Neonatal Parenteral Nutrition (PN)

Overview

- Case study
- Indications and Rationale
  - Energy requirements
  - Fluid requirements
  - Dextrose
  - Amino Acids
  - Lipids
- Deficiencies
- Monitoring
- Review of case

Case

3-week-old boy born at 23-week gestation developed septic shock, renal failure, necrotizing enterocolitis, and bowel perforation. He was treated with peritoneal washouts, drains, antimicrobials, and bowel rest. PN was started on DOL#1, but lipids were intermittently held since birth due to fluid overload and hypertriglyceridemia. He was later diagnosed with intestinal failure-associated liver disease (IFALD) (direct bilirubin > 2 mg/dL) and essential fatty acid deficiency (EFAD) (T:T > 0.2). What is the most appropriate IV lipid emulsion (ILE) for this infant?

A) Hold ILE
B) 100% soybean oil ILE 0.5 g/kg
C) Mixed oil ILE 3 g/kg
D) 100% fish oil ILE 1 g/kg

Indications and Rationale: Common Indications – Term and Preterm Infants

- Inability to feed due to GI condition or illness
- Failure to meet energy requirements by enteral nutrition
- Anticipated NPO > 3-5 days
- Increased metabolic demands during critical illness

Worthington P, *et al. J Parenter Enteral Nutr.* 2017;41(3):324-77.
Pediatric Nutrition Support Core Curriculum. Editor: Mark Corkins. ASPEN, 2015.
Robinson DT, *et al. J Parenter Enteral Nutr.* 2023;47(7):830-58.

Indications and Rationale: Specific Indications – Preterm Infants

- Higher nutritional requirements for growth and development
- PN should be started after birth as soon as vascular access is obtained
- Gastrointestinal immaturity preventing full enteral feeding

Worthington P, *et al. J Parenter Enteral Nutr.* 2017;41(3):324-77.
Pediatric Nutrition Support Core Curriculum. Editor: Mark Corkins. ASPEN, 2015.
Robinson DT, *et al. J Parenter Enteral Nutr.* 2023;47(7):830-58.

Starter PN

- A stock PN for immediate delivery of basic nutrition until a custom PN is ordered
  - Amino acids, dextrose, and calcium
  - No other electrolytes
  - Additional intravenous fluids with electrolytes may be ordered as needed

- Early initiation of PN is critical for premature infants
  - Supports growth and development
  - Prevents catabolism

Robinson DT, *et al. J Parenter Enteral Nutr.* 2023;47(7):830-58.

Neonatal PN: Energy Requirements

Preterm Infant (kcal/kg/day)	110 – 120
Term Infant (kcal/kg/day)	90 - 100

- Establish daily energy requirements
  - Consider additional kcal based on clinical condition and postnatal growth
- Calculate energy needs using current dry weight or birth weight if not yet regained

Mirtallo J, *et al. J Parenter Enteral Nutr.* 2004;28(6):S39–S70.
Joosten K, *et al. Clin Nutr.* 2018;37(6 Pt B):2309-314.
Pediatric Nutrition Support Core Curriculum. Editor: Mark Corkins. ASPEN, 2015.

Neonatal PN: Fluid Requirements

	Day of Life (birth)	Day of Life 1	Day of Life 2+
Preterm Infant (mL/kg/day)	80 - 100	120	140
Term Infant (mL/kg/day)	60 - 80	100	100 – 120

- Establish total fluid limit or allowance
- Determine PN volume

  PN = Total Fluid Requirement - (Medications + Flushes + Enteral Nutrition + IVF)

Mirtallo J, *et al. J Parenter Enteral Nutr.* 2004;28(6):S39–S70.
Pediatric Nutrition Support Core Curriculum. Editor: Mark Corkins. ASPEN, 2015.

Neonatal PN: Fluid Requirements – Cont'd

- Adjust fluid requirements for specific clinical situations

- **Increase** fluids: consider increasing fluid intake in cases of elevated insensible losses or excessive fluid output
  - Diarrhea
  - High ostomy outputs
  - Polyuria
  - Phototherapy for jaundice
  - Extensive skin injuries
  - Sepsis

Mirtallo J, *et al. J Parenter Enteral Nutr.* 2004;28(6):S39–S70.
Pediatric Nutrition Support Core Curriculum. Editor: Mark Corkins. ASPEN, 2015.

Neonatal PN: Fluid Requirements – Cont'd

- Adjust fluid requirements for specific clinical situations

- **Reduce** fluids: consider reducing fluid intake in scenarios where insensible losses are decreased or there is fluid overload
  - Double walled isolators for premature or critically ill infants
  - Ascites due to liver or renal failure
  - Pulmonary edema
  - Congestive heart failure

Mirtallo J, *et al. J Parenter Enteral Nutr.* 2004;28(6):S39–S70.
Pediatric Nutrition Support Core Curriculum. Editor: Mark Corkins. ASPEN, 2015.

Neonatal PN: Dextrose

	Initiation	Advance By	Goals
Preterm Infant (mg/kg/min)	5 – 7	1 - 2 (or 1-2.5% dextrose)	10-14 (max 14 – 18)
Term Infant (mg/kg/min)	6 - 9	1 - 2 (or 2.5 – 5% dextrose)	10-14 (max 14 – 18)

- Advance until energy goals met
- Monitor blood glucoses with target blood glucose 70-150 mg/dL
  - Premature infants < 28 weeks are at increased risk of hyperglycemia
  - Insulin should not be used given risk of hypoglycemia
- Maintain minimum Glucose Infusion Rate (GIR) 6 mg/kg/min for brain's energy needs
- Note that GIR > 12.5 mg/kg/min may stimulate lipogenesis from excess glucose

Bresson JL, *et al. Pediatr Res.* 1989;25(6):645-48.
Ramel S, *et al. Neoreviews* 2020;21(2):e89-e97.
Pediatric Nutrition Support Core Curriculum. Editor: Mark Corkins. ASPEN, 2015

Neonatal PN: Amino Acids

	Initiate at Goal
Preterm Infant (g/kg/day)	3 (max 3.5)
Term Infant (g/kg/day)	2.5 – 3

- Start protein at goal
  - Gradual advancement delays reaching target needs, leading to net negative nitrogen balance
  - Limited benefit with protein dose > 3.5 g/kg/day

- Initiating protein > 3 g/kg/day has been linked to sepsis in premature infants

Robinson DT, *et al. J Parenter Enteral Nutr.* 2023;47(7):830-58.
Strømmen K, *et al. Clin Nutr ESPEN.* 2017;18:16-22.

