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# Nutrition Strategies for Managing Intestinal Rehabilitation in Short Bowel Syndrome Patients

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BEST CHILDREN'S HOSPITALS U.S.News & WORLD REPORT RANKED IN 9 SPECIALTIES 2023-2024

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# Disclosures

- Speaker's bureau
  - Alcresta Therapeutics
  - Abbott Nutrition
  - Nutricia North America
  - Takeda

# Objectives

- Understand the role nutrition plays in the intestinal adaptation process
- Explore the transition from parenteral to enteral nutrition in infants with SBS
- Discuss how micro and macronutrients can address malnutrition with short bowel syndrome
- Review a case study on an infant transitioning from PN to an amino acid-based formula

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# Nutritional Strategies
# What formula and Why?

# Case Study

- This is a 5-month-old patient who presented for a second opinion with a history of NEC
- 55 cm of intestinal plus the entire colon
- Advancement has been limited by diarrhea including episodes of blood being in the stool.
- Infant initially on a extensively hydrolyzed formula for the last 3 months
- Continues to have  intermittent blood in the stool in addition to diaper rash/diarrhea

- Next Steps…

# Formula/Protein

- No significant difference in absorption between hydrolyzed and non-hydrolyzed formulas.
  - N=10 infants randomized crossover study
  - No difference in nitrogen balance or intestinal permeability
- Short bowel syndrome
  - Hydrolyzed and amino acid-based formulas
    - Non-IgE-mediated milk protein allergy in patients with short bowel syndrome
  - Shorter duration of TPN dependence
    - Amino acid-based formulas, Breast milk



Ksiazyk et al. *JPGN*. 2002; Andorsky et al. *J Pediatr.* 2001; 139:27-33; Bines et al. *JPGN.* 1998; 27(5):614-616; Degreef et al. *Journal of Nutrition and Metabolism.* 2010; Kaufman et al. *J Pediatr.* 1997;131:356-61.

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# Stimulants of Adaptation

- **Enteral nutrition**
  - Absence of enteral nutrition
    - Mucosa atrophies
    - Decreases in enzyme and nutrient transporter activity
  - Long Chain Triglyceride
    - Enhance intestinal hyperplasia
  - Short chain fatty acids
    - Increase nutrient transporter expression and absorption



*Best Prac & Res Clinical Gastro.* 2016:30:249-261.

# Fat

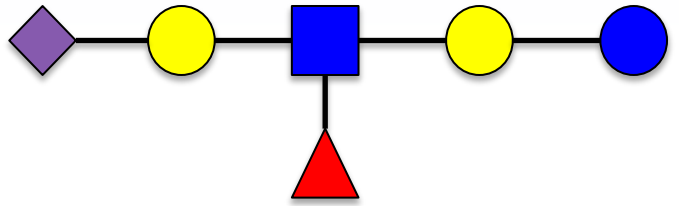
- Long chain Triglycerides (LCT)
  - Require bile acids to absorb LCT
  - Ileal resection, loss of enterohepatic circulation
- Medium Chain Triglycerides (MCT) can be directly absorbed
  - Slightly less calories
  - Less helpful adaptation
  - Improved absorption in preserved colon
- Elemental and casein hydrolysate formulas
  - High in MCT
  - More calories from fat even in setting of malabsorption, intestinal resection

**Fat composition in the formula**



DiBaise et al. *Am J of Gastro.* 2004;99;1823-1832; Jeppesen and Mortensen. *Gut*. 1998;478-483

# Human Milk Oligosaccharides (HMO)



- > 200 human milk oligosaccharides
- Carbohydrate polymers
- 3rd most common component after carbohydrates and lipids, > protein
- Minimal present in bovine based formula
- Components
  - Glucose, Galactose
  - N-acetylglucasamine, Fucose
  - N-acetylneuraminic acid

Image Credit from Bode lab. www.bodelab.com.

