Pediatric Parenteral Nutrition

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Parenteral Nutrition (PN)

- PN is lifesaving for many pediatric patients
- Associated with complications
  - Immediate
  - Long term
- PN process involves multiple disciplines and professions
- Potential for medication errors
- "High risk" therapy per Institute for Safe Medication Practices (ISMP)

PN Ordering and Compounding Concepts

To start writing the order

- Fluid rate
  - Maintenance
  - Other losses
    - Gastric
    - Wound
    - Chest tube
- Glucose tolerance
  - Stress
  - Medications (steroids)
  - Disease (pancreatitis)
- Underlying disease
  - Renal failure
  - Liver disease
- Access
  - Peripheral
    - Max peripheral osmolality (1000 – 1000 mOsm/L)
    - Limit dextrose (10 – 12.5%)
    - Limit K (40 mEq/L)
    - Limit Ca (10 – 20 mEq/L)
    - Limit amino acids, Na
    - Not quite CVL
  - CVL

Fluid (kcal) requirements

- < 1 - 1.5 kg
  - 150 ml/kg
- 1.5 - 2.5 kg
  - 120 ml/kg
- Up to 10 kg
  - 100 ml/kg
    - (up to 1000 ml)
- >10 – 20 kg
  - 1000 ml + 50 ml/kg for each kg from 10 – 20
    - (up to 1500 ml)
- >20 kg
  - 1500 ml + 20 ml/kg for each kg > 20

Holliday and Siegel, Pediatrics 1957
Protein

- Preterm infants: 3 – 3.5 g/kg/day
- Term infants: 2.5 – 3 g/kg/day
- Children: 1.5 – 2 g/kg/day
- Adolescents: 0.8 – 1.2 g/kg/day
- Increased needs with critical illness
- Limit to 2.5 g/kg/day (infants) with liver disease

Protein and Cysteine

- Pediatric amino acid product + cysteine for infants < 1 year of age
  - Trophamine
  - Premasol
  - Aminosyn PF
- Standard amino acid product for older children
  - Travasol
  - Aminosyn

Dextrose

- Limited to 10 – 12.5% in peripheral PN
- Up to 25% (or higher) in central PN
- Ideally should not exceed glucose oxidation rate or glucose infusion rate (GIR) in long term PN patients

Example PN Order

Glucose Infusion Rate

Glucose infusion rate or GIR (mg/kg/min) =

\[
\text{Dextrose (g/day)} \times 1000 / \left( 24 \text{ (h/day)} \times 60 \text{ (min/h)} \times \text{weight (kg)} \right)
\]

GIR

\[
\text{Dextrose (g/kg/day)} / 1.44
\]

\[
\text{GIR} = 13.9 \text{ mg/kg/min}
\]
Basic Compounding Concepts

- Components available in known concentrations
  - Amino acids (10 – 15%)
  - Dextrose (50 – 70%)
  - Calcium gluconate (~ 0.5 mEq/ml)
  - Electrolytes, vitamins/trace elements, other additives
- Sterile water to make the final volume of solution

Osmolarity of Parenteral Nutrients

- Amino acids 100 mOsm / %
- Dextrose 50 mOsm / %
- Lipids 1.7 mOsm / %
- Sodium, potassium 2 mOsm / mEq
- Calcium gluconate 1.4 mOsm / mEq
- Magnesium sulfate 1 mOsm / mEq

Example peripheral solution

3 kg infant on peripheral PN (300 ml volume):
- 10% dextrose 500 mOsm/L
- 2.5% AA 250 mOsm/L
- Na/K (2 mEq/kg each) 80 mOsm/L
- Ca (10 mEq/L) 10 mOsm/L
- Mg (0.4 mEq/kg) 4 mOsm/L

844 mOsm/L
44 kcal/kg/day (not including lipid calories)

