Renal Nutrition for the Intensive Care Nursery

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Level IV ICN
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• No disclosures
Outline

1) Overview of the nutritional state of the preterm infant
2) Discuss the renal consequences of the preterm infant
ICN Vocabulary 101

- **Gestational age**: birth age (weeks)
- **Corrected age**: chronological age – gestational age
  - 12 week old (3m) former 30 week premie has a corrected age of 2 weeks (12-10wks)
- **Trimester 1 and 2**: gestation weeks 1-27
- **Trimester 3**: gestation weeks 28-40
- **Preterm**: Gestational age <37 weeks
- **Extremely Low Birth Weight (ELBW)**: <1000gm birth weight
- **Very Low Birth Weight (VLBW)**: <1500gm birth weight
- **Low Birth Weight (LBW)**: <2500gm birth weight
- **SGA**: Small for Gestational Age (<10%ile birth weight)
- **IUGR**: Intrauterine Growth Restriction – medical diagnosis, see criteria
- **Fenton Growth Charts**: used for preterm infants until 50 weeks Post Menstrual Age (PMA)
  **When transition to WHO Chart, make sure to correct for age to ensure smooth transition between charts**

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Case Study – J.C.

- 33 weeker, birth weight 1.79kg (4#) 28%ile for weight
- Mom provided breastmilk for ~2 months
- C-section due to non-reassuring heart tones
- Antenatal procedures: vesicocentesis and vesicoamniotic shunt
- Postnatal renal diagnoses: Oligohydramnios (low amniotic fluid) and solitary left cystic dysplastic kidney
- Other pertinent diagnoses: Bladder outlet obstruction (suprapubic catheter placement), Imperforate anus (colostomy with MF on DOL 2), and Pulmonary hypoplasia with Pneumothorax requiring mechanical ventilation and chest tube initially.
### Nutritional Concerns for the Preterm Infant

- Calories
- Fat
- Protein
- Water
- Sodium
- Potassium
- Chloride
- Iron
- Zinc
- Copper
- Selenium
- Iodine
- Calcium
- Phosphorus
- Magnesium
- Vitamin D
- Slowed gastric emptying
- Less acidic stomach pH
<table>
<thead>
<tr>
<th>Nutrient</th>
<th>Age if Preterm (wk)</th>
<th>Premature Infant Cord Blood (SD)</th>
<th>Term Infant Cord Blood (37–41 wk)</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ferritin (µg/dL)</td>
<td>23</td>
<td>63 (27–35)</td>
<td>171</td>
<td>Siddappa et al, 2007 104</td>
</tr>
<tr>
<td>TIBC (µmol/L)</td>
<td>24–29</td>
<td>31 (17.4 (10.7)</td>
<td>42 (36–49.5)</td>
<td>Sweet et al, 2001 105</td>
</tr>
<tr>
<td>Iron (µmol/L)</td>
<td></td>
<td>17.4 (10.7)</td>
<td>20.8 (8.8)</td>
<td>Makhoul et al, 2004 106</td>
</tr>
<tr>
<td>Selenium (µg/dL)</td>
<td>23</td>
<td>45.85 (15.4)</td>
<td>68.4 (26.6)</td>
<td>Elizabeth et al, 2001 107</td>
</tr>
<tr>
<td>Total protein (g/dL)</td>
<td>&lt;37</td>
<td>4.24 (0.5)</td>
<td>5.50 (0.735)</td>
<td></td>
</tr>
<tr>
<td>Albumin (g/dL)</td>
<td></td>
<td>1.84 (0.264)</td>
<td>2.494 (0.391)</td>
<td></td>
</tr>
<tr>
<td>Calcium (mg/dL)</td>
<td></td>
<td>5.67 (0.89)</td>
<td>8.08 (0.96)</td>
<td></td>
</tr>
<tr>
<td>Triglycerides (mg/dL)</td>
<td></td>
<td>52.10 (18.87)</td>
<td>66.66 (20.3)</td>
<td></td>
</tr>
<tr>
<td>Total cholesterol (mg/dL)</td>
<td></td>
<td>51.46 (19.39)</td>
<td>69.79 (19.81)</td>
<td></td>
</tr>
<tr>
<td>Magnesium (mg/dL)</td>
<td></td>
<td>1.62 (0.31)</td>
<td>1.96 (0.19)</td>
<td></td>
</tr>
<tr>
<td>Zinc (µg/dL)</td>
<td></td>
<td>70.25 (24.25)</td>
<td>92.24 (19.40)</td>
<td></td>
</tr>
</tbody>
</table>
Calories, Fat, and Protein

