Anorexia
Assessment

• Prenatal and perinatal history
  - ACE inhibitors, NSAIDs COX-2 inhibitors

• Prenatal ultrasound
  - Renal size, echogenicity, structural malformations, amniotic fluid volume, bladder size

• Drug administration

• Family history
Physical Exam

- Blood pressure
  - High: PCKD, AKI, arterial or venous thrombosis
  - Low: Volume depletion, hemorrhage, sepsis
- Ascites, edema - GU obstruction, cong. nephrotic syndrome
- Abdominal mass (2/3 are GU in origin)
- Genitalia
- Evidence of oligohydramnios
- Ears, eyes
Laboratory Studies

- Chemistry panel: sodium, potassium, chloride, bicarbonate, blood urea nitrogen, creatinine, calcium, phosphorus, magnesium, total protein, albumin
- Urine studies: urinalysis, urine culture, random urine protein/creatinine, urine electrolytes
- Arterial blood gas
- Complete blood count, coagulation studies
Urinary Studies

- Assessment of fractional excretion of sodium can help to differentiate the prerenal (hypovolemia) from intrinsic (acute tubular necrosis) causes of AKI, although in premature infants this metric may not be as helpful.

\[
\text{FENa, percent} = \frac{\text{UNa} \times \text{PCr}}{\text{PNa} \times \text{UCr}} \times 100
\]
## Diagnostic Indexes in Acute Kidney Injury

<table>
<thead>
<tr>
<th>Test</th>
<th>Prerenal AKI</th>
<th>Intrinsic AKI</th>
</tr>
</thead>
<tbody>
<tr>
<td>BUN/Cr ratio (mg/mg)</td>
<td>&gt;30</td>
<td>&lt;20</td>
</tr>
<tr>
<td>FE_{Na} (%)</td>
<td>≤2.5</td>
<td>≥3.0</td>
</tr>
<tr>
<td>Urinary Na (mEq/L)</td>
<td>≤20</td>
<td>≥50</td>
</tr>
<tr>
<td>Urinary Osm (mOsm/kg)</td>
<td>≥350</td>
<td>≤300</td>
</tr>
<tr>
<td>Urinary specific gravity</td>
<td>&gt;1.012</td>
<td>&lt;1.014</td>
</tr>
<tr>
<td>Ultrasonography</td>
<td>Normal</td>
<td>May be abnormal</td>
</tr>
<tr>
<td>Response to volume challenge</td>
<td>UO &gt;2 mL/kg/h</td>
<td>No increase in UO</td>
</tr>
</tbody>
</table>

AKI, acute kidney injury; BUN, blood urea nitrogen; Cr, creatinine; FENa, fractional excretion of sodium (Na); Osm, osmolality; UO, urinary output.
Imaging

• Renal ultrasound with doppler
  - Look for presence or absence of kidneys
  - Size
  - Presence or absence of hydronephrosis
  - Bladder distension
  - Blood flow to kidneys
Imaging

• Voiding cystourethrogram
  - Identify lesions of lower urinary tract such as posterior urethral valves
  - Evaluate reflux
Medical Management of AKI

• Prerenal
  - Give adequate volume
    ▪ Isotonic saline (NS) 10-20 mL/kg over 1-2 hours, may give more quickly if in shock, may need to repeat
    ▪ Clinical evaluation of volume status-BP, heart rate, perfusion, ECHO
    ▪ Monitor weights every 12-24 hours, Strict I and O
    ▪ Support blood pressure
  - Treat underlying condition (sepsis, etc)
Prerenal Failure-Fluid Management

- Once baby is euvoletic, fluid administration should be limited to insensible losses and urine replacement
  - 30-60 mL/kg/day
Medical Management

- Monitor fluid and electrolyte abnormalities closely: every 6-12-24 hours
- Monitor urine output
- Monitor weight
- Calcium/phosphorus abnormalities
- Correct acidosis
Medical Management

• Remove potassium and phosphorus from fluids
• Treat hypertension
• Adjust/discontinue medications
• Placement of Foley catheter to monitor urine output and rule out lower urinary tract obstruction
• Provide adequate nutrition-fats and carbohydrate
Asphyxia and AKI

- In neonates with perinatal asphyxia, adenosine receptor antagonists (theophylline) may prevent AKI by inhibiting the adenosine-induced vasoconstriction.
- Prophylactic theophylline, given early after birth, associated with better kidney function
- KDIGO guidelines recommend a single dose of theophylline for asphyxiated infants at risk for AKI.
Diuretics in AKI