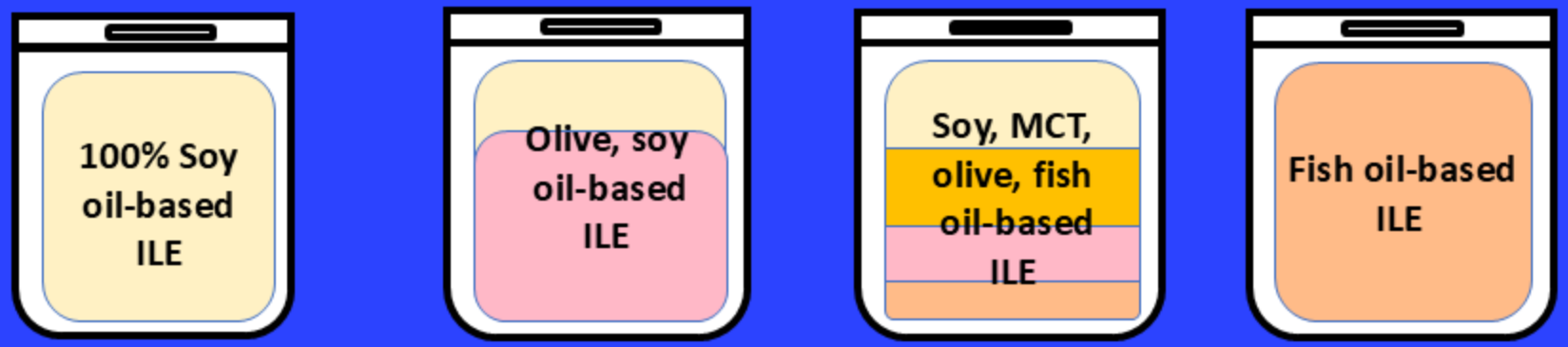
Neonatal PN: Lipids

	Initiation	Advance By	Goals
Preterm Infant (g/kg/day)	1	0.5 – 1	3
Term Infant (g/kg/day)	1	0.5 – 1	3

- Advance gradually to minimize risk of hypertriglyceridemia
- Infuse over 12 - 24 hours depending on formulation and clinical condition
- Insufficient lipids can cause essential fatty acid deficiency (EFAD)
- Excess lipids can cause hypertriglyceridemia

Mirtallo J, *et al. J Parenter Enteral Nutr.* 2004;28(6):S39–S70.

Types of Intravenous Lipid Emulsions (ILEs)



	100% SO-ILE	OO, SO-ILE	SO, MCT, OO, FO-ILE	FO-ILE
Indication	ILE < 2 weeks EFAD	ILE > 2 weeks	ILE > 2 weeks	IFALD EFAD
Advantages	↑↑↑ EFA	Sufficient EFA ↓ Phytosterols	Sufficient EFA ↓ Phytosterols	Sufficient EFA ↓ Triglycerides ↓↓ Phytosterols
Disadvantages	↑ Triglycerides ↑ Phytosterols	EFAD *	EFAD *	↓ Energy density

* If inadequately dosed

Mirtallo J, *et al. Nutr Clin Pract.* 2020;35:769-82.
Calkins KL, *et al. Neoreviews* 2020;21(2):e109-e119.

NASPGHAN FOUNDATION

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Neonatal PN: Types of ILEs

Oil Source	SO-ILE	OO, SO-ILE	SO, MCT, OO, FO-ILE	FO-ILE
SO (%)	100	20	30	0
MCT (%)	0	0	30	0
OO (%)	0	80	25	0
FO (%)	0	0	15	100

Chan AP, *et al. Clin Perinatol.* 2023;50(3):575-89.
Calkins KL, *et al. Neoreviews* 2020;21(2):e109-e119.

Neonatal PN: Types of ILEs

Fatty Acid	SO-ILE	OO, SO-ILE	SO, MCT, OO, FO-ILE	FO-ILE
Caprylic	0	0	17% ± 0.2%	0
Capric	0	0	12% ± 0.2%	0
Linoleic, ω-6	44%-62%	18%	14%-25%	1.5%
α-Linolenic, ω-3	4%-11%	1.7%	1.5%-3.5%	1.1%
ARA, ω-6	0	0.16%	0.5%	0.2%-2%
DHA, ω-3	0	0	1%-3.5%	14%-27%
EPA, ω-3	0	0	1%-3.5%	13%-26%
Oleic acid, ω-9	19%-30%	60%	23%-35%	4%-11%
ω-6:ω-3	7:1	9:1	2.5:1	1:8

Chan AP, *et al. Clin Perinatol.* 2023;50(3):575-89.
Calkins KL, *et al. Neoreviews* 2020;21(2):e109-e119.

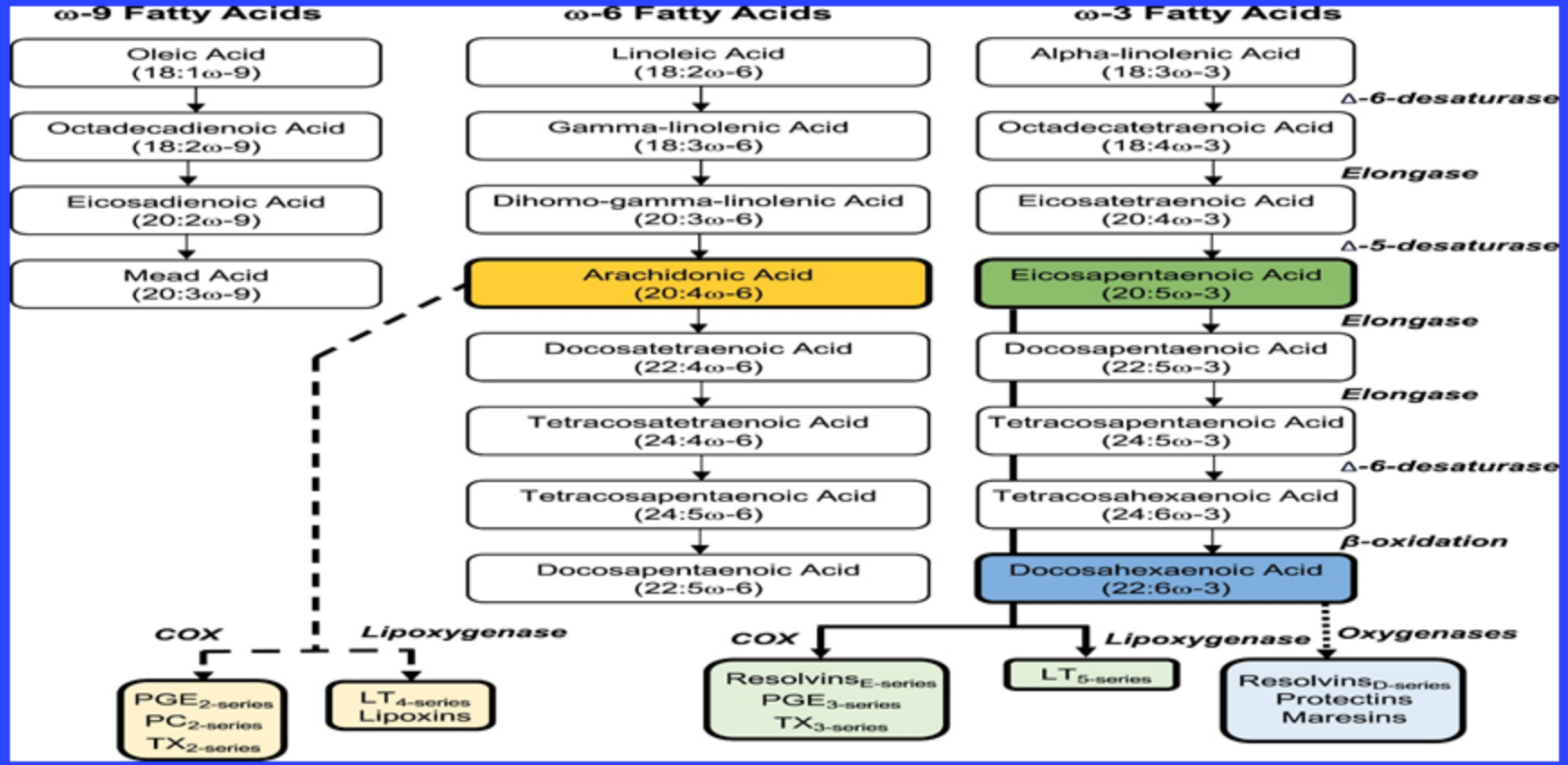
Essential Fatty Acid Deficiency

- Definition
  - Insufficient supply of essential ω-6 linoleic acid and ω-3 α-linolenic acid (LA) and
  - Triene:Tetraene (T:T) or Mead acid:Arachidonic ratio > 0.2