Sodium

<table>
<thead>
<tr>
<th></th>
<th>meq/L</th>
<th>100 ml/kg</th>
<th>75 ml/kg</th>
</tr>
</thead>
<tbody>
<tr>
<td>1/4 NS</td>
<td>38.5</td>
<td>3.85 meq/kg</td>
<td>2.7 meq/kg</td>
</tr>
<tr>
<td>1/3 NS</td>
<td>51</td>
<td>5.1 meq/kg</td>
<td>2.8 meq/kg</td>
</tr>
<tr>
<td>1/2 NS</td>
<td>77</td>
<td>7.7 meq/kg</td>
<td>5.8 meq/kg</td>
</tr>
<tr>
<td>LR</td>
<td>130</td>
<td>13 meq/kg</td>
<td>9.8 meq/kg</td>
</tr>
<tr>
<td>NS</td>
<td>154</td>
<td>15.4 meq/kg</td>
<td>11.6 meq/kg</td>
</tr>
</tbody>
</table>

Usual dosing: 2 – 4 meq/kg

Na during AmphoB Therapy
Anion with Na and K

- Mostly use Cl
- Acetate (OAc)
  - Bicarbonate incompatible with PN (Ca & magnesium)
  - Precursor salt (e.g., acetate) converted in vivo to bicarbonate
- Generally give 0.5 – 1 meq/kg in VLBW neonates
- Increased needs with greater stool/ostomy output
- Phos
  - NaPO$_4$ preferred over KPO$_4$ (decreased aluminum content)

Calcium and Phosphorus

- Maximum mineral bone accretion in utero at ~ 36 wks gestation
- Impossible to give the minerals supplied in utero via PN due to Ca phosphate solubility
- Early studies evaluated how to simulate in utero accretion at lower doses
- 1.7 mg Ca:1 mg P ratio optimal (approximately 3 mEq Ca:1.3 mmol P)

Calcium and Phosphorus

- Calcium dosing (with appropriate phosphorus)
  - Young infants: 2.5 – 3.5 mEq/kg/day (in appropriate ratio with phosphorus)
  - Older infants, children: 1.5 – 2.5 mEq/kg/day
  - Adolescents: ≤ 1 meq/kg, 10 mEq/L of PN

- Phosphorous dosing
  - Young infants: 1 – 1.4 mmol/kg/day (in appropriate ratio with calcium)
  - Older infants, children: 1 mEq Ca/1 mmol P
  - Kcal intake: 15 mmol P/1000 kcal

Preventing Calcium Phosphate Solubility Issues

- Alteration of solution pH (decreased)
  - Pediatric amino acid solutions
  - Addition of L-cysteine
- Increased amino acid and dextrose concentrations
- Final concentrations of each
- Decreased solution temperature
- Utilize calcium phosphate solubility software
- Add phosphate product first, calcium product last
- Calcium gluconate preferred salt
- Filtering solution with 0.2 micron filter

% Dissociation of Ca Gluconate and Ca Chloride

D10%, standard amino acids, no cysteine

D10%, 2.4% pediatric amino acids + cysteine

**IV Fat Emulsion (IVFE)**

- Soybean oil based emulsion
- Primarily long chain fat
- Dose:
  - Term and preterm infants: up to 3 g/kg/day
  - Older children: < 30% total calories as fat
  - Liver disease: limit to 1 g/kg/day

**Novel IV Fat Emulsions**

- Omegaven (omega 3 fish oil) – not approved for use in US; must obtain under investigational IND
- Clinolipid (20% soybean oil/80% olive oil) – not approved for pediatric patients; clinical trial actively recruiting
- SMOF (soybean, MCT, olive oil, fish oil) – clinical trial underway

**Total Nutrient Admixtures (TNA)**

- Lipids are negatively charged particles
- Limits to Ca/P/Zn/Mg/Fe additions
- Stability is pH & multivalent cation dependent
- Cannot visualize particulates
- Cannot use 0.2 micron filter (use 1.2 micron)
- Not recommended in infants/children

**Total nutrient admixtures**

**Standardized or Premixed PN**
Standardized PN Solutions

- Also referred to as premixed PN
- Clinimix (amino acids, dextrose, electrolytes)
- Sulfite free, sterile, nonpyrogenic, hypertonic solutions
- 1 and 2 liter dual chamber bags
  - Amino acids with electrolytes
  - Dextrose with calcium
  - Seal must be broken and contents mixed well prior to administration
- For central and peripheral PN administration
- MVI added by the Le Bonheur pharmacy