• Higher metabolic demand
  • 120+kcal/kg enteral

• Fat
  • 3+gm fat/kg

• Protein
  • 3.5-4gm/kg enteral until 40 wks PMA (aka baby due date)

• Fluid: maintenance 120ml/kg for preterm infant
  • 140-160ml/kg for growth, depends on formula/breastmilk fortifiers

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Fetal-Infant Growth Table for Preterm Infants
2013 Fenton Growth Chart

<table>
<thead>
<tr>
<th>PMA (weeks)</th>
<th>Males Weight (grams/day)</th>
<th>Males Length (cm/week)</th>
<th>Males OFC (cm/week)</th>
<th>Females Weight (grams/day)</th>
<th>Females Length (cm/week)</th>
<th>Females OFC (cm/week)</th>
</tr>
</thead>
<tbody>
<tr>
<td>24 – 28</td>
<td>15</td>
<td>1.4</td>
<td>1</td>
<td>14</td>
<td>1.4</td>
<td>0.9</td>
</tr>
<tr>
<td>28 – 32</td>
<td>25</td>
<td>1.4</td>
<td>1</td>
<td>24</td>
<td>1.4</td>
<td>1</td>
</tr>
<tr>
<td>32 – 36</td>
<td>34</td>
<td>1.3</td>
<td>0.8</td>
<td>33</td>
<td>1.3</td>
<td>0.9</td>
</tr>
<tr>
<td>36 – 40</td>
<td>30</td>
<td>1</td>
<td>0.6</td>
<td>28</td>
<td>1</td>
<td>0.6</td>
</tr>
<tr>
<td>40 – 44</td>
<td>33</td>
<td>0.9</td>
<td>0.5</td>
<td>28</td>
<td>0.8</td>
<td>0.5</td>
</tr>
<tr>
<td>44 – 48</td>
<td>32</td>
<td>0.8</td>
<td>0.4</td>
<td>28</td>
<td>0.7</td>
<td>0.4</td>
</tr>
<tr>
<td>48 – 50</td>
<td>15</td>
<td>0.4</td>
<td>0.2</td>
<td>13</td>
<td>0.3</td>
<td>0.2</td>
</tr>
</tbody>
</table>
Water, Sodium, Potassium, & Chloride

• ~7 to 14 days to adjust to extraterine environment

• Monitor electrolytes and I&Os, but often no intervention until >2 weeks of age
Iron

- AAP iron recommendation for preterm infants: 2-4mg/kg supplemental iron, daily total max of 15mg/day.
  - Epogen requires higher FeSO4 dosage (4-6mg/kg/day)
- Higher fractional iron absorption compared to term infants.
- Breastmilk is low in Iron (~0.3mg/L).
- Term infants have sufficient iron stores to last until ~4 months of age. Preterm infants have lower storage levels and deplete those levels quickly during first few weeks of postnatal growth.
Zinc

• Essential for many enzymatic rxns
• Plays important role in growth and tissue differentiation
• Deficiency can cause stunted growth, increased infection risk, and poor neurodevelopment
• Can inhibit copper absorption
• No reliable biomarker. Serum or plasma levels are used, but these are not sensitive enough to detect marginal deficiency.
• Colostrum is high in zinc. Breastmilk zinc levels decrease over the first three months of lactation. Belief that infants meet zinc requirements with intake from breastmilk combined with gradual release of stored zinc in hepatic metallothionein. “However, these mechanisms are insufficient in infant with a birth weight <1500-2000gm” ….immature liver!
Calcium and Phosphorus

• 80% of minerals are accreted in bone during the third trimester

• Increased risk for rickets/osteopenia of prematurity

• Ca:Phos ratio for optimal bone absorption 1.8:1
Slowed Gastric Emptying

- Peristalsis requires maturation of the GIT
- Reaches “normal” by ~6-8 months of age, corrected
- Increases propensity for emesis
Stomach pH