- Risk Factors
  - Prematurity, as maternal transfer of EFAs occurs mainly in the 3rd trimester
  - Low birth weight
  - Prolonged withdrawal, restriction or inappropriate dosage of IV lipids

Lagerstedt SA, *et al. Mol Genet Metab.* 2001;73(1):38-45.

Metabolism of Polyunsaturated Fatty Acids



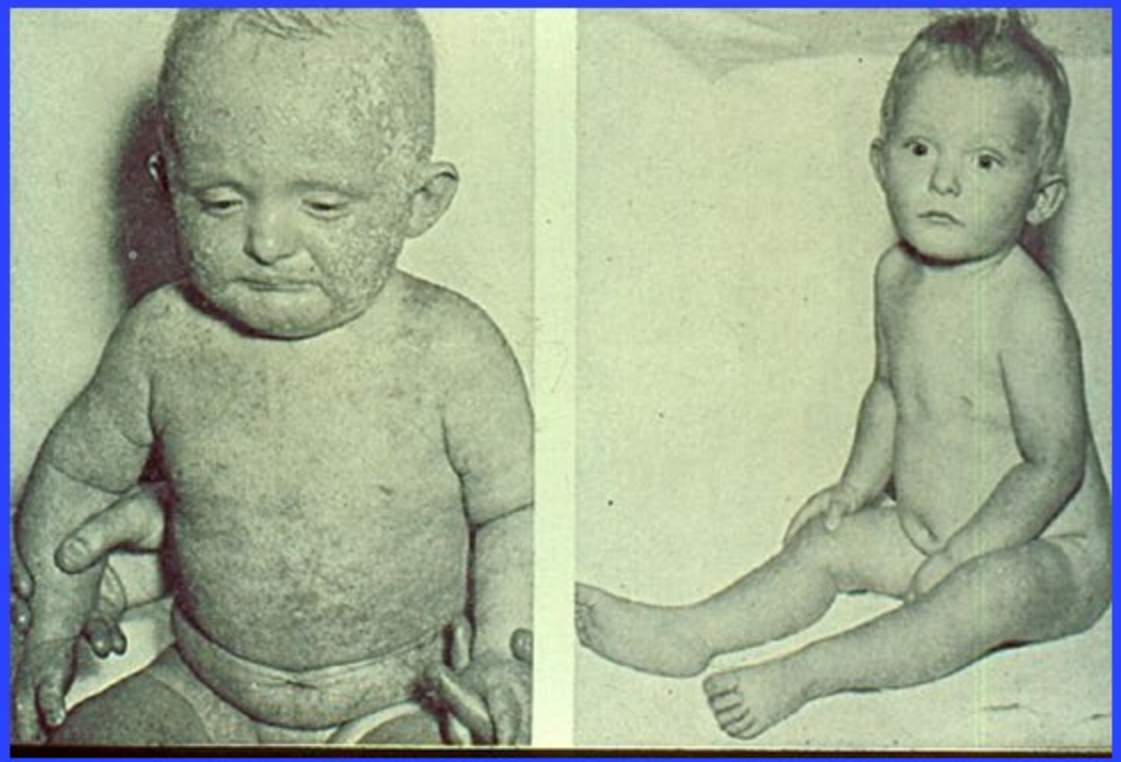
↓ LA leads to, by default, elongation of OO(18:1ω-9), resulting in
↑Mead Acid (20:3ω-9) and a
↑ T:T ratio [Mead Acid (20:3ω -9):Arachidonic Acid(20:4ω-6)]

Chan AP, *et al. Clin Perinatol.* 2023;50(3):575-89.

Essential Fatty Acid Deficiency

- Biochemical Indicators (T:T > 0.2)
  - ↑ LFTs
  - ↑ Triglyceride
  - ↓ Platelet

- Physical Signs (T:T > 0.4)
  - Dry, scaly rash
  - Poor wound healing
  - Growth restriction
  - Increased infection risks
  - Bleeding



Child with essential fatty acid deficiency (left) after successful treatment (right)

Uauy R, *et al. Semin Pereinatol.* 1989;13:118-30.

Essential Fatty Acid Deficiency

- Prevention
  - Provide IV lipids at appropriate dosage
  - Fish oil provides "conditionally essential" fatty acids, arachidonic acid and docosahexaenoic acid (DHA), that can be retro converted to linoleic acid and eicosapentaenoic acid (EPA), respectively
- Treatment
  - Administer either 100% soybean oil or 100% fish oil IV lipid

	SO-ILE	SO, MCT, OO, FO-ILE	FO-ILE
Minimum Dosage (g/kg)	**0.5 – 1.0**	2.2 – 3.0	**1.0 – 1.5**

Gramlich L, *et al. J Parent Enteral Nutr.* 2019;43(6):697-707.
Gura K, *et al. J Pediatr.* 2020;219:98–105.e4.
de Meijer VE, *et al. J Pediatr Gastroenterol Nutr.* 2010;50:212–18.

Hypertriglyceridemia

- Definition
  - Triglyceride level > 250-300 mg/dL
- Risk Factors
  - Prematurity (< 28 weeks' gestation)
  - Low birth weight (< 1000 g)
  - IV lipid (based on dose ,concentration, oil source)
  - Sepsis
  - Renal failure
  - Corticosteroids
  - Dextrose overfeeding
  - Essential fatty acid deficiency
  - Inborn errors of metabolism
  - Carnitine deficiency

Chan AP, *et al. Neoreviews* 2022;23(8):e528-e540.
Mirtallo J, *et al. J Parenter Enteral Nutr.* 2004;28(6):S39–S70.
Lapillonne A, *et al. Clin Nutr.* 2018;37(6 Pt B):2324–336.

