Components of PN

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Typical Nutritional Components of PN

Water

Macronutrients

- Protein
- Carbohydrate
- Fat

Micronutrients

- Electrolytes & Minerals
- Vitamins
- Trace elements

Other additives

- Heparin
- Cysteine
- Carnitine
- Medications (e.g., famotidine, insulin)

PN Macronutrients

- Three major macronutrients
  - Carbohydrates (Dextrose)
  - Fat (Intravenous Lipid Emulsion - ILE)
  - Protein (Amino Acids - AA)

- Macronutrients may be combined in PN solution as follows
  - 2-in-1: Dextrose + AA (lipids administered separately)
  - 3-in-1: Dextrose + AA + Lipids

Components of PN: Macronutrient Guidelines - Infants

Infants (< 1 yr)	Initiation		Advance By		Goals	
	Preterm	Term	Preterm	Term	Preterm	Term
Protein (g/kg/day)*	1 – 3 (3 – 4 max)	2.5 – 3	_	_	3 – 4	2.5 – 3
Dextrose (mg/kg/min)	6 – 8	6 – 8	1 – 2	1 – 2	10 – 14 (max 14 – 18)	10 – 14 (max 14 – 18)
ILE (g/kg/day)**	0.5 – 1	0.5 – 1	0.5 – 1	0.5 – 1	3 (max 0.15 g/kg/hr)	2.5 – 3 (max 0.15 g/kg/hr)

*Protein can be initiated at goal. **ILE doses based on soybean oil emulsion.

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Corkins MR, *et al. The A.S.P.E.N. Pediatric Nutrition Support Core Curriculum*, 2nd Ed. ASPEN;2015.

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Components of PN: Macronutrient Guidelines - Children

Children (1-10 yr)	Initiation	Advance By	Goals
Protein (g/kg/day)	1.5 – 2.5	–	1.5 – 2.5
Dextrose (mg/kg/min)	3 – 6	1 – 2	8 – 10
ILE (g/kg/day)**	1 – 2	0.5 – 1	2 – 2.5

**ILE doses based on soybean oil emulsion.

Corkins MR, *et al. The A.S.P.E.N. Pediatric Nutrition Support Core Curriculum*, 2nd Ed. ASPEN;2015.

Components of PN: Macronutrient Guidelines – Adolescents

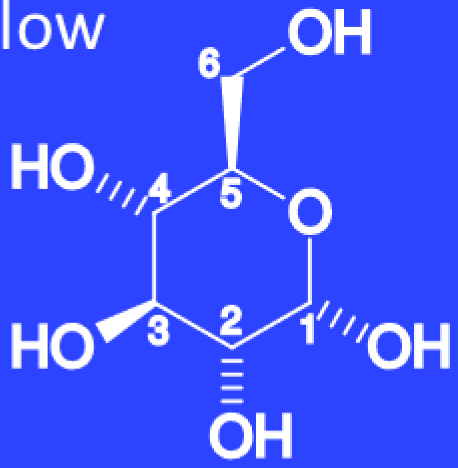
Adolescents	Initiation	Advance By	Goals
Protein (g/kg/day)	0.8 – 2	–	0.8 – 2
Dextrose (mg/kg/min)	2.5 – 3	1 – 2	5 – 6
ILE (g/kg/day)**	1	1	1 – 2

**ILE doses based on soybean oil emulsion.

Corkins MR, *et al. The A.S.P.E.N. Pediatric Nutrition Support Core Curriculum*, 2nd Ed. ASPEN;2015.

Macronutrients: Carbohydrates

- Dextrose (D-glucose monohydrate) is the primary carbohydrate
  - Monohydrate form provides 3.4 kcal/g
  - Enteral carbohydrates provide approximately 4 cal/g
- Typically, 40-55% of caloric intake comes from dextrose
- Intravenous dextrose must be slowly introduced to allow appropriate endogenous insulin response
- Toxicity
  - Hyperglycemia, glucosuria and osmotic diuresis
- Glucose provision typically expressed as % dextrose



Glucose Infusion Rate (GIR)

- GIR needs vary with age of patient
- GIR (mg/kg/min) = (Dextrose (g/dL) x Infusion Rate (mL/hr) x 0.167)/wt(kg)
- Typical glucose oxidation rate under most circumstances = 7-13mg/kg/min
  - Beyond this, fat synthesis increases leading to increased respiratory quotient (RQ: CO_2/O_2)
  - In the presence of pulmonary disease, large energy intake may lead to CO_2 retention
- Glucose oxidation rate changes with GIR based on age
  - Neonates, infants: 12.5 mg/kg/min
  - Children, adolescents: 6 mg/kg/min

Bresson JL, *et al. Pediatr Res.* 1989;25(6):645-48.