- Premature infants aged 3-13 days, formula (Harries 1968)
- Full term newborns aged 5-13 days, breast milk (Mason 1962)
- Premature infants aged 1 month, formula (Roman 2007)
- Healthy infants aged 1-6 months, formula (Cavell 1983)
- Healthy young men aged 27-32 years, casein protein solution (Calbet 2004)
- Healthy young men aged 27-32 years, whey protein solution (Calbet 2004)
- Healthy young adults aged 21-35 years, a meal of hamburger, bread, potatoes, ketchup, mayo, tomato, lettuce, and milk (Dressman 1990)
- Healthy elderly adults aged 65-83 years, a meal of hamburger, bread, potatoes, ketchup, mayo, tomato, lettuce, and milk (Russell 1993)
Summary of Preterm Infant Nutrition

• Starting at low to deficient levels of many micro- and all macronutrients
• Not just small adults. Underdeveloped organs, and body mechanisms and processes.
• Comorbidities often require change from preterm formulas and breastmilk fortifiers. This has consequences.
• What do to? Monitor closely. Labs, nutrition focused physical exam, growth, and tolerance.
# Isocaloric Comparison, per kg

<table>
<thead>
<tr>
<th></th>
<th>Breastmilk, term, unfortified</th>
<th>Breastmilk fortified with HMF [24]</th>
<th>Similac Special Care High Protein</th>
<th>Similac PM 60:40</th>
<th>Renastart</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calories, kcal</td>
<td>120</td>
<td>120</td>
<td>120</td>
<td>120</td>
<td>120</td>
</tr>
<tr>
<td>Protein, gm</td>
<td>1.8</td>
<td>3.8</td>
<td>4</td>
<td>2.6</td>
<td>1.9</td>
</tr>
<tr>
<td>Na, mEq</td>
<td>1.2</td>
<td>1.8</td>
<td>2.3</td>
<td>1.2</td>
<td>2.6</td>
</tr>
<tr>
<td>K, mEq</td>
<td>1.8</td>
<td>3.7</td>
<td>4</td>
<td>2.5</td>
<td>0.7</td>
</tr>
<tr>
<td>Ca, mg</td>
<td>49</td>
<td>182</td>
<td>216</td>
<td>67</td>
<td>1.3</td>
</tr>
<tr>
<td>Phos, mg</td>
<td>25</td>
<td>102</td>
<td>120</td>
<td>34</td>
<td>1.4</td>
</tr>
<tr>
<td>Vitamin A, IU</td>
<td>386</td>
<td>1243</td>
<td>1500</td>
<td>360</td>
<td>109</td>
</tr>
<tr>
<td>Vitamin D, IU</td>
<td>4</td>
<td>179</td>
<td>180</td>
<td>72</td>
<td>50</td>
</tr>
<tr>
<td>Fe, mg</td>
<td>0.12</td>
<td>0.6</td>
<td>2.2</td>
<td>0.8</td>
<td>1</td>
</tr>
</tbody>
</table>

[20kcal/oz] = 180ml/kg  [24kcal/oz] = 150ml/kg  [26kcal/oz] = 140ml/kg
J.C.

- TPN/IL
- Breastmilk
- Breastmilk fortified with Similac PM 60:40
- Breastmilk fortified with Solcarb, alternating with Sim PM 60/40
- Breastmilk fortified with Solcarb, alternating with Renastart
- Similac PM 60:40 + SolCarb + Renastart
- Renastart

What to give? When to change? Consequences to watch out for?
Monitor labs, tolerance, growth….
and have close communication between renal and ICN teams.
The Kidney and the Preterm Infant
Kidney Formation

- 5 weeks gestation – metanephric, or definitive, kidney begins to form
- Metanephric kidney is functional during the second half of pregnancy (week 20+)
- 34-36 weeks gestation – nephrogenesis complete
  - 800,000 to 1.2 million nephrons per kidney of term infant
- Genetic differences have been associated with CAKUT in humans
- Note: Bladder and urethra are formed during the second and third months of gestation (weeks 4-12)
Pathophysiology of Preterm Kidney Disease