- Will not alter course, but may increase urine output
- Lasix (furosemide) 1-2 mg/kg/dose
  - Can increase urine flow rate—decreases intratubular obstruction
  - Inhibits Na/K/ATPase, which limits oxygen consumption in already damaged tubules
- Mannitol is not recommended and should be avoided
Dopamine in AKI

- Neonates with hypotension who have received fluid or are euvolemic may require inotropic and systemic vasoactive support
- Renal dose dopamine 1-3-5 mcgram/kg/min)
  - Increases renal blood flow by promoting vasodilatation
  - Improves urine output by promoting naturiesis
- However, no studies have proven benefit
Hyponatremia in AKI

- Hyponatremia is frequently dilutional and best treated with fluid restriction rather than additional sodium.
- However, Na less than 120 mEq/L (120 mmol/L) may be associated with seizures and lethargy.
- Administration of 3% hypertonic saline or NS to increase sodium to 130 mEq/L (130 mmol/L).
- NS may have too much fluid volume.
Sodium Replacement

To treat severe hyponatremia: $Na = 115 \text{ mmol/L}$

- Amount of sodium (mmol) = 
  \[ \text{desired } Na - \text{actual } Na (\text{mmol/L}) \times 0.6 \times \text{total body water } L/\text{kg} \times \text{weight (kg)} \]

Example: $(130 - 115) \times 0.6 \times 2 = 18 \text{ mmol (mEq) needed}$

$3\% = 513 \text{ mEq/L} = 35 \text{ ml to give over 6 hrs}$
$\text{NS} = 154 \text{ mEq/l} = 116 \text{ mL} = \text{TOO MUCH FLUID}$
Ongoing Sodium Replacement

- Neonates may also have high urinary losses of sodium due to immature kidneys or obstructive lesions so may need significant sodium replacement in daily fluid.
- Measure urinary sodium every 6 hours, especially if in high urine output failure.
Hyperkalemia in AKI

• Common complication in AKI as the kidney tightly regulates potassium balance and excretes 90% of dietary potassium intake

• Can be life threatening and lead to cardiac arrhythmias, cardiac arrest and death
Hyperkalemia

- $K > 6 \text{ mEq/L}$
- Document hyperkalemia with arterial or venous sample (heelstick may have hemolysis)
- Emergency if $K > 8 \text{ mEq/L}$
- Remove all $K$ from IVF!
- Treat immediately
Hyperkalemia

- Obtain electrocardiogram (ECG) in the event of hyperkalemia
  - Tall peaked T waves
  - Prolonged PR interval
  - Flattening of P waves
  - Widening QRS complexes
  - Ventricular tachycardia, ventricular fibrillation
## Treatment of Hyperkalemia

<table>
<thead>
<tr>
<th>Intervention</th>
<th>Dose</th>
<th>Mechanism</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sodium bicarbonate</td>
<td>1 mEq/kg IV over 10-30 min</td>
<td>Shifts K into cells</td>
</tr>
<tr>
<td>Calcium gluconate (10%)</td>
<td>0.5-1.0 mL/kg IV over 5-10 min</td>
<td>Stabilizes cardiac membrane potential</td>
</tr>
<tr>
<td>Insulin/Glucose</td>
<td>Glucose 0.5 g/kg; insulin 0.1U/kg IV over 30 min</td>
<td>Stimulates cellular uptake of K</td>
</tr>
</tbody>
</table>
## Treatment of Hyperkalemia

<table>
<thead>
<tr>
<th>Intervention</th>
<th>Dose</th>
<th>Mechanism</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sodium polystyrene sulfonate (Kayexalate)</td>
<td>1 g/kg PO or PR in sorbitol</td>
<td>Exchanges Na for K across colonic mucosa</td>
</tr>
<tr>
<td>Furosemide</td>
<td>1-2 mg/kg IV</td>
<td>Increases urinary excretion of K</td>
</tr>
<tr>
<td>Albuterol-β₂-adrenergic agonist</td>
<td>Nebulized 2.5 mg</td>
<td>Stimulatory effect on Na⁺ – K⁺ ATPase, intracellular shift of K</td>
</tr>
</tbody>
</table>
Calcium-Phosphorus in AKI

- **Hyperphosphatemia**
  - Dietary Phos restriction
  - Use low phosphorus formulas and add phosphorus binders such as calcium carbonate to formula