# Human Milk: Nucleotides

- Nucleotides
  - 2-5% of the nonprotein fraction of breast milk
  - Provide important cellular and metabolism functions
- Highest components
  - Cytidine 5' MNP (CMP)
  - Uridine 5'monophosphate
  - Adenosine 5' monophosphate
  - Guanosine 5' monophosphate
  - Inosine 5' monophosphate
- Vary depending on the individual, Time of year, stage of lactation



Hodgkinson et al *Nutrition Research* 2022;99:13-24

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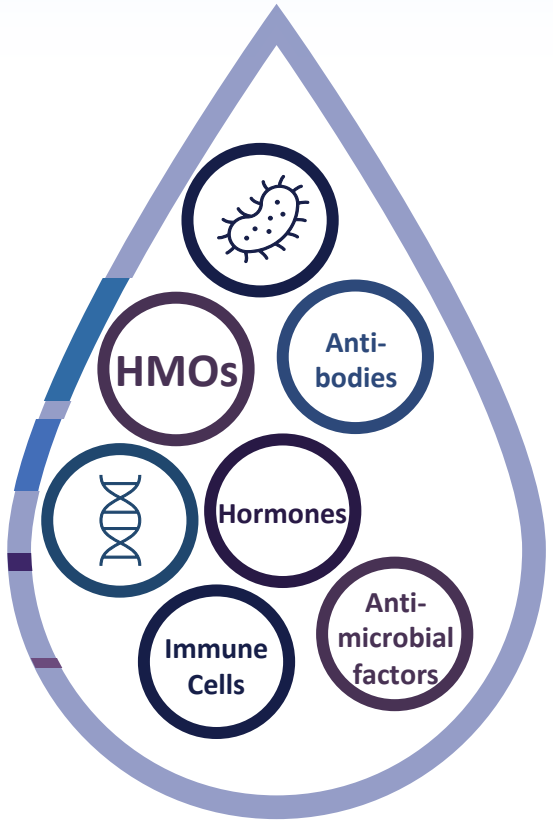
# Role of Nucleotides

**The FDA does not set recommended levels of nucleotides for infant formula.**

Nucleotides are not essential.
**HOWEVER, during periods of rapid growth or disease, nucleotide synthesis may not be able to keep up with demand.**

- Intestinal growth and differentiation
- Intestinal repair
- Somatic growth
- Iron absorption
- Intestinal flora
- Lipid metabolism
- Immune function




**HUMAN MILK COMPOSITION**



(1) Abrams S, Bergner EM. Is it time to review the current nutrient requirements for infant formulas principally established in 1980? *Adv Nutr*. 2023. (2) Hodgkinson A, et al. Nucleotides: an updated review of their concentration in breastmilk. *Nutr Res*. 2022;99:13-24. (3) Thorell, et al. Pediatr Res. 1996;40:845-52. (4)Thorell et al. reported a mean of 54mg/l (5.4mg/100ml) in milk collected between 3 and 24 weeks lactation.

# Not all formulas are equal

| Feeding Substrate | Nucleotide Content |
|---|---|
| Human Milk | 5.4 mg/100 mL |
| Energy and Nutrient Dense Formula | 4.3 mg/100 mL |
| Amino Acid Infant Formula with DHA/ARA | 2.86 mg/100 mL* |
| Extensively Hydrolyzed Infant Formula | 2.4 mg/100 mL* |

** When prepared at standard dilution of 20 kcal/fl oz*

Common nucleotides added to formula:

- cytidine 5′-monophosphate
- disodium uridine 5′-monophosphate
- adenosine 5′-monophosphate
- disodium guanosine 5′-monophosphate



Hodgkinson A, et al. Nucleotides: an updated review of their concentration in breastmilk. *Nutr Res*. 2022;99:13-24[13]

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## Next Steps…

- Allergy, non IgE mediated
- Elemental formula
  - Amino acid-based infant formula with nucleotides
  - Bleeding resolved over the next 3-4 weeks with better enteral tolerance

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- **Elemental formula**
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# Enteral Regimen/Diet