Hypertriglyceridemia

Management of HTG	Comments
Ensure lab specimen is not contaminated	
Avoid excessive dextrose infusions	May limit nonprotein calories
Administer ILE over longer period	
Treat sepsis and renal failure	
Normalize serum calcium to optimize LPL activity	
Minimize use of medications associated with HTG (corticosteroids, chlorothiazide)	
Reduce ILE dose or pause ILE	Ensure infant's risk for EFAD is low and ILE dose will not cause an EFAD
Change ILE type to include fish oil	ω-3 fatty acids in fish oil enhance lipid utilization, accelerate lipid clearance, and suppress lipogenesis
Heparin	Induces triglyceride clearance, but increased bleeding risk should be considered
Carnitine	Enhances fatty acid oxidation, but evidence on clinical effectiveness is limited

Chan AP, *et al. Neoreviews* 2022;23(8):e528-e540

Growth Monitoring Charts

- Growth curves used to track weight, length, and head circumference for age
- Selection of growth chart depends on patient age, gender, institutional preference, and specific underlying conditions (Down syndrome, Rett syndrome, etc.)
  - **Olsen**: up to 36 weeks gestational age
    - Intrauterine growth curves based on data from US
  - **Fenton**: most used, best between 36-50 weeks corrected age
    - Combination of intrauterine and postnatal curves based on data from Canada, Australia, Italy, Scotland, Germany, and US
  - **World Health Organization**: after 4-8 weeks post-term until 2 years old
    - International postnatal growth standards based on breastfed children

Olsen IE, *et al. Pediatrics* 2010;125(2):e214–e224.
Fenton TR, *et al. BMC Pediatr.* 2013;13:59.
WHO Multicentre Growth Reference Study Group. *Acta Paediatr.* 2006;450(Suppl):76–85.

Growth Monitoring Target Goals

- Once birth weight is achieved, the following growth goals should be targeted
- Accurate growth monitoring may be difficult if edema is present

	Weight	Length	Head Circumference
Preterm Infant	15-20 g/kg/day	1 cm/week	0.7 cm/week
Term Infant (0 – 3 months)	30 g/day	0.75 cm/week	0.5 cm/week

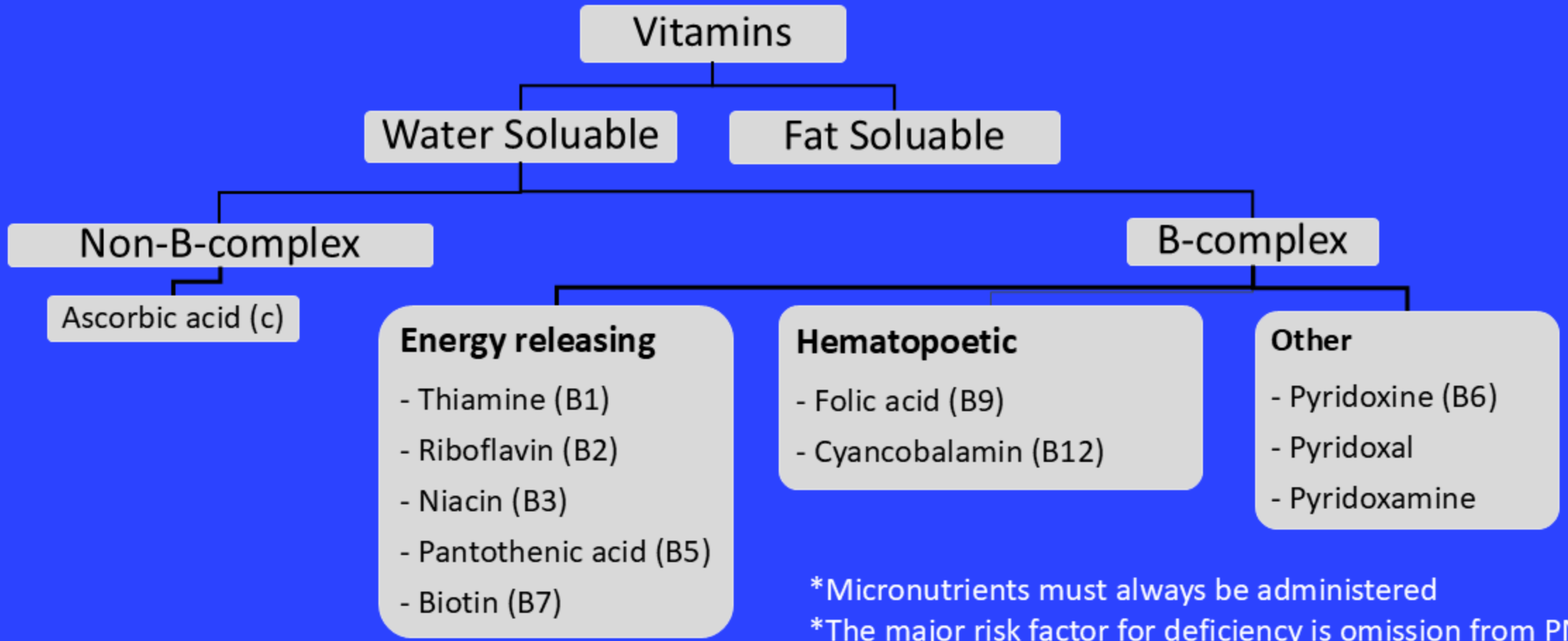
Water as Nutrition. In: Nutritional Needs of the Preterm Infant: Scientific Basis and Practical Guidelines. Editor: Tsang. Baltimore 1992.
Fenton TL, *et al. J Pediatr.* 2018;196:77-83.

Neonatal PN: Heparin

- Prophylactic to prevent thrombosis
- Reduces the formation of a fibrin sheath around the catheter
- May reduce phlebitis with peripheral intravenous access
- May facilitate lipid clearance; increased lipolysis and release of free fatty acids
- Reduces the incidence of culture-positive catheter-related sepsis
- Heparin dosing
  - 1 unit/mL full-term infants-adults
  - 0.5 units/mL preterm and VLBW infants (<1500g)
- Cons: ↑risk for heparin-induced thrombocytopenia and heparin medication interactions

Birch P, *et al. Arch Dis Child Fetal Neonatal Ed*. 2010;95(4):F252-7.
Uslu S, *et al. J Perinatol.* 2010;30(12):794-9.
Kerner JA. "Parenteral Nutrition" in Nutrition in Pediatrics 3rd Editon, 2003:969.

Essential Micronutrients: Organic



*Micronutrients must always be administered

*The major risk factor for deficiency is omission from PN

Birch P, *et al. Arch Dis Child Fetal Neonatal Ed*. 2010;95(4):F252-7.
Uslu S, *et al. J Perinatol.* 2010;30(12):794-9. Randolph AG, et al. Chest 1998;113(1):165-71.
Kerner JA. "Parenteral Nutrition" in Nutrition in Pediatrics 3rd Editon, 2003:969.

Essential Micronutrients: Inorganic

- Micronutrients must always be administered
- The major risk factor for deficiency is omission from PN

Electrolytes	Minerals
Sodium	Iron
Potassium	Iodide *
Mangesium	Zinc
Phosporus	Copper
Calcium	Chromium
	Manganese
	Selenium
	Cobalt
	Molybdenum

* PN Iodine not available in the USA

Birch P, *et al. Arch Dis Child Fetal Neonatal Ed*. 2010;95(4):F252-7.
Uslu S, *et al. J Perinatol.* 2010;30(12):794-9. Randolph AG, et al. Chest 1998;113(1):165-71.
Kerner JA. "Parenteral Nutrition" in Nutrition in Pediatrics 3rd Editon, 2003:969.