Contents of Premixed PN Solutions Used at Le Bonheur

<table>
<thead>
<tr>
<th>Solution</th>
<th>Amino g (LC)</th>
<th>Dextrose g (LC)</th>
<th>Electrolytes mEq/L</th>
<th>Dextrose in 2L (g)</th>
</tr>
</thead>
<tbody>
<tr>
<td>3.5% AA/6% Dextrose + 4.25</td>
<td>15</td>
<td>70</td>
<td>70</td>
<td>1020</td>
</tr>
<tr>
<td>Electrolytes</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4.25% AA/8% Dextrose + 4.25</td>
<td>25</td>
<td>70</td>
<td>70</td>
<td>1020</td>
</tr>
</tbody>
</table>

*Electrolyte composition of all solutions contain:
- 36 mEq/L sodium
- 30 mEq/L potassium
- 5 mEq/L magnesium
- 4.5 mEq/L calcium
- 39 mEq/L chloride
- 15 mmol/L phosphate

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Clinimix use at Le Bonheur

- Retrospective review (Oct 2010 to April 2012)
- 69 patients received 74 courses of premixed PN
  - 5 patients received 2 separate courses
- Mean duration 5.6 ± 6.2 days (1-31)
- 15 courses (20%) required change to individualized PN

Characteristics of Patients Receiving Premixed PN (n=74)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yr)</td>
<td>1-18 (17)</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>4.9 ± 2.5 (1.5-15)</td>
</tr>
<tr>
<td>Sex (M:F)</td>
<td>36:38</td>
</tr>
<tr>
<td>Central venous access (%)</td>
<td>60 (80%)</td>
</tr>
<tr>
<td>Central access at PN initiation (%)</td>
<td>40 (53%)</td>
</tr>
<tr>
<td>Hospital unit</td>
<td>36 (50%)</td>
</tr>
<tr>
<td>Intensive care unit (%)</td>
<td>26 (35%)</td>
</tr>
<tr>
<td>General medical ward (%)</td>
<td>49 (67%)</td>
</tr>
<tr>
<td>Preoperative (%)</td>
<td>53 (72%)</td>
</tr>
<tr>
<td>Cancer</td>
<td>22 (30%)</td>
</tr>
<tr>
<td>Chronic disease (%)</td>
<td>31 (42%)</td>
</tr>
<tr>
<td>Urinary tract infection (%)</td>
<td>17 (23%)</td>
</tr>
<tr>
<td>Transplant (renal failure)</td>
<td>17 (23%)</td>
</tr>
<tr>
<td>Uncontrolled sepsis (%)</td>
<td>4 (5%)</td>
</tr>
<tr>
<td>Paraplegia</td>
<td>4 (5%)</td>
</tr>
</tbody>
</table>

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Electrolyte Imbalance Necessitating Change to Individualized PN (n=15)

<table>
<thead>
<tr>
<th>Electrolyte Imbalance</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Metabolic alkalosis</td>
<td>11 (73%)</td>
</tr>
<tr>
<td>Hypokalemia</td>
<td>2 (13%)</td>
</tr>
<tr>
<td>Hypophosphatemia</td>
<td>3 (20%)</td>
</tr>
<tr>
<td>Hypomagnesemia</td>
<td>2 (13%)</td>
</tr>
<tr>
<td>Hypophosphatemia and hypokalemia</td>
<td>1 (7%)</td>
</tr>
<tr>
<td>Hypophosphatemia and metabolic alkalosis</td>
<td>1 (7%)</td>
</tr>
</tbody>
</table>

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Metabolic alkalosis defined as elevated serum bicarbonate
Clinimix use at Le Bonheur: Nutrition Goals

- 49 patients received PN > 48 hours
  - 29% of patients received PN for ≤ 2 days

- Goal protein achieved in 48/49 (98%)
  - 1 patient made protein goals with supplemental EN

- Goal calories achieved in 33/49 (67%)
  - 7 initiated on EN and PN calories not advanced

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Reasons total caloric goals unmet by premixed PN (n=16)