- Amino Acid/hydrolysate/breast milk
  - 20 kcal/oz-30 kcal/oz
- May dilute to 10 or 15 kcal/oz
  - Decreasing the osmotic load to reduce diarrhea
- Avoid fruit juices/fruits
  - Worsen D-lactic acidosis
  - Diarrhea
- More concentrated the formula the increased chance of osmotic diarrhea

# Fiber

- Soluble fiber is fermented by colonic bacteria
  - Short chain fatty acids; acetate, butyrate, proprionate
    - Colonocyte fuel/health
    - Enterocyte proliferation
    - Water and sodium resabsorption
- Delays gastric emptying
- Decreases gut transit
- Increase fluid absorption decreasing fluid losses





Drenckpohl et al. *Nutr in Clin Practice.* 2005:20:674-7; Alam et al. *Arch Dis Child.* 2005;90:195-9.

# Blended Formula

- Many commercial blended feeds now available
  - Some are milk free and also free of other possible allergens (soy, nuts)
- May or may not be nutritionally complete
- No universal viscosity
  - May need slight warming before hanging or dilution with water or oral rehydration solution
- Calorically dense and will need dilution for tolerance
  - mOsm of pediatric free amino acid formula at standard dilution is ~550/kg H2O
  - mOsm of blended formula ~482/kg H2O

# Transition to Blenderized Formulas

9/10 transitioned to 100%
7/9 entire colon present
Average of 67 days

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**Feeding outcomes and history from 10 patients with intestinal failure who transitioned to tube feeding formula with real food ingredients**

| Patient | Days[1] | Age[2] (months) | Gender | Gestational Age (weeks) | Diagnosis | Bowel length (cm) | Ileocecal Valve[3] | Colon | Previous Formula | Dairy Exposure | 1 yr Weight gain (kg) |
|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | 17 | 12 | F | 36 | Gastroschisis | All | X | All | AAF | Y | 1.86 |
| 2 | 18 | 16 | F | 37 | Gastroschisis/malrotation | 38 | | Partial | AAF | Y | 4.8 |
| 3 | 322 | 32 | F | 25 | NEC | 47 | X | Partial | AAF | N | 2.6 |
| 4 | 17 | 30 | M | 24 | NEC | 63 | X | All | AAF | N | 2.5 |
| 5 | Failed | 18 | F | 24 | NEC | All | | Partial | AAF | N | n/a |
| 6 | 98 | 23 | F | 38 | Atresia/malrotation | All | X | All | AAF | N | 1.3 |
| 7 | 2 | 30 | M | 28 | NEC | 34 | X | All | HF | Y | 2.6 |
| 8 | 16 | 18 | F | 26 | NEC | 52 | X | All | AAF | N | 3.66 |
| 9 | 26 | 30 | F | 24 | NEC | 46 | X | All | AAF | Y | 3 |
| 10 | 90 | 72 | F | 33 | Atresia/malrotation | 45 | X | All | HF | Y | 1 |

F = female; M= male; NEC = necrotizing enterocolitis; AAF= Amino acid-based formula; HF = hydrolyzed formula
[1]Days to transition to tube feeding formula with real food ingredients
[2]Age at transition
[3]X= yes

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*Table adapted from Nutr Clin Pract.* 2017;32:277-281.