Comparison of Infant and Child Dosing of Electrolyte and Minerals

	Infant (0 – 5 kg)	Infant / Child (5 – 20 kg)
Sodium	2 – 5 mEq/kg	2 – 6 mEq/kg
Potassium	2 – 4 mEq/kg	2 – 3 mEq/kg
Chloride	2 – 5 mEq/kg	2 – 5 mEq/kg
Acetate	Balance	Balance
Calcium	1 – 4 mEq/kg	0.5 – 1 mEq/kg
Phosphorus	2 – 4 mEq/kg	1 – 2 mEq/kg
Magnesium	0.3 – 0.5 mEq/kg	0.3 – 0.5 mEq/kg

*Assumes normal age-related organ function and normal losses

Klein RE. Pediatric Nutrition Handbook 8th Edition 2020.

Electrolytes: Acid / Base Balance

- Chloride: provided as Na chloride, K chloride, and as part of cysteine hydrochloride
  - Avoid prolonged use of chloride free-PN without close monitoring as it may increase the risk of metabolic alkalosis
- Bicarbonate can't be added to PN due to compatibility issues
- Acetate: provided as Na or K acetate
  - K acetate has significantly lower aluminum content (200 mcg/L) compared to Na acetate (360 mcg/L)
  - Metabolized to bicarbonate and added to counter metabolic acidosis

Smith BS, *et al. Am J Health Syst Pharm.* 2007;64:730–39.
Bohrer D, *et al. J Parenter Enteral Nutr.* 2002;26:382–89.
Bishop NJ, *et al. N Engl J Med.* 1997;336:1557–61.

Calcium and Phosphorus Challenges

- Due to rapid bone accretion, infants require much higher Ca and Phos content per PN volume and per kg body weight than older children and adults
  - Risk of precipitation is much greater in infants and should be considered with every PN order
- Metabolic bone disease is common in preterm infants and those receiving long-term PN
  - Monitor serum levels closely
  - Adjust Ca and Phos daily in PN if needed
  - Ca and Phos should be dosed in a ratio that optimizes their deposition into bone

Mihatsch W, et al. *Clin Nutr.* 2018;37:2360-65.
Groh-Wargo S, *et al. Clin Perinatol.* 2022;49:355-79.
Porcelli PJ, *et al. J Am Coll Nutr.* 1997;16(3):283-7.

Calcium and Phosphorus Challenges – Cont'd

- Ideal Ca:Phos ratio = 1.3-1.7:1 by weight ratio (mg: mg)
  = 1.1-1.3:1 molar ratio (mmol:mmol or mEq:mEq)
  = 0.8-1.0** molar ratio during first 5-7 days in newborn preterm infants at risk for postnatal hypercalcemia and hypophosphatemia

- Ca and Phos in PN are based on both recommended intakes and ratios of these nutrients and the compounding limits of solubility

**In early PN when calcium and phosphorous intakes are low, and protein and energy are optimized it is recommended to use a molar Ca:P ratio below1 (0.8-1.0) to reduce the risk of early postnatal hypercalcemia and hypophosphatemia.

Mihatsch W, et al. *Clin Nutr.* 2018;37:2360-65.
Groh-Wargo S, *et al. Clin Perinatol.* 2022;49:355-79.
Porcelli PJ, *et al. J Am Coll Nutr.* 1997;16(3):283-7.

Calcium/Phosphorus Solubility & Cysteine

- Cysteine is considered an essential amino acid for preterm infants
- Can be added to the PN solution
- Lowers pH of the solution allowing increased solubility of Ca and Phos
- Cysteine improves nitrogen balance in extremely low birth weight infants
- Dosing recommendation is 40 mg cysteine/g of pediatric amino acid solution
- Addition of cysteine may necessitate supplementation with acetate in preterm infants and possibly other patients prone to acidosis

Groh-Wargo S, *et al. Clin Perinatol.* 2022;49:355-79.
Shulman RJ, *et al. J Pediatr Gastroenterol Nutr.* 2003;36:587–607.
Plogsted S, *et al. Nutr Clin Pract.* 2015;30(4):579-80.

Carnitine

- May aid triglyceride clearance
  - Facilitates transport of fatty acids across the mitochondrial membrane
- Conditionally essential in the preterm infant
- Serum levels decrease when carnitine is not added to PN
- Consider supplementation
  - Extremely low birth weight premature infants
  - Children on long-term PN (> 2 weeks)
  - Hypertriglyceridemia
  - Significant liver disease

Vanek VW, *et al. Nutrition Clin Pract.* 2012;4:440-91.
Crill CM, *et al. Nutr Clin Pract.* 2007;22:204-13.

Carnitine – Cont'd

- Recommended initial dose is Carnitine 2 – 5 mg/kg/day. This may be increased up to 20 mg/kg/day as clinically needed.
- The treatment dose for deficiency is Carnitine 20 mg/kg/day
- Patients with inborn errors of metabolism require very high doses of carnitine (i.e., 50-100mg/kg) and ideally should be administered separate from the PN solution to ensure the full dose is received

Vanek VW, *et al. Nutrition Clin Pract.* 2012;4:440-91.
Crill CM, *et al. Nutr Clin Pract.* 2007;22:204-13.

Multivitamin Products and Their Dosages

INFLUVITE ® 2 vial system (4mL of vial 1, 1 mL of vial 2)	
Vitamin A: 2300 IU	Vitamin D: 400 IU
Vitamin E: 7 IU	Vitamin K: 200 mcg
Vitamin C: 80 mg	Thiamin 1.2 mg
Riboflavin 1.4 mg	Niacin 17 mg
Dexpanthenol 5 mg	VitaminB6: 1 mg
VitaminB12: 1 mcg	Biotin 20 mcg
Folic acid 140 mcg	
Infants ≥3 kg: 100% of Vial 1 (4 mL) & Vial 2 (1 mL) Infants 1-3 kg: 65% of Vial 1 (2.6 mL) & Vial 2 (0.65 mL) Infants < 1 kg: 30% of Vial 1 (1.2 mL) & Vial 2 (0.3 mL)	

http://www.hospira.com/Files/MVI_pediatric_PI.pdf
http://www.infuvite.com.PDF/infuvite_PackageInsert.pdf

Suggested Intakes of Parenteral Vitamins in Infants and Children

Vitamin	Term Infants and Children Dose/day (identical to currently available formulations)	Preterm Infants Dose/kg body weight (maximum not to exceed term infant dose)	
		Current suggestions (40% of currently available formulations)	Best Estimate * for New Formulations
A (mcg)	700	280	500
E (mg)	7	2.8	2.8
K (mcg)	200	80	80
D (IU)	400	160	160
Ascorbic acid (mg)	80	32	25
Thiamin (mg)	1.2	0.48	0.35
Riboflavin (mg)	1.4	0.56	0.15

*Because of elevated levels of water-soluble vitamins, the current proposal is to reduce the intake of water-soluble vitamins and increase retinal.

Greene HL, *et al. Am J Clin Nutr.* 1988;48:1324-42.