- Placental Insufficiency
  - Blood flow↓
  - Cerebral redistribution
  - Protein delivery↓
    - Oxygen delivery↓
  - Intrauterine Growth Restriction
    - Cell migration failure

Low Nephron Endowment
- Developmental Disruption
- Low Birth Weight

Morphologic Changes
- Hypoperfusion
- Nephrotoxicity

Antenatal Findings
- Premature Birth
- Postnatal
INFLAMMATION
• Intrauterine life of the kidney
  • Minor role: regulating salt and water balance (placenta is primary regulator)
  • Major role: manager of amniotic fluid by forming and excreting urine

• Extrauterine life of the kidney – progressive maturation of function
  • Maintain a stable balance of body chemicals (waste, drugs)
  • Production of urine
  • Regulator of salt, potassium, and acid content
  • Hormone production that affect the function of other organs (Vitamin D, erythropoietin)
## Kidney maters with age

<table>
<thead>
<tr>
<th>Age</th>
<th>GFR (mL/min/1.73 m²)</th>
<th>RBF (mL/min/1.73 m²)</th>
<th>Max Urine Osm (mOsm/kg)</th>
<th>Serum Creatinine (mg/dL)</th>
<th>Fe Na (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Newborn</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Premature (30-34 weeks)</td>
<td>14 ± 3</td>
<td>40 ± 6</td>
<td>480</td>
<td>0.6-1.3 *</td>
<td>2-6</td>
</tr>
<tr>
<td>Term</td>
<td>21 ± 4</td>
<td>88 ± 4</td>
<td>800</td>
<td>0.6-1 *</td>
<td>&lt;1</td>
</tr>
<tr>
<td>1-2 weeks</td>
<td>50 ± 10</td>
<td>220 ± 40</td>
<td>900</td>
<td>0.27-0.5 *</td>
<td>&lt;1</td>
</tr>
<tr>
<td>6 months-1 year</td>
<td>77 ± 14</td>
<td>352 ± 73</td>
<td>1200</td>
<td>0.18-0.29 *</td>
<td>&lt;1</td>
</tr>
<tr>
<td>1-3 years</td>
<td>96 ± 22</td>
<td>540 ± 118</td>
<td>1400</td>
<td>0.24-0.43 †</td>
<td>&lt;1</td>
</tr>
<tr>
<td>Adult</td>
<td>118 ± 18</td>
<td>620 ± 92</td>
<td>1400</td>
<td>0.6-1.3</td>
<td>&lt;1</td>
</tr>
</tbody>
</table>

**TABLE 93.2, Normal Values for Renal Function, Adapted from references.**

Fe Na, Fractional excretion of sodium; GFR, glomerular filtration rate; Osm, osmolality; RBF, renal blood flow.

* Based on enzymatic or Jaffe creatinine measurements.

† Based on IMDS-traceable creatinine measurements.
GFR and RBF

- Hurried activation of the Renin-Angiotensin-Aldosterone System (RAAS)
- Key factor in development of genetic hypertension, vascular dysfunction, vessel rigidity, and further constriction

<table>
<thead>
<tr>
<th>Age</th>
<th>GFR (mL/min/1.73 m²)</th>
<th>RBF (mL/min/1.73 m²)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Newborn</td>
<td></td>
<td></td>
</tr>
<tr>
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</tr>
<tr>
<td>Adult</td>
<td>118 ± 18</td>
<td>620 ± 92</td>
</tr>
</tbody>
</table>
Measuring Kidney Function

- Creatinine level most commonly used indicator of kidney function
  - Influenced by age, muscle mass, and maturity
- Immediately postnatal, serum Cr reflective of maternal kidney function/maternal Cr level.
  - Term infants – decline in Cr over first two weeks of life
  - Preterm infants – decline in Cr over 1-2 months due to low GFR and poor tubular reabsorption of Cr
  - Failure of Cr level to fall is indicator of impaired renal function
- Ultrasound can identify hydronephrosis, cystic kidney disease, and abnormalities in kidney size and position.
  - Also screening tool for nephrocalcinosis due to CLD and long-term loop diuretic therapy
  - Complete US >48 hours of life due to “normalization”/establishment of UOP