# Blenderized Formulas

## Patient symptoms on commercially available blenderized feedings

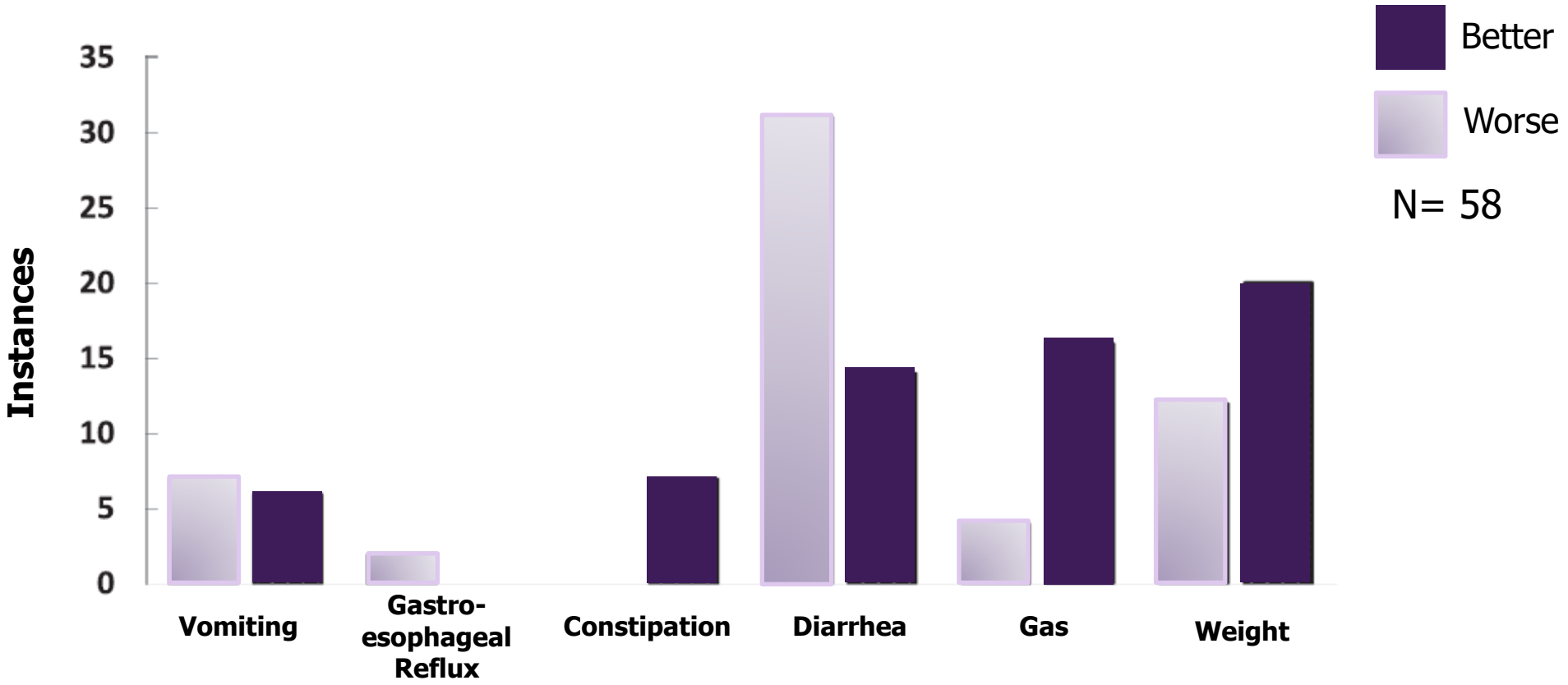


Figure adapted from Zong et al. *Nutr Clin Pract*. 2022;37:913-920.

# Route of feedings

- Continuous feedings can be beneficial
  - Nasogastric vs Gastric
  - Combination or continuous/bolus feedings
    - May encourage oral skills
- Shorter the remnant bowel, the less likely to tolerate bolus or oral feedings
- GER or motility disorders are common
  - Nasojejunal/Gastrojejunal
- If volume sensitive
  - More concentrated formulas 24 kcal/oz or greater
  - Increase caloric intake without increasing volume/fluid load especially in sensitive children

# Formula Additives

Electrolyte additives:

- Sodium Chloride (table salt)
- ~100 mEq/ teaspoon

- Na Bicarbonate (Baking Soda)
- ~60 mEq/ teaspoon

Fat/CHO Modulars:

- Duocal Powdered carbohydrate®
- 59% CHO, 41% Fat (35% MCT)
  - No protein
  - 42 kcal/tablespoon
- Liquigen®
  - Emulsified MCT
  - 67.5 kcal/tablespoon
- Vegetable/Coconut/Olive Oil
  - 128 kcal/tablespoon