Suggested Intakes of Parenteral Vitamins in Infants and Children – Cont'd

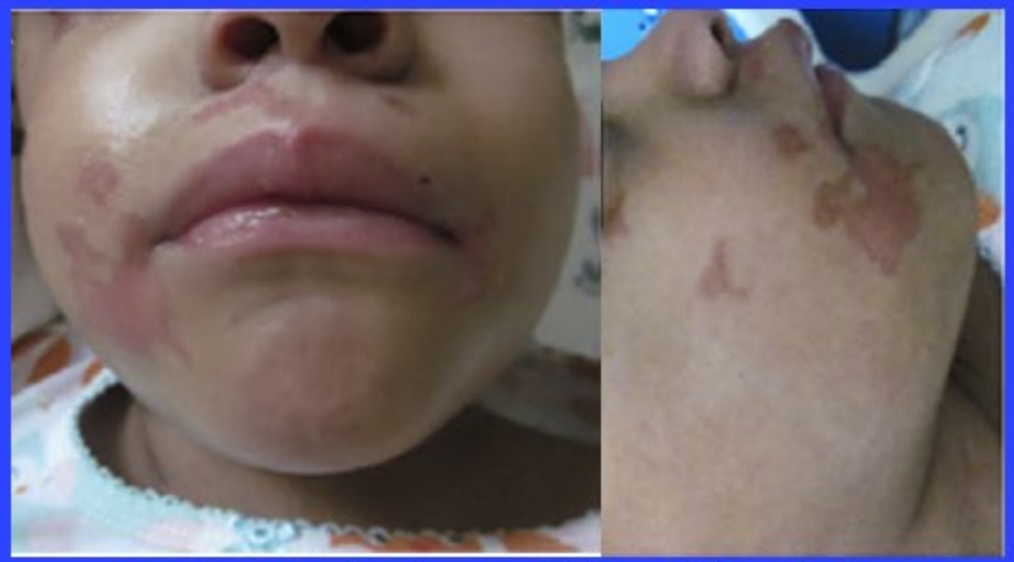
Vitamin	Term Infants and Children Dose/day (identical to currently available formulations)	Preterm Infants Dose/kg body weight (maximum not to exceed term infant dose)	
		Current suggestions (40% of currently available formulations)	Best Estimate * for New Formulations
Pyridoxine (mg)	1	0.4	0.18
Niacin (mg)	17	6.8	6.8
Pantothenate (mg)	5	2	2
Biotin (mcg)	20	8	6
Folate (mcg)	140	56	56
Vitamin B12 (mcg)	1	0.4	0.3

*Because of elevated levels of water-soluble vitamins, the current proposal is to reduce the intake of water-soluble vitamins and increase retinal.

Greene HL, *et al. Am J Clin Nutr.* 1988;48:1324-42.

Multivitamins (MVI)

- Must always be administered
- Omission from PN is associated with an increased risk for onset of severe metabolic derangements
- Intolerance of MVIs may occur due to an anaphylactoid reaction to polysorbate – the solubilizing vehicle



Nonimmunologic anaphylactoid rash due to polysorbate–a solubilizing vehicle for MVIs*

Greene HL, *et al. Am J Clin Nutr.* 1988;48(5):1324-42. CDC. MMWR Weekly 1997;46(23);523-28.
Darlington WS, *et al. Pediatric Blood Cancer* 2015;62:2232.
Coors EA, et al. *Ann Allergy Asthma Immunol.* 2005;95:693-99.

MVI Shortage Considerations

- Risk factor for deficiency
  - Omission from PN
    - National shortages
    - History of anaphylactoid reaction to polysorbate 80 (vehicle for MVI)
  - Vitamin A is susceptible to photodegradation and oxidization

- If no pediatric MVI is available, use adult products at reduced doses
  - Infants <2.5 kg or <36 gestation age, can receive an Adult MVI dose of 1 mL/kg up to 2.5 mL/day
  - Vitamin K: daily dose is 200 mcg/day
  - Thiamine: 0.35 to 0.5 mg/kg/day, max 1.2 mg/day

Greene HL, *et al. Am J Clin Nutr.* 1988;48(5):1324-42. CDC. MMWR Weekly 1997;46(23);523-28.
Darlington WS, *et al. Pediatric Blood Cancer* 2015;62:2232.
Coors EA, et al. *Ann Allergy Asthma Immunol.* 2005;95:693-99.

Neonatal PN: Photodegredation and Oxidation

- Light exposure generates peroxide/free radical formation in PN solutions
  - Both dextrose and AA solutions containing vitamins and intravenous lipid emulsions are prone to peroxidation
  - Premature infants are most susceptible to consequences of peroxide formation in PN admixtures because of immature defense mechanisms and conditions associated with oxidative stress e.g., bronchopulmonary dysplasia, necrotizing enterocolitis, and retinopathy of prematurity
  - Covering PN bags and IV tubing with light protective covers or use of tinted bags and tubing reduces peroxide formation

Robinson DT, *et al. Nutr Clin Pract*. 2021;36:927-41.

Thiamine Deficiency

- Thiamine is a coenzyme in biochemical reactions for energy formation, including carbohydrate metabolism, decarboxylation of α-keto acids, pyruvate, and branched-chain amino acids, and transketolase reactions of the pentose phosphate pathway
- **Source:** 5 mL Pediatric MVI contains thiamine 1.2 mg
- **Risk: o**mission of PN multivitamins for ≥ 10+ days
- Thiamine can be given separately when MVIs are not available
- **Treatment:** IV thiamine 25-50 mg

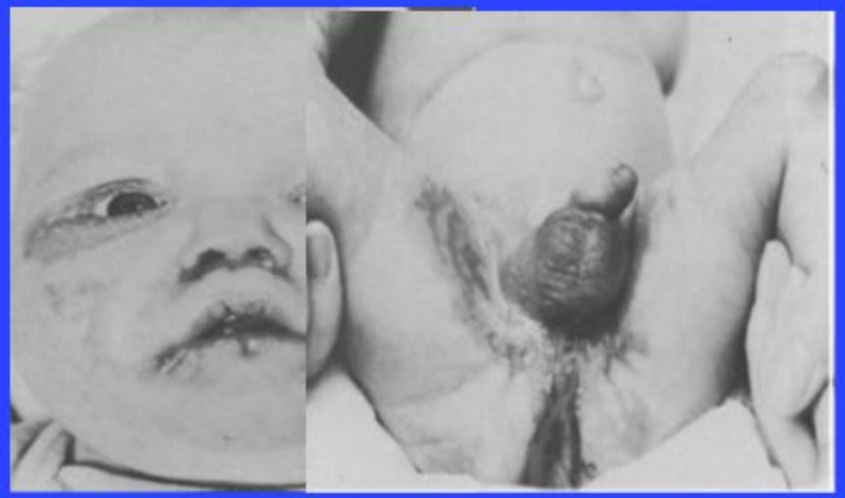
SYMPTOMS/SIGNS

- Severe lactic acidosis
- Increased anion gap
- Metabolic acidosis refractory to sodium bicarbonate
- Tachycardia
- Hypotension
- Lethargy
- Beriberi

Robinson DT, *et al. Nutr Clin Pract*. 2021;36:927-41.