<table>
<thead>
<tr>
<th>Reason</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peripheral access only</td>
<td>4 (25)</td>
</tr>
<tr>
<td>No lipids (request of consulting service)</td>
<td>2 (13)</td>
</tr>
<tr>
<td>No lipids due to lipid shortage and anticipated short PN course</td>
<td>1 (6)</td>
</tr>
<tr>
<td>Lipid intolerance</td>
<td>1 (6)</td>
</tr>
<tr>
<td>Anticipated short PN course</td>
<td>1 (6)</td>
</tr>
</tbody>
</table>

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Clinimix use at Le Bonheur

- Advantages
  - Conserves overall PN product supply
  - Cost savings to patient and hospital
  - Effective
  - Minimal compounding time / human manipulation

- Disadvantages
  - Fixed amount of electrolytes
  - Ca/phos dosing not ideal for infants
  - May require use of additional IVF

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Standardized PN: Triple Chamber Solutions

- Available January 2015
- Kabiven (central) and Perikabiven (peripheral)
- 3.3% amino acids, 9.7% dextrose, 3.9% lipids (Kabiven)
- 2.4% amino acids, 6.7% dextrose, 3.5% lipids (Perikabiven)
- Electrolyte composition not ideal
  - Lower Na
  - Lower calcium/phosphorus
  - Greater magnesium

Calculations
Counting Parenteral Kilocalories

- Dextrose = 3.4 kcal/g
  (\% dextrose \times \text{volume} = \text{g})

- Fat = 9 kcal/g

<table>
<thead>
<tr>
<th></th>
<th>10% IVFE</th>
<th>20% IVFE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fat kcal/ml</td>
<td>0.9</td>
<td>1.8</td>
</tr>
<tr>
<td>Glycerol kcal/ml</td>
<td>0.2</td>
<td>0.2</td>
</tr>
<tr>
<td>Total kcal/ml</td>
<td>1.1</td>
<td>2</td>
</tr>
</tbody>
</table>

- Protein = 4 kcal/g

Example Peripheral Solution: Calories

3 kg infant on peripheral PN (300 ml volume):

- 10% dextrose 102 kcal/day
- 2.5% amino acids 30 kcal/day

132 kcal/day divided by 3 kg = 44 kcal/kg/day
(calculation does not include lipid calories)

Example Calories: Lipids

- Lipids at 1 g/kg/day x 3 kg = 3 g/day
- 3 g + 20 g/100 mL (i.e., 20\% emulsion) = 15 mL
- 15 mL/24 hours = 0.625 mL/hr
- Round rate to 0.6 mL/hr x 24 hrs/day = 14.4 mL
- 14.4 mL/day x 2 kcal/mL = 28.8 kcal/day or 9.6 kcal/kg/day

Long Term Management: CIRCLE

- Children’s Intestinal Rehabilitation Center at Le Bonheur (CIRCLE)
  - Interprofessional team
  - Goal to improve intestinal rehabilitation through care coordination
  - Clinic for outpatients twice per month since 2010
- CIRCLE inpatient service started July 2015
  - Covered by pediatric gastroenterologists (Drs. Corkins, Lazar, Sevilla)
  - See existing CIRCLE inpatients, CIRCLE outpatients admitted to Le Bonheur, and any inpatient consults
  - If a CIRCLE patient is admitted under your care, please consult CIRCLE Service

PN Safety

PN and Past Medication Errors

- Deaths in home patients related to Ca/P precipitation and pulmonary emboli
- Death of patient receiving 50% dextrose for 2 days
- Infant deaths related to incorrect dextrose %
- Irreversible brain damage in a neonate receiving PN with no dextrose
- Iron overload and liver toxicity in a child receiving iron dextran via PN

PN and Past Medication Errors

- Infection in children (2 deaths) from contaminated PN
- NICU outbreak related to contaminated IV lipids
- Death of a child receiving high potassium PN at home
- Magnesium toxicity in 2 premature infants related to compounder malfunction
- Death of a preterm infant due to zinc overload/toxicity
- Death of a toddler due to heparin overdose

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Fatal 1,000-fold overdoses can occur, particularly in neonates, by transposing mcg and mg.