# Management of Intestinal Failure Patient

- What route?
  - NG, G-tube, GJ, NJ tube
- What Formula?
  - MCT vs LCT
  - Osmotic
  - Fiber content
- Advancement of feedings
  - Consider changing formula
  - Addition of fiber supplements
- Diarrhea
  - Formula
  - Fiber Supplements
  - Anti-motility agents

# TPN Management

# Components of Nutritional Support

- **TPN**
  - **Macronutrients**
  - **Electrolytes**
  - **Vitamins**
  - **Trace Elements**
  - **Lipid minimization/alternative lipids**

- Enteral Nutrition
  - Type – Polymeric, Extensively hydrolyzed, Amino-Acids, Blenderized
  - Route-NG, NJ G, GJ

**Hurt et al.** ***J Parenter Enteral Nutr.*** **2011;35(5 Suppl):60S-72S.**

# Writing your Parenteral Nutrition

# Pediatric GI Electrolyte Losses

| | Sodium *(mEq/L)* | Potassium *(mEq/L)* | Chloride (mEq/L) | Bicarbonate (mEq/L) |
|---|---|---|---|---|
| Gastric | 140 | 15 | 155 | - |
| Ileostomy | 80-140 | 15 | 115 | 40 |
| Colostomy | 50-80 | 10-30 | 40 | 20-25 |
| Secretory | 60-120 | | | |
| Diarrhea | 30-40 | 10-80 | 10-110 | 30 |
| Normal Stool | 5 | 10 | 10 | 0 |

Wessel et al. *Semin Perinatol.* 2007;31(2):104-11.

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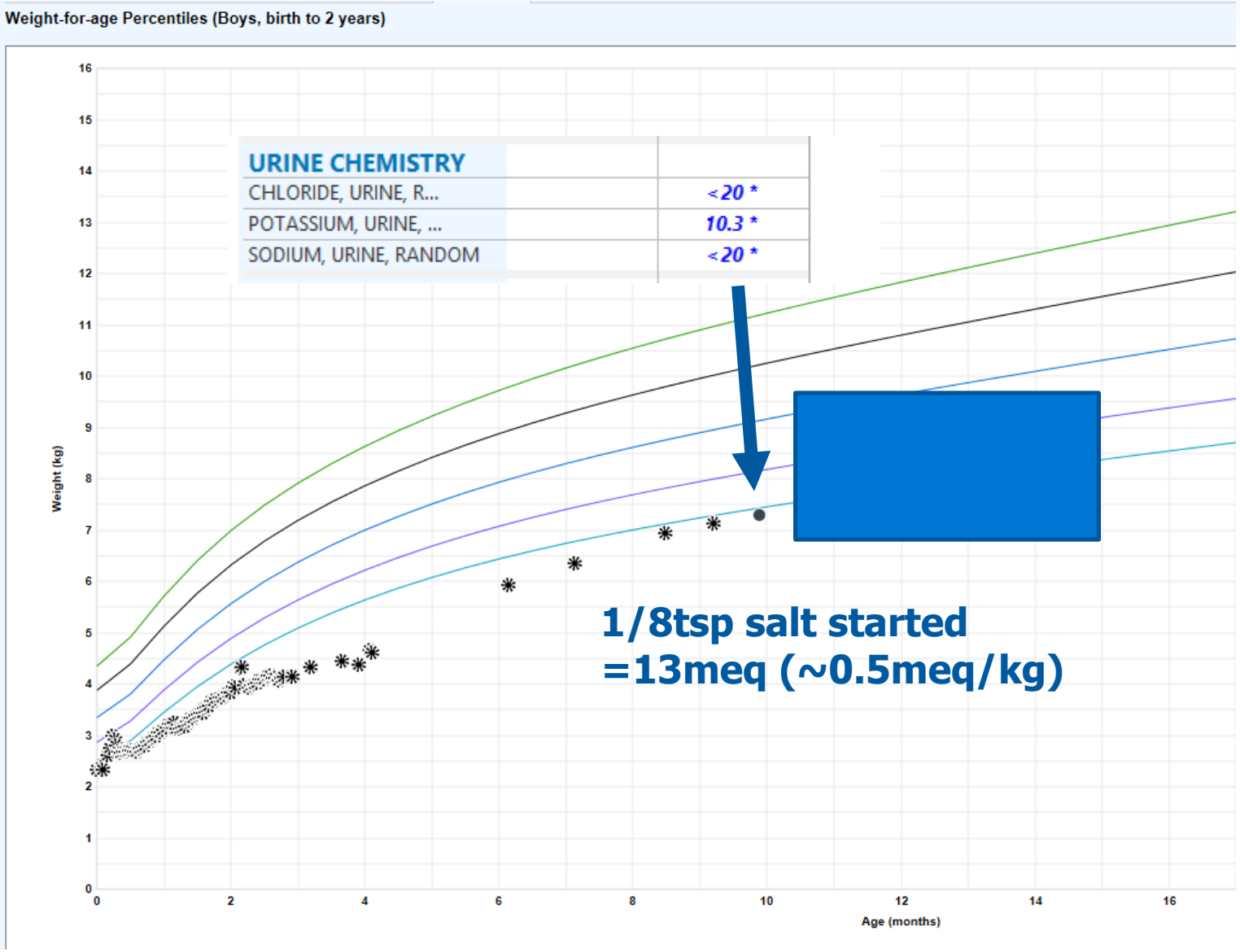
# Urine electrolytes