GIR – Cont'd

- Multiple online calculators exist
- Online tools may allow calculation of total GIR across multiple infusions with different dextrose concentrations
(i.e., dextrose-containing fluids + PN + compounded medication solutions)
- www.nicutools.org ("glucose delivery")

Bresson JL, *et al. Pediatr Res.* 1989;25(6):645-48.

Macronutrients: Dextrose / GIR Minimum Requirements

Minimum Dextrose Requirements Based On Age

Age	GIR (mg/kg/min)	g/kg/day
Newborn	7.9	11.5
Children	4.7	6.8
Adolescents	1.9	2.7
Adult	1.0	1.4

- These are the estimated minimum dextrose intakes to meet energy needs of the brain and other glucose-dependent organs
- If patients develop persistent hyperglycemia (>180mg/dL) at these minimum levels, consider providing insulin therapy based on GIR instead of further reduction of dextrose concentration

Corkins MR, *et al. The A.S.P.E.N. Pediatric Nutrition Support Core Curriculum*, 2nd Ed. ASPEN;2015.
Jones MO, *et al. J Pediatr Surg.* 1993;28(9):1121-25.

Macronutrients: Protein

- Major physiological functions of protein
  - Structure (i.e., muscle)
  - Function (i.e., enzymes, transport proteins)
  - Nitrogen donor to other compounds (i.e., nucleic acids, carnitine, taurine)
- Protein should not be considered a main energy source
- Protein requirements vary by age and disease state

Kashyap S. *Curr Opin Pediatr.* 2008;20(2):132-36.

Macronutrients: Amino Acid (AA) Solutions

- Infant protein needs
  - Conditional AA needed: histidine, taurine, cysteine
    - Immature synthetic abilities
    - Cysteine added in infants < 1 kg to improve nitrogen balance
      - Also decreases PN solution pH, allowing more calcium and phosphate to be added
  - Infant AA solutions are modelled off the serum AA patterns seen in breastfed infants
    - Further study of infant AA requirements ongoing
  - Excess protein intake leads to azotemia (elevated blood urea nitrogen, other compounds in blood)

Kashyap S. *Curr Opin Pediatr.* 2008;20(2):132-36.

Examples of AA Solutions (per 100 mL)

	Amino acid	Aminosyn II®	Novamine® 10%	Premasol® 10%	Trophamine® 10%	Aminosyn® PF	Travasol®
Essential	Isoleucine (g)	0.72	0.6	0.82	0.82	0.76	0.6
	Leucine (g)	0.94	0.73	1.4	1.4	1.2	0.73
	Lysine (g)	0.72	0.58	0.82	0.82	0.677	0.58
	Methionine (g)	0.40	0.40	0.34	0.34	0.18	0.40
	Phenylalanine (g)	0.44	0.56	0.48	0.48	0.427	0.56
	Threonine (g)	0.52	0.42	0.42	0.42	0.512	0.42
	Tryptophan (g)	0.16	0.18	0.20	0.20	0.18	0.18
	Valine (g)	0.8	0.58	0.78	0.78	0.673	0.58

Examples of Amino Acid Solutions (per 100 mL)

	Amino acid	Aminosyn II®	Novamine® 10%	Premasol® 10%	Trophamine® 10%	Aminosyn® PF	Travasol®
Nonessential	Aspartic Acid (g)	-	-	0.32	0.32	0.527	-
	Serine (g)	0.42	0.50	0.38	0.38	0.495	0.50
	Glutamic Acid (g)	-		0.50	0.50	0.82	-
	Alanine (g)	1.28	2.07	0.54	0.54	0.698	2.07
	Proline (g)	0.86	0.68	0.68	0.68	0.812	0.68
Conditionally Essential	Arginine (g)	0.98	1.15	1.2	1.2	1.227	1.15
	Glycine (g)	1.28	1.03	0.36	0.36	0.385	1.03
	Glutamine (g)	-	-	0.50	0.50	-	-
	Taurine (g)	-	-	0.025	0.025	0.070	-
	Cysteine (g)	-	-	< 0.016	< 0.016	-	-
	Histidine (g)	0.3	0.48	0.48	0.48	0.31	0.48
	Tyrosine (g)	0.444	0.04	0.24	0.24	0.044	0.04