Biotin Deficiency

- Cofactor for four distinct carboxylases that catalyze essential functions in human intermediary metabolism
- **Source:** 5 mL Pediatric MVI contains Biotin 20 □g
- **Risk:** omission of PN multivitamins
- **Symptoms:** alopecia totalis, hypotonia, scaly skin rash, and characteristic well-demarcated periorificial dermatitis



Well demarcated" periorificial and perianal rash

- **Diagnosis:** ↓urinary biotin, ↑urinary organic acids: methylcrotonyl-coenzyme A carboxylase, & propionyl-coenzyme A carboxylase (indicative of a deficiency of biotin-dependent enzymes)

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Robinson DT, *et al. Nutr Clin Pract.* 2021;36:927-41.
Mock MM, *et al. J Pediatrics* 1985;106(5):762-69.

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Recommended Dosing of Trace Minerals

Trace Element	Preterm Neonates	Term Neonates 3 – 10 kg	Children 10 – 40 kg	Adolescents > 40 kg
Zinc	400 mcg/kg	250 mcg/kg	50 mcg/kg (max 5000 mcg/d)	2 – 5 mg
Copper	20 mcg/kg	20 mcg/kg	20 mcg/kg (max 500 mcg/d)	200 – 500 mcg
Manganese	1 mcg/kg	1 mcg/kg	1 mcg/kg (max 5000 mcg/d)	40 – 100 mcg
Chromium	0.05 – 0.3 mcg/kg	0.2 mcg/kg	0.2 mcg/kg (max 5 mcg/d)	5 – 15 mcg
Selenium	2 mcg/kg	2 mcg/kg	2 mcg/kg (max 100 mcg/d)	40 – 60 mcg

*Note: These requirements are different than the multi-trace element products currently available in the USA.

Iron (Fe)

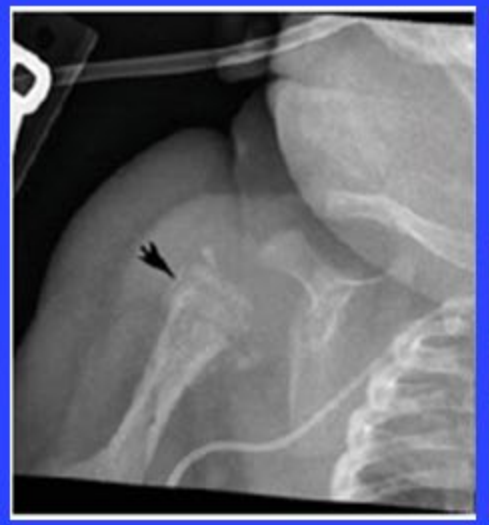
- Parenteral formulation: Fe Dextran
- Controversial; not recommended as a routine additive
- Iron dextran requires a test dose and carries an FDA black box warning
- Not a component of current multiple trace element preparations (limited stability in PN)
- **Risks**: potential for increased sepsis; oxidant; risk for anaphylaxis
- **Avoid**: in infants < 2 months age; chronic blood transfusions; Fe-overload conditions
- Dose: 0.1 - 0.2 mg/kg/day for infants > 2 months of age or those with Fe deficiency

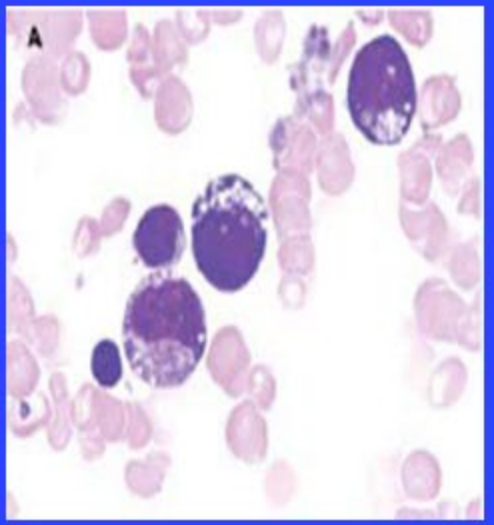
Greene HL, et al. Am J Clin Nutr. 1988;48(5):1324-42.

Copper Deficiency

- Required for co-factor in cuproenzymes
- **Source:** present in Multrys® or individually dosed
- **Risk:** omission from PN
- **Deficiency effects:** anemia, neutropenia, and metabolic bone disease
- **Diagnosis:** ↓serum/plasma Copper & Ceruloplasmin
- **Prevention:** always include copper and monitor q1-3 months

Irregular metaphysis & osteopenia



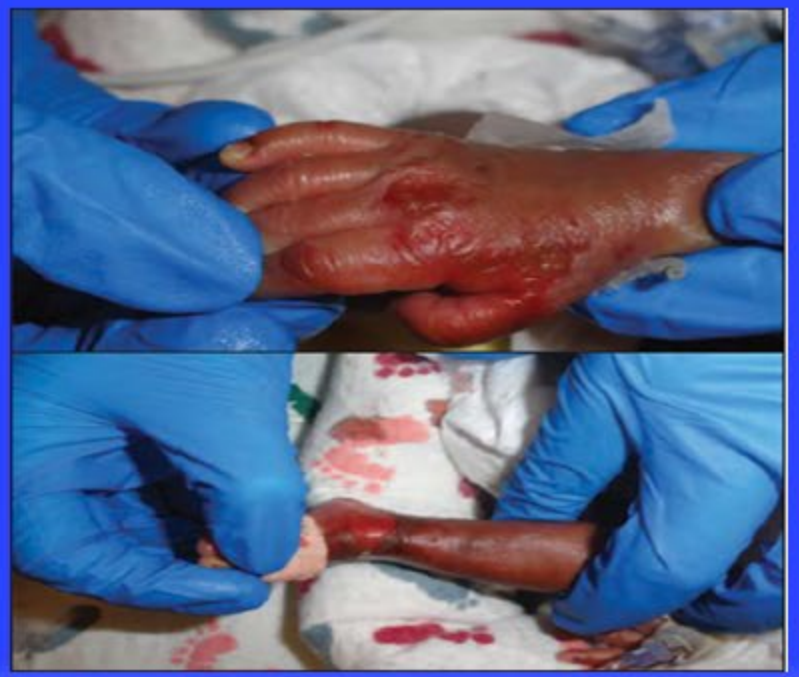


Vacuolated marrow precursors

Marquardt ML, *et al Pediatrics* 2012;130(3);e695-8.
Angotti LB, *et al. Pediatr Blood Cancer* 2008;51(5);693-5.
Norton SA, *et al. MMWR.* 2013;62(7):134-7.

Zinc Deficiency

- Required co-factor for enzymes involved maintenance of structural integrity of proteins, regulation of gene expression
- **Source:** **m**ultitrace and/or individually dosed
- **Risk:** omission from PN
- **Deficiency effects**: alopecia, acral skin rash, impaired wound healing, growth retardation, diarrhea, hypogeusia
- **Diagnosis:** ↓serum/plasma Zinc
- **Prevention:** always include Zinc and monitor every 1-3 months



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Ruktanonchai D, *et al. MMWR.* 2013;62(7):134-7.

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Selenium (Se)

- Should be provided to all patients at initiation of PN
- Omit in patients with renal disease
- Increased requirement with oxidative stress, critical illness, and losses (e.g., fistula output, burns, drains)
- Se status: monitor plasma Se together with a measure of systemic inflammation (↑ C-reactive protein is associated with ↓ plasma Se)

Shenkin A. Gastroenterology 2009;137(5 Suppl):S61-9.