- Na,K-ATPase (sodium pump)
- Urine $Na^+$, $Cl^-$, and $K^+$
  - Weekly while in-patient
- Total body Na+ <u>replete</u>:
  - $Na^+ > 40$ mEq/L
  - $K^+ < 2 \times Na$
- Total body $Na^+$ <u>depletion</u>:
  - $Na^+ < 40$ mEq/L
  - $K^+ > 2 \times Na$
- If deplete, kidneys are spilling potassium to conserve sodium

| URINE CHEMISTRY | | |
|---|---|---|
| CHLORIDE, URINE, R... | *<20 ** | *37 ** |
| POTASSIUM, URINE, ... | *10.8 ** | *22.0 ** |
| SODIUM, URINE, RANDOM | *29 ** | *75 ** |


Weight-for-age Percentiles (Boys, birth to 2 years)
URINE CHEMISTRY
CHLORIDE, URINE, R... <20 *
POTASSIUM, URINE, ... 10.3 *
SODIUM, URINE, RANDOM <20 *
1/8tsp salt started
=13meq (~0.5meq/kg)
Weight (kg)
Age (months)
0
1
2
3
4
5
6
7
8
9
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16
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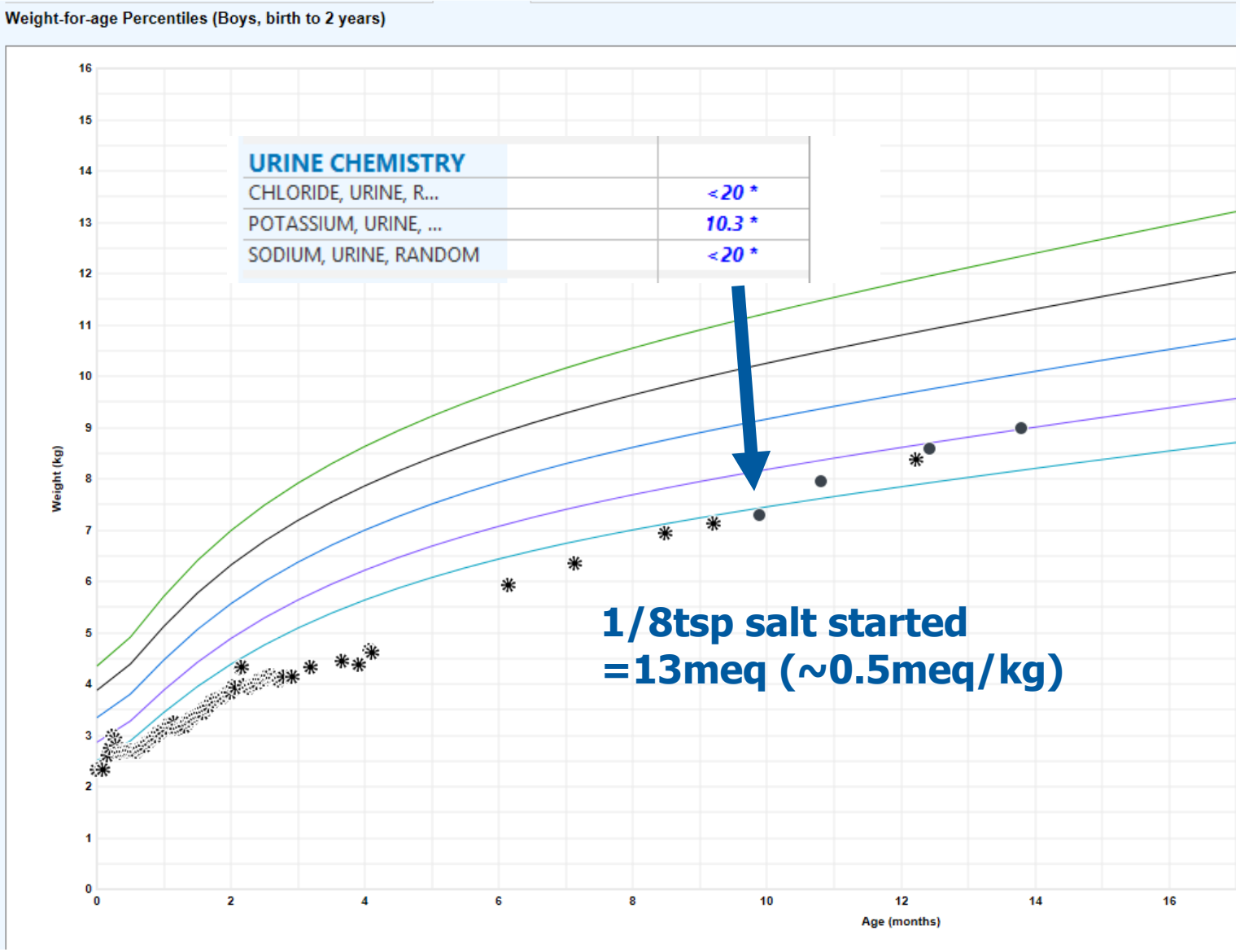
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# Stool output replacement

- Baseline 40 ml/kg/day from rectum
- Accept up to 60 ml/kg/day  from a stoma
- Calculate the maintenance fluid and incorporate the average amount of output into the TPN to minimize replacement
- Patient is positive by 100 ml/daily and is receiving maintenance fluids
  - Consider adding an additional 10 ml/kg of fluids
  - Patient is positive by 600 ml/day and stool output is 45 ml/kg/ day
  - Receiving 75 ml of replacement each day
    - Increase the replacement regimen 60 ml/kg/day

# Macronutrients

# Dextrose

- Dextrose is 3.4 kcal/gram
- Provides 50-60% of caloric intake
- Glucose Infusion Rate (GIR): mg/kg/min
  - How quickly dextrose is delivered to the patient
- Excessive GIR can result in hyperglycemia, hypertriglyceridemia, fatty liver or excessive CO2 production

GOAL GIR

Premature infant: 8-12mg/kg/min

Infant: 12-14mg/kg/min

Child (1-10yrs): 8-10mg/kg/min

(11-18yrs): 5-6mg/kg/min

**MAX**: 12-16mg/kg/min

# Calculating Glucose Infusion Rate (GIR)

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- Version 1: mg/kg/min

- Version 2: $\frac{\text{Dex \% x highest rate of TPN}}{6 \times \text{kg}}$

- Example:

  TPN order: 798mL (@42mL/hr x 18 hours + 2hrs of ramps= 20 hours), D12% (95.76 grams), weight: 8kg

  - Version 1: 95.76 grams dex x 1000= 95760mg/8kg/1140minutes= 10.5
    - 1140 minutes= 19 hours, I use 19 hours because the TPN is 18 hours + 2 hour ramps= 20 hours

  - Version 2: $\frac{12 \times 42}{6 \times 8} = 10.5$

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# Amino Acids

- Amino acids are 4 kcal/gram
- Provides 10-20% of total daily calories
- Excessive amino acid infusions (>4g/kg/day) may result in azotemia
  - High level of nitrogen containing compounds in the blood
- Trophamine
  - Under 10kg
  - liver dysfunction
  - Burns
  - Sepsis
- Plenamine
  - Pediatric patients >10kg
  - Adults >18yrs

# Lipids

- Typically 20-40% of daily calories
- Do not exceed >60% of daily calories from fat due to risk for ketosis
- Provides 10 Cal/gram
- Prevents essential fatty acid deficiency by providing Linoleic Acid (omega 6) and A-Linolenic Acid (omega 3)
- Monitor TG when advancing IV lipid solutions
  - Hold lipids if TG >500
- Lipid choices
  - Intralipid®
  - SMOF®
  - Omegaven®

# Comparison of commercially available lipid emulsions in the United States

| Oil | Intralipid | Omegaven | SMOFlipid |
|---|---|---|---|
| Approved for pediatric use | Yes | Yes | Yes |
| Soybean | 100% | | 30% |
| MCT | | | 30% |
| Olive | | | 25% |
| Fish | | 100% | 15% |
| Essential Fatty Acids (% by weight) | | | |
| Linoleic | 50 | 4.4 | 21.4 |
| α-Linolenic | 9 | 1.8 | 2.5 |
| EPA | 0 | 19.2 | 3 |
| DHA | 0 | 12.1 | 2 |
| ARA | 0 | 1-4 | 0.15-0.6 |

SMOF= soybean, medium-chain triglyceride, olive oil, fish oil; MCT= medium chain triglyceride; EPA= eicosapentaenoic acid; DHA= docosohexaenoic acid; ARA= arachidonic acid


# Therapies

- Lipid Minimization
  - 1 gm/kg/day or withdrawal of SOLE
  - Risk for EFAD
- Composite Lipid Emulsions
  - Have less phytosterols
  - 2.5-3 gm/kg/day of SMOF= at risk for EFAD if minimize
- Omegaven
  - 1 gm/kg

# Short bowel syndrome/IBD: Nutrition prescription

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- Macronutrient needs: degree of malabsorption may lead to higher nutrition needs
- Fluid needs: Maintenance x 1.2-1.5 depending on stool output/ostomy
- TPN:
  - CHO: keep GIR <15mg/kg/min
  - Protein: infant up to 3.5-4g/kg post-surgery; children: 1.5-3g/kg
  - Fat: provide < 30-40% of total kcals (Intralipid, Omegaven, SMOF)
- EN:
  - Continuous feedings preferred, slow, controlled advancement
- Oral feeds: Start small amounts ASAP to maintain oral feeding skills
  - Focus on proteins, vegetables, limit simple carbohydrates

# Monitoring

- Growth
  - Weight
  - Length/height
  - Head circumference
- Laboratory
  - Electrolytes/minerals
  - Triglycerides
  - Liver and renal function
  - Hemoglobin
- Long Term TPN monitoring
  - Trace elements (copper, zinc, selenium), carnitine and vitamin levels
  - Iodine
  - Fatty acid profile

**Use the Gut when Possible**

# References

Drenckpohl et al. *Nutr in Clin Practice.* 2005:20:674-7;
Alam et al. *Arch Dis Child.* 2005;90:195-9.
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# Questions???