Conditions With Altered Protein Needs

- Increased protein needs (from RDA)
  - Malnutrition
  - Enteric/urinary protein losses
  - Physiologic stress
  - Drugs (i.e., corticosteroids)
  - Burns

Macronutrients: Intravenous Fat Emulsions (ILE)

- Fats
  - Concentrated source of calories
  - Meets essential fatty acid needs

- Multiple lipid solutions available providing triglycerides derived from different oils

- Essential fatty acid (EFA) needs: 1-4% calories (minimum) must come from a combination of linoleic and linolenic acid to meet EFA needs
  - Serum triene:tetraene ratio > 0.2 reflects EFA deficiency
  - Ratio may not accurately reflect EFA deficiency if both EFAs low

Wolfram G, *et al. J Parenter Enteral Nutr.* 1978;2(5):634-9.

Macronutrients: ILE – Cont'd

- Fats are infused over 24 hours to maximize tolerance
  - Monitor triglycerides to assess tolerance
  - Neonates: triglyceride levels <200 mg/dL
  - Children: triglyceride levels <300-400 mg/dL

- Fat decreases the osmolality of the PN solution
  - More concentrated form of calories compared to dextrose and amino acids

Wolfram G, *et al. J Parenter Enteral Nutr.* 1978;2(5):634-9.

Macronutrients: Comparison of ILE

Component	Intralipid®	Omegaven®	ClinoLipid® / ClinOleic®	SMOFLipid®
Soybean oil, %	100		20	30
Medium-chain triglycerides, %				30
Olive oil, %			80	25
Fish oil, %		100		15
Glycerol, g/100 mL	2.25	2.5	2.25	2.5
Egg phospholipid, g/10 mL	1.2	1.2	1.2	1.2
Phytosterols, mg/100 ml	439 ± 5.7	3.66	274 ± 2.6	207
Vitamin E, mg/100 mL	3.8	15 - 30	3.2	16 - 23
LA, %	50	4.4	18.5	21.4
ALA, %	9	1.8	2	2.5
EPA, %	0	19.2	0	3
DHA, %	0	12.1	0	2
ARA, %	0	1 - 4	0	0.15 - 0.6

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Anez-Bustillos L, *et al. Nutr Clin Pract*. 2016;31(5):596-609.

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Micronutrients Overview

- General principle: monitor regularly and adjust in PN if needed
- Maintain homeostasis
- Weight-based supplementation appropriate starting point
- Alterations may be necessary by disease states
  - Neonatal period
  - Critical illness
  - Renal disease
  - Liver disease

Corkins MR, *et al. The A.S.P.E.N. Pediatric Nutrition Support Core Curriculum*, 2nd Ed. ASPEN;2015.
Denne SC. *Semin Neonatol.* 2001;6(5):377-82.

Micronutrients Overview – Cont'd

Sodium
- Consider acid-base balance, fluids & diuretic therapy

Potassium
- Consider renal function, diuretic therapy, gastrointestinal losses, medication interactions (including insulin), sodium in PN, dextrose administration

Calcium
- Consider phosphate levels, bone health, serum albumin level

Phosphate
- Consider ionized calcium levels, renal function, bone health
- Calcium and phosphate requirements higher in preterm infants

Magnesium
- Consider potassium, calcium, phosphate levels, renal losses, gastrointestinal losses, bone health, medication interactions (including PPI therapy), clinical signs and symptoms

Corkins MR, *et al. The A.S.P.E.N. Pediatric Nutrition Support Core Curriculum*, 2nd Ed. ASPEN;2015.
Denne SC. *Semin Neonatol.* 2001;6(5):377-82.