<table>
<thead>
<tr>
<th>Age</th>
<th>GFR (mL/min/1.73 m²)</th>
<th>Serum Creatinine (mg/dL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Newborn</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Premature (30-34 weeks)</td>
<td></td>
<td>0.6 - 1.3 *</td>
</tr>
<tr>
<td>Term</td>
<td></td>
<td>0.6 - 1 *</td>
</tr>
<tr>
<td>1-2 weeks</td>
<td></td>
<td>0.27 - 0.5 *</td>
</tr>
<tr>
<td>6 months-1 year</td>
<td></td>
<td>0.18 - 0.29 *</td>
</tr>
<tr>
<td>1-3 years</td>
<td></td>
<td>0.24 - 0.43</td>
</tr>
<tr>
<td>Adult</td>
<td></td>
<td>0.6 - 1.3 *</td>
</tr>
</tbody>
</table>
First 2 months of life, Cr went from 5.2 to 3.

Ref range: 0.06-0.45

Months 2-4 of life, Cr increased from 3 to 4.1.
## Neonatal AKI Definition 2013

<table>
<thead>
<tr>
<th>Stage</th>
<th>Serum creatinine (μmol/l) rise by</th>
<th>Serum creatinine rise × reference value*</th>
<th>Urinary output (ml/kg/h)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>&lt; 26.5</td>
<td>&lt; 1.5</td>
<td>≥0.5</td>
</tr>
<tr>
<td>1</td>
<td>≥26.5 (48 h)</td>
<td>≥1.5–1.9 (7 days)</td>
<td>&lt;0.5 × 6–12 h</td>
</tr>
<tr>
<td>2</td>
<td></td>
<td>≥2–2.9</td>
<td>&lt;0.5 × &gt; 12 h</td>
</tr>
<tr>
<td>3</td>
<td>≥221 or dialysis</td>
<td>≥3</td>
<td>&lt;0.3 × ≥ 24 h or anuria x ≥12 h</td>
</tr>
</tbody>
</table>

1.*Reference creatinine is defined as the lowest previous serum creatinine value
Urine

• Concentration – allows for fluid conservation
  • Neonatal urine <1.004 specific gravity
  • Clear and nearly colorless is WNL

<table>
<thead>
<tr>
<th></th>
<th>&gt;2yr &amp; Adults</th>
<th>Term Neonates</th>
<th>Preterm Neonates</th>
</tr>
</thead>
<tbody>
<tr>
<td>1500 mOsm/kg</td>
<td>800 mOsm/kg</td>
<td>600 mOsm/kg</td>
<td></td>
</tr>
</tbody>
</table>

• Dilution – allows for free water excretion

<table>
<thead>
<tr>
<th></th>
<th>&gt;2yr &amp; Adults</th>
<th>Term Neonates</th>
<th>Preterm Neonates</th>
</tr>
</thead>
<tbody>
<tr>
<td>50 mOsm/kg</td>
<td>50 mOsm/kg</td>
<td>70 mOsm/kg</td>
<td></td>
</tr>
</tbody>
</table>

• Maximal renal concentration and dilution requires structural maturity, well-developed tubular transport mechanisms, and an intact hypothalamic-renal vasopressin axis. ……why growth and maturation is one of the best “treatments”
Sodium and Growth

- Net storage of 1-1.5mmol Na/kg/day to build extracellular compartment
- Sodium dependent Na-Hydrogen antiporter system located in the cell wall.
  - Antiporter increases the action of Na/K ATPase and stimulated growth by alkalization of the cell interior.
- Antiporter activity diminished in sodium depleted and acidotic state → growth failure regardless of macronutrient intake.
References


  - Chapter 92: Fluid, Electrolytes, and Acid-Base Homeostasis


- National Kidney Foundation, kidney.org

- Protein Digestion of Baby Foods: Study Approaches and Implications for Infant Health - Scientific Figure on ResearchGate. Available from: https://www.researchgate.net/figure/Postprandial-gastric-pH-of-healthy-infants-and-adults_fig2_319631155 [accessed 5 Jan, 2020]