- **Hypocalcemia**
  - Treat with calcium gluconate 10% at 0.5-1.0 mL/kg
Acid-Base Balance

- Metabolic acidosis is common because of the role of the kidney in excreting net acids generated by body metabolism
- Treat if pH < 7.2 or plasma bicarbonate is less than 12 mEq/l (12 mmol/L)
- Administer IV or oral sodium bicarbonate
- Give NaHCO₃ to maintenance fluids or feeds to prevent acidosis or sodium acetate in parenteral nutrition
- Treatment of acidosis decreases amount of ionized calcium so monitor iCa levels to prevent tetany or seizures
Hypertension

• Fluid overload may result in mild hypertension
  - Treat with fluid restriction and anti-hypertensives

• Severe hypertension should make one think of renal artery or venous thrombosis
Nutrition in AKI

- Need to provide adequate nutrition to prevent tissue breakdown and catabolic state
- Human breast milk or renal formula (PM 60/40)
- May need high calorie additives
- May need IV nutrition—minimum of 50 kcal/kg day and 1-2 g/kg/day of protein
## Composition of Human Milk and Renal Formulas

<table>
<thead>
<tr>
<th>Formula</th>
<th>Kcal/mL or oz</th>
<th>Protein (g)</th>
<th>CHO (g)</th>
<th>Fat (g)</th>
<th>Na (mEq)</th>
<th>K (mEq)</th>
<th>Ca (mg)</th>
<th>Phos (mg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Human preterm</td>
<td>0.67 (20)</td>
<td>14</td>
<td>66</td>
<td>39</td>
<td>11</td>
<td>15</td>
<td>248</td>
<td>128</td>
</tr>
<tr>
<td>Human term</td>
<td>0.67 (20)</td>
<td>10</td>
<td>72</td>
<td>39</td>
<td>7</td>
<td>13</td>
<td>280</td>
<td>147</td>
</tr>
<tr>
<td>Renal</td>
<td>0.67 (20)</td>
<td>15</td>
<td>69</td>
<td>38</td>
<td>7</td>
<td>15</td>
<td>378</td>
<td>189</td>
</tr>
</tbody>
</table>
Renal Replacement Therapy

What for?

- Ultrafiltration
  - Severe fluid overload-remove water
- Dialysis
  - Remove solutes
Indications for Renal Replacement Therapy

- Hyperkalemia
- Hyponatremia
- Acidosis
- Hypocalcemia
- Hyperphosphatemia
- Volume overload
- Uremic symptoms
- Inability to provide adequate nutrition
Renal Replacement Therapy

• Peritoneal dialysis-
  - Preferred in neonatal population
• Continuous renal replacement therapy
• Hemodialysis-intermittent
Peritoneal Dialysis

- Most often used in neonatal population
  - Less difficult technically, does not require vascular access or anticoagulation
  - Very effective in newborns due to greater ratio of peritoneal membrane surface area to body surface area
Peritoneal Dialysis of the Newborn

- Hyperosmolar dialysate repeatedly infused into and drained out of peritoneal cavity through a catheter
- Vary cycle length, dwell time, osmolar concentration of dialysate
- Contraindication-recent abdominal surgery, NEC, VP shunt
Continuous Renal Replacement Therapy (CRRT)

- Neonate’s blood is continuously circulated through a pump-driven extracorporeal circuit containing a highly permeable hemofilter
- Need central vascular access and continuous anticoagulation
- Can be used with ECMO
- Advantage is can carefully control fluid removal, good for very unstable babies
CRRT

Now have devices to use in babies as small as 2000 g

• CVVH-An ultrafiltrate of plasma is removed, a portion of which is returned to the patient in the form of a physiologic replacement fluid

• CVVH-D--In continuous venovenous hemodialysis, countercurrent dialysate is used rather than replacement fluid to achieve solute removal.
Hemodialysis

- Short term is less common, but possible
- Involves intermittent 3-4 hour treatments in which fluids and solutes are rapidly removed from the infant using an extracorporeal dialyzer with rapid countercurrent dialysate flow
- Treatment of choice for hyperammonemia
- Need major vascular access and may have hemodynamic instability
Outcome of Neonatal AKI

- Mortality 25-78% depending on underlying cause, other organ involvement, GA
- Oliguria may last for several weeks
- Polyuria with increased sodium and potassium losses may complicate recovery
- Outcome for nonoliguric AKI is better than anuric/oliguric
- May progress to renal disease later in childhood and chronic renal failure so need long term follow up
Thank you-Any Questions?