Electrolyte and Mineral Requirements

	Preterm Neonates	Infants / Children	Adolescents / Children > 40 kg
Sodium (mEq/kg/day)	2 - 5	2 – 5	80 – 150 mEq/day
Potassium (mEq/kg/day)	2 – 4	2 – 4	40 – 60 mEq/day
Calcium (mEq/kg/day)	2 – 4	0.5 – 4	10 – 20 mEq/day
Phosphorus (nmol/kg/day)	1 - 2	0.5 – 2	10 – 40 mmol/day
Magnesium (mEq/kg/day)	0.3 – 0.5	0.3 – 0.5	10 – 30 mEq/day
Acetate	As needed to maintain acid-base balance		
Chloride	As needed to maintain acid-base balance		

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Corkins MR, *et al. The A.S.P.E.N. Pediatric Nutrition Support Core Curriculum*, 2nd Ed. ASPEN;2015.
Denne SC. *Semin Neonatol.* 2001;6(5):377-82.

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Micronutrients: Calcium / Phosphate

- Limitations to amounts of calcium and phosphate that may be supplied in PN
  - Calcium and phosphate may precipitate depending on the amounts added to PN solutions
  - Cysteine lowers pH and may be added to neonate/infant PN to increase solubility of Ca and Phosphate

- Factors affecting solubility include
  - Temperature
  - Type of AA product
  - pH of the final solution
  - Lighting
  - Concentration of calcium and phosphate
  - Dextrose concentration
  - Cysteine
  - Order of mixing

Corkins MR, *et al. The A.S.P.E.N. Pediatric Nutrition Support Core Curriculum*, 2nd Ed. ASPEN;2015.
Denne SC. *Semin Neonatol.* 2001;6(5):377-82.

Micronutrients: Trace Elements

- Numerous minerals are integrated into various physiologic functions
- Commercial PN products contain zinc, copper, chromium, manganese
  - Higher amounts of certain trace elements are present in PN solutions due to contamination during manufacturing
- Optimal requirements of trace elements for children are not well understood

Corkins MR, *et al. The A.S.P.E.N. Pediatric Nutrition Support Core Curriculum*, 2nd Ed. ASPEN;2015.
Denne SC. *Semin Neonatol.* 2001;6(5):377-82.

Micronutrients: Trace Elements – Cont'd

- In patients with liver disease, copper and manganese doses often need adjustment
  - Excreted via bile
  - Levels need to be monitored in patients with cholestasis
- In patients with renal disease, selenium and chromium need to be used with caution
  - Levels need to be monitored
- Manganese can be present as a contaminant in PN solutions
  - Monitor for manganese toxicity in long-term PN patients
- Chromium may not be needed in patients on long-term PN

Corkins MR, *et al. The A.S.P.E.N. Pediatric Nutrition Support Core Curriculum*, 2nd Ed. ASPEN;2015.
Denne SC. *Semin Neonatol.* 2001;6(5):377-82.

Components of PN: Trace Elements

Solution Name	Multrys®	Tralement®
Age indication	Neonatal/Pediatric	Pediatric/Adolescent/Adult
Weight indication	< 10 kg	≥ 10 kg
Trace element in 1 mL solution (mcg)		
Zinc (Zn)	1,000	3,000
Copper (Cu)	50	300
Selenium (Se)	6	55
Manganese (Mn)	3	60

Micronutrients: Iron (Fe)

- Iron deficiency is common in PN recipients
  - Also consider other non-iron deficiency causes of anemia
  - Consider enteral supplementation over parenteral route for treatment
  - Addition of Fe to PN requires consideration due to potential increased risk of sepsis (pro-oxidant), and anaphylaxis (FDA black box warning)
- Consider supplementation in patients who have been NPO
  - Avoid Fe in patients receiving frequent blood transfusions due to possibility of Fe overload
- Parenteral Fe preparations
  - Iron sucrose
  - Iron dextran
  - Ferric carboxymaltose (small risk of hypophosphatemia)

Talathi S, *et al. J Pediatr Gastroenterol Nutr.* 2023;76(5):672-83.
Khaodhiar L, *et al. J Parenter Enteral Nutr.* 2002;26(2):114-19.