September 6, 2007

6 week old infant dies after receiving PN with 60 times more sodium than prescribed.

April 11, 2011

Contaminated PN solutions lead to deaths in Alabama hospitals.

April 11, 2011

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PN Safety at Le Bonheur

- PN solutions compounded at Le Bonheur
  - also for Methodist Glown and South NICUs
- CPOE / Abacus software system for PN
- Standardized PN process for Methodist / Le Bonheur system
  - Standard order form
  - Standard limits for pediatric patients

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PN Safety at Le Bonheur

- PN additives ordered as amount per kg per day
- Abacus system limits
  - Neonates, peds < 40 kg or > 40 kg
  - Central v. peripheral access
- Multiple double check systems in place
  - Physician to PN Service
  - PN Service to Pharmacy
  - Nursing to PN Service and Pharmacy

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Compounder Limits

- Inherent system limits generally prevent large errors
- Institution specific limits can allow a more specific supplementation range

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Pharmacist writes paper PN order with Physician co-signature

Pharmacist enters PN order into compounder software program; faxes order to pharmacy

IV pharmacist verifies faxed order against compounder order

Second pharmacist verification

PN compounded

IV pharmacist checks compounded PN against paper order, compounder label and compounder report

PN infused to Patient at 8PM

Nurse checks PN label against paper order prior to infusion
### Le Bonheur System Limits

<table>
<thead>
<tr>
<th>Additive</th>
<th>&lt;1 yr Central</th>
<th>≤ 1 yr Peripheral</th>
<th>Peds ≤ 40 kg Central</th>
<th>Peds ≤ 40 kg Peripheral</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calcium per day</td>
<td>40 mEq/day</td>
<td>40 mEq/day</td>
<td>60 mEq/day</td>
<td>60 mEq/day</td>
</tr>
<tr>
<td>Calcium per kg</td>
<td>1.1 mEq/kg</td>
<td>0.7 mEq/kg</td>
<td>1.1 mEq/kg</td>
<td>0.7 mEq/kg</td>
</tr>
<tr>
<td>Calcium per L</td>
<td>0.06 mEq/L</td>
<td>0.06 mEq/L</td>
<td>0.06 mEq/L</td>
<td>0.06 mEq/L</td>
</tr>
<tr>
<td>Magnesium per kg</td>
<td>0.06 mEq/kg</td>
<td>0.06 mEq/kg</td>
<td>0.06 mEq/kg</td>
<td>0.06 mEq/kg</td>
</tr>
<tr>
<td>Magnesium per L</td>
<td>NA</td>
<td>NA</td>
<td>12.1 mEq/L</td>
<td>12.1 mEq/L</td>
</tr>
</tbody>
</table>

### Le Bonheur System Limits: Zinc

<table>
<thead>
<tr>
<th>Additive</th>
<th>&lt;1 yr Central</th>
<th>≤ 1 yr Peripheral</th>
<th>Peds ≤ 40 kg Central</th>
<th>Peds ≤ 40 kg Peripheral</th>
</tr>
</thead>
<tbody>
<tr>
<td>Zinc per day</td>
<td>6.1 mg/day</td>
<td>6.1 mg/day</td>
<td>6.1 mg/day</td>
<td>6.1 mg/day</td>
</tr>
<tr>
<td>Zinc per kg</td>
<td>0.05 mg/kg</td>
<td>0.05 mg/kg</td>
<td>0.05 mg/kg</td>
<td>0.05 mg/kg</td>
</tr>
</tbody>
</table>

### Home PN and Errors

- Dextrose % much lower than prescribed
- Phosphorous and/or calcium removed from PN
- Protein product substitution
- PNs compounded as TNAs with potentially unstable concentrations of base components and additives
- PNs mixed with incorrect dextrose concentration
- Over or under doses prescribed when transcribing to home PN order form
- PN solutions not delivered to home

### Discharge on Home PN

- Complicated process
- Multiple disciplines involved
- Potential for errors throughout process
- Need to assess competency of the home care companies
- Plan in place for appropriate follow-up and monitoring
- Initial and periodic review of home PN orders

**COMMUNICATION IS KEY TO A SAFE DISCHARGE!!**