Chromium (Cr)

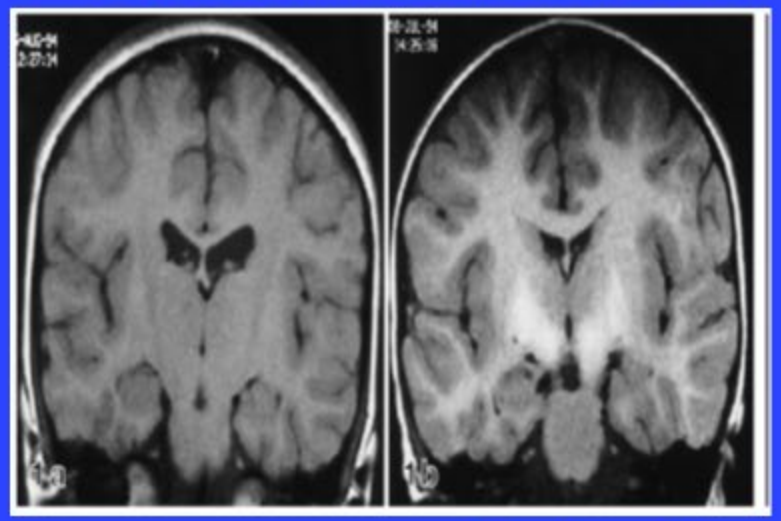
- Recent data suggests the need to lower the recommended amount of Cr in PN
- Cr improves glucose tolerance in VLWB and ELBW at risk for perinatal hyperglycemia
- Current PN components are contaminated with Cr
- Omit Cr in patients with renal disease or on long-term therapy with PN

Capone K, *et al. Nutr Clin Pract*. 2018;33(3):426-32.
Moukarzel A. *Gastroenterology* 2009;137(5 Suppl):S18-28.

Manganese

- Required for mucopolysaccharide metabolism
- Normally regulated through restricted enteric absorption
- **Source:** Multrys®
- **Toxicity:** manganese deposition in basal ganglia => dopamine depletion
  => Parkinsonian symptoms
- **Diagnosis:** ↑plasma concentrations
- **Prevention:** discontinue Multrys®
  in chronic PN and give trace minerals individually

Mn deposition in subthalamic nuclei



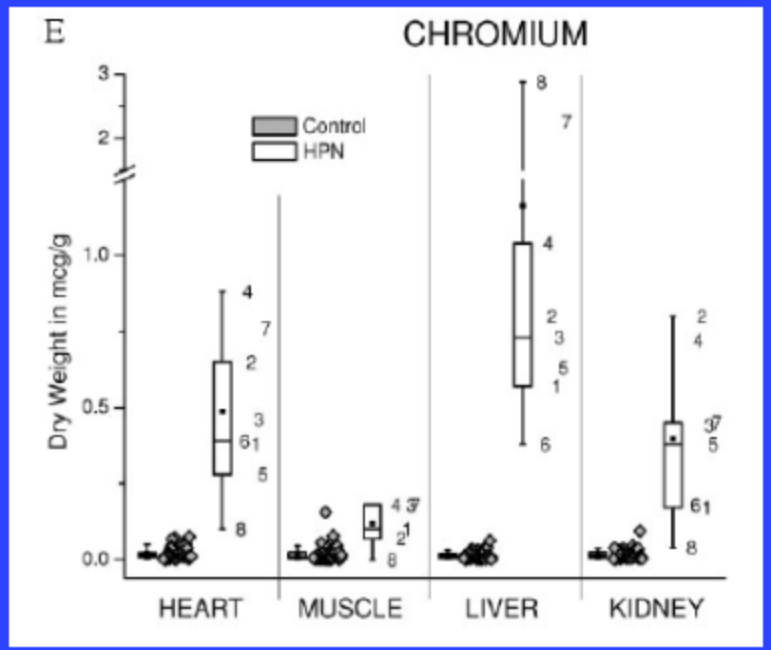
Control Mn deposition

Quaghhebeur G, *et al. Neuroradiology* 1996;38(7):680-83.
Howard L, *et al. J Parenter Enteral Nutr.* 2007;31(5):388-96.

Chromium

- Required for glucose regulation, ↑insulin sensitivity
- **Source:** Multrys® & natural contaminant in PN solutions
- **Risk:** chronic deposition in tissues:
  Kidneys => ↑long-term risk for nephropathy
- **Diagnosis:** ↑serum/plasma concentrations
- **Prevention:** discontinue multi-trace in chronic PN and give other trace minerals individually

Chromium accumulation in tissues



Quaghhebeur G, *et al. Neuroradiology* 1996;38(7):680-83.
Howard L, *et al. J Parenter Enteral Nutr.* 2007;31(5):388-96.

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PN Monitoring

Trace Element	Initial	With Every Change in PN Order	Weekly Until Stable	Monthly / as Indicated
Electrolytes	√	√	√	
Glucose	√	√	√	
Calcium	√	√	√	
BUN	√	√	√	
Creatinine	√	√	√	
Magnesium	√	√	√	
Phosphorus	√	√	√	
ALT	√		√	
AST	√		√	
Alkaline phosphatase	√		√	

PN Monitoring – Cont'd

Trace Element	Initial	With Every Change in PN Order	Weekly Until Stable	Monthly / as Indicated
Total protein	√		√	
Albumin	√		√	
GGT	√		√	
Prealbumin	√		√	
Triglycerides	√	√	√	
Conjugated bilirubin	√		√	
CBC	√		√	√
Iron studies				√
Trace elements				√
Vitamins				√

Case

3-week-old boy born at 23-week gestation developed septic shock, renal failure, necrotizing enterocolitis, and bowel perforation. He was treated with peritoneal washouts, drains, antimicrobials, and bowel rest. PN was started on DOL#1, but lipids were intermittently held since birth due to fluid overload and hypertriglyceridemia. He was later diagnosed with intestinal failure-associated liver disease (IFALD) (direct bilirubin > 2 mg/dL) and essential fatty acid deficiency (EFAD) (T:T > 0.2). What is the most appropriate IV lipid emulsion (ILE) for this infant?

A) Hold ILE
B) 100% soybean oil ILE 0.5 g/kg
C) Mixed oil ILE 3 g/kg
D) 100% fish oil ILE 1 g/kg

Case: Review

3-week-old boy born at 23-week gestation developed septic shock, renal failure, necrotizing
oneal
washouts,
, but
lipids were
hypertrigly
ated liver
disease (IF
cy (EFAD)
(T:T > 0.05
fant?

A) Hold I
B) 100%
C) Mixed
D) 100% fish oil ILE 1 g/kg

EFAD can develop rapidly in premature infants who do not receive an adequate amount of lipid. Therefore, ILE withholding and ILE dose restriction is not appropriate for premature infants. ILEs should be given consistently to prevent an EFAD. The optimal type and dose of ILE depends on the patient's age, liver status, clinical goal, and nutritional goals. In this case, a 100% fish oil ILE dosed at ≥ 1 g/kg/day can safely and effectively treat the infant's EFAD, IFALD, and hypertriglyceridemia.