Micronutrients: Zinc (Zn)

- Important trace element for growth, wound healing
- Signs of zinc deficiency
  - Dermatitis, alopecia, diarrhea, immune deficiency
- Zinc excreted mainly in stool
  - Increased needs in diarrhea, hypercatabolic states, ostomy losses, intrathoracic/peritoneal drains, mucositis
- Measures of zinc status
  - Serum zinc is a poor measure of total body zinc status
  - Low alkaline phosphatase may be a better marker of zinc deficiency but is not diagnostic
- May increase PN intake to 1.5 - 2x usual dosing if increased metabolic demand (to maintain one line)
- Monitor for copper deficiency

Corkins MR, et al. The A.S.P.E.N. Pediatric Nutrition Support Core Curriculum, 2nd Ed. ASPEN;2015.

Micronutrients: Copper (Cu)

- Copper deficiency is rare, except in patients with cholestasis
  - Risk factors: malabsorption, prematurity, severe malnutrition
  - May present with anemia (hypochromic, microcytic), leukopenia, neutropenia, bone abnormalities
- Biliary tract is the primary route for Cu excretion
  - Patients with cholestasis have decreased excretion, may be at increased risk for toxicity
  - Note that patients without cholestasis can also have elevated Cu levels
- Monitor through serum Cu and ceruloplasmin levels
  - Clinical picture should be evaluated to assess Cu status
    - Toxicity may present similarly to Wilson's disease: cirrhosis, neurological disorders, renal damage
    - Deficiency may present similarly to B_{12} deficiency, with cardiac disease, arthritis, loss of hair pigmentation, neurologic abnormalities, pancytopenia

Corkins MR, et al. The A.S.P.E.N. Pediatric Nutrition Support Core Curriculum, 2nd Ed. ASPEN;2015.

Micronutrients: Manganese (Mn)

- Deficiency very uncommon in humans
- Mn contamination is commonly found through manufacturing of various PN components
- Biliary tract primary route for Mn excretion
  - Patients with cholestasis may have decreased Mn excretion
- Toxicity
  - Symptoms include insomnia, headache, forgetfulness, anxiety, cholestasis, Parkinson's disease-like illness
  - Best assessed through MRI brain (accumulation in basal ganglia)
- Monitoring
  - Regular monitoring of patients receiving chronic PN
  - Erythrocyte or whole-blood Mn concentrations should be measured

Corkins MR, et al. The A.S.P.E.N. Pediatric Nutrition Support Core Curriculum, 2nd Ed. ASPEN;2015.

Micronutrients: Selenium (Se)

- Deficiency may develop within 6 weeks of being Se-free in PN
  - Can cause cardiomyopathy, growth retardation, pseudo-albinism, white fingernails, hypothyroidism
  - Patients should be supplemented if on exclusive PN for > 4 weeks

- Toxicity rare
  - May cause nausea, diarrhea, irritability, fatigue, peripheral neuropathy, hair loss, nail changes
  - In patients with impaired renal function, reduce Se from PN

- Monitoring
  - Total plasma selenium, glutathione peroxidase, C-reactive protein
  - In presence of systemic inflammation, Se levels may decrease
  - Close monitoring in patients with renal dysfunction

Corkins MR, et al. The A.S.P.E.N. Pediatric Nutrition Support Core Curriculum, 2nd Ed. ASPEN;2015.

Micronutrients: Chromium (Cr)

- Excreted in kidneys
- Common contaminant in PN solutions
  - Contamination can increase delivery by 10-100%. Deficiency is rare.
- Chromium deficiency symptoms primarily involve reversible glucose intolerance that does not improve with insulin
- Monitoring
  - Close monitoring in patients with renal dysfunction
  - Consider monitoring both serum Cr concentrations and HbA1C levels regularly in long-term PN patients
  - Best method for diagnosing Cr deficiency is demonstrating insulin resistance that improves with Cr supplementation, and reappears after supplementation is withdrawn

Corkins MR, et al. The A.S.P.E.N. Pediatric Nutrition Support Core Curriculum, 2nd Ed. ASPEN;2015.

Micronutrients:
Multivitamin Vials - Pediatric

Multi-vitamins in PN typically supplied as 2 injectable vials (Vial 1, Vial 2)

Infuvite® Pediatric Vial #1 contents (per 4 mL)

Active Ingredient	Quantity
Ascorbic acid (Vitamin C)	80 mg
Vitamin A* (as palmitate)	2,300 IU (equals 0.7 mg)
Vitamin D_3* (cholecalciferol)	400 IU (equals 10 mcg)
Thiamine (Vitamin B_1) (as the hydrochloride)	1.2 mg
Riboflavin (Vitamin B_2) (as riboflavin 5-phosphate sodium)	1.4 mg
Pyridoxine HCl (Vitamin B_6)	1 mg
Niacinamide	17 mg
Dexpanthenol (as *d*-pantothenyl alcohol)	5 mg
Vitamin E* (*dl*-α-tocopheryl acetate)	7 IU (equals 7 mg)
Vitamin K_1*	0.2 mg

*Polysorbate 80 is used to water solubilize the oil-soluble vitamins A, D, E, and K.

Infuvite® Pediatric Vial #2 contents

Active Ingredient	Quantity
Folic acid	140 mcg
Biotin	20 mcg
Vitamin B_{12} (cyanocobalamin)	1 mcg

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U.S. Food and Drug Administration. "FDA Online Label Repository." Accessed September 19, 2024. https://labels.fda.gov/.

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Micronutrients:
Multivitamin Vials - Adult

Multi-vitamins in PN typically supplied as 2 injectable vials
(Vial 1, Vial 2; note differences in dosing and volume)

Infuvite® Adult Vial #1 contents (per 5 mL)	
Ascorbic acid (Vitamin C)	200 mg
Vitamin A* (as palmitate)	3,300 IU
Vitamin D_3* (cholecalciferol)	200 IU
Thiamine (Vitamin B_1) (as the hydrochloride)	6 mg
Riboflavin (Vitamin B_2) (as riboflavin 5-phosphate sodium)	3.6 mg
Pyridoxine HCl (Vitamin B_6)	6 mg
Niacinamide	40 mg
Dexpanthenol (as *d*-pantothenyl alcohol)	15 mg
Vitamin E* (*dl*-α-tocopheryl acetate)	10 IU
Vitamin K_1*	150 mcg

Infuvite® Adult Vial #2 contents (per 5 mL)	
Folic acid	600 mcg
Biotin	60 mcg
Vitamin B_{12} (cyanocobalamin)	5 mcg

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U.S. Food and Drug Administration. "FDA Online Label Repository." Accessed September 19, 2024. https://labels.fda.gov/.

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Acid Base / Balance

- May be managed by addition or removal of sodium, potassium acetate
  - Acetate = bicarbonate precursor

- Bicarbonate contraindicated in PN
  - Calcium / phosphate precipitation
  - High Na load
  - Generates CO_2 in PN bag

Corkins MR, et al. The A.S.P.E.N. Pediatric Nutrition Support Core Curriculum, 2nd Ed. ASPEN;2015.

Heparin

- Prophylactic anticoagulant used to prevent thrombosis
- Reduces formation of fibrin sheath around catheter
  - May reduce phlebitis with peripheral IV access
  - May facilitate lipid clearance (increases lipolysis and releases free fatty acids)
- Heparin dosing
  - 1 unit/mL full-term infants to adults
  - 0.5 units/mL preterm and VLBW infants (< 1500 g)

Corkins MR, et al. The A.S.P.E.N. Pediatric Nutrition Support Core Curriculum, 2nd Ed. ASPEN;2015.

Case: Review

- Jerry is a previously healthy 13-year-old male. He was transferred from an outside hospital after undergoing exploratory laparotomy for a complicated perforated appendicitis. Due to extensive lysis of adhesions and inflamed bowel, the decision was made to create an ileostomy 100 cm distal to the ligament of Treitz.
- Since surgery he has been having 75 - 100 mL/kg of ostomy output daily. He will be NPO for at least 1 week while receiving IV antibiotics for his intra-abdominal infection secondary to intestinal perforation.

Question: What is the most appropriate way to provide adequate hydration and nutrition to GE?

Case: Review

- Jerry is a previously healthy 13-year-old male. He was transferred from an outside hospital after undergoing exploratory laparotomy fo … of ac … e an ile …
- Si … out d … antibiotics for his intra-abdominal infection secondary to intestinal perforation.

- GE was initiated on PN through a tunneled central line with an initial caloric delivery of 1700 kcal
- 3 months after initial ostomy creation, ostomy was taken down and intestines placed in continuity
- PN weaned inpatient over 14 days after ostomy take down
- He continues to require micronutrient supplementation (B_{12}, Zn), but eats a regular diet by mouth and has no activity restrictions

Question: What is the most appropriate way to provide adequate hydration and nutrition to GE?

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