

Pediatric Parenteral Nutrition

A Comprehensive Review



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Speaker Disclosure goes here

Objectives

- To understand the history, indications, route of administration, components, monitoring, and complications related to parenteral nutrition for pediatric patients
- To understand the indications, components, and monitoring related to parenteral nutrition for neonatal patients
- To understand the role and implementation of parenteral nutrition in the critically ill and specialized patient populations
- To understand the background, implementation, monitoring, and complications related to home parenteral nutrition

Glossary

AA	Amino acid	IVFE	Intravenous fat emulsion
AAP	American Academy of Pediatrics	K	Potassium
ASPEN	American Society for Parenteral & Enteral Nutrition	MCT	Medium chain tryglicerides
Cr	Chromium	Mg	Magnesium
CRP	C-reactive protein	Mn	Manganese
Cu	Copper	Na	Sodium
DHA	Docosahexaenoic acid	NEC	Necrotizing enterocolitis
DRI	Dietary Reference Intakes	Phos	Phosphorus
EN	Enteral nutrition	PICC	Peripherally inserted central catheter
EFA	Essential fatty acid	PN	Parenteral nutrition
EFAD	Essential fatty acid deficiency	PNALD	Parenteral nutrition-associated liver disease
GIR	Glucose infusion rate	PT	Prothrombin time
HCl	Hydrochloric acid	PTT	Partial thromboplastin time
HPN	Home Parenteral Nutrition	REE	Resting Energy Expenditure
IBD	Inflammatory Bowel Disease	SBS	Short Bowel Syndrome
iCa	Ionized calcium	Se	Selenium
IV	Intravenous	VLBW	Very low birth weight
IVF	Intravenous fluid	WHO	World Health Organization

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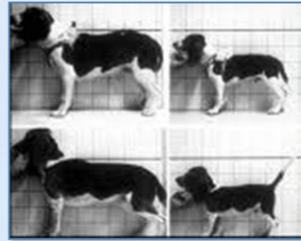
- Parenteral Nutrition for the Pediatric Patient
- Parenteral Nutrition for the Neonatal Patient
- Parenteral Nutrition for the Specialized Patient
- Home Parenteral Nutrition
- Cases
- Questions & Answers



Parenteral Nutrition For The Pediatric Patient

Parenteral Nutrition - History

- **Late 1930s**
 - positive nitrogen balance with infusion of protein hydrolysates in children
- **1944**
 - glucose, casein, olive oil/lecithin preparation in 5-month-old marasmic infant for 5 days via peripheral vein
- **1961**
 - safe intravenous fat preparation
- **1966**
 - administration of hypertonic dextrose /amino acid solutions via central lines in beagle puppies
- **1968**
 - First clinical report of successful use of PN in infant with short bowel syndrome resulting in normal growth and development*



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*Dudrick et al. *Surgery* 1968;64:134-142.

Sukarochana et al. *Surg Gyn Obstetr.* 1965;121:79.

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In 1966 an animal model of short bowel syndrome was created at the University of Pennsylvania. Beagle puppies were given PN via a central line and shown to have normal rates of growth. In the slide the puppies on the left received PN and had normal rates of growth as compared to the puppies on the right who did not have a central line.

Parenteral Nutrition - History

- **Mid-1970s**
 - protein hydrolysates replaced by crystalline amino acid solutions resulting in fewer allergic reactions
- **1980**
 - Infant-specific crystalline amino acid solutions
- **1981**
 - Pediatric-specific vitamin and mineral solutions
- **1988**
 - Guidelines for vitamin and mineral dosing for neonate and pediatric patients.

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


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Greene HL, Hambidge KM, Schanler R, et al. Guidelines for the use of vitamins, trace elements, calcium, magnesium, and phosphorus in infants and children receiving total parenteral nutrition: report of the Subcommittee on Pediatric Parenteral Nutrient Requirements from the Committee on Clinical Practice Issues of the American Society for Clinical Nutrition. *Am J Clin Nutr.* 1988 Nov;48(5):1324-42.

Parenteral Nutrition - Indications

- Always use Enteral Nutrition (EN) whenever possible
- Use PN only when
 - Unable to meet nutritional requirements via the GI tract
 - Bowel dysfunction resulting in inability to tolerate EN for
 - 1-3 days in infants
 - 4-5 days in children and adolescents
 - 7-10 days in adults
- **PN should ONLY be used when there is NO reason to use EN.**

Braunschweig et al. *Amer J Clin Nutr.* 2001;74(4):534-42.


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The benefits of EN include: reduction of gut atrophy. Improvement of gut motility, reduction in infections (enhanced gut immune function and avoidance of translocation), cost effectiveness and the fact that it is less likely to overfeed the patient.

The limitations of PN include that it is more likely to underfeed the patient. Contraindications to enteral feeding include: a nonfunctional gut, anatomical disruption, obstruction, ischemia, peritonitis and severe shock states; frequent interruptions for fasting for diagnostic and other procedures limit efficacy of EN, especially in malnourished patients and the risk of aspiration

Braunschweig CL. et al. Enteral compared with parenteral nutrition: a meta-analysis. *Amer J Clin Nutr.* 2001;74(4):534-42.

Parenteral Nutrition - Timing

- **Timing of nutrition may be as or more important than route**
 - A meta-analysis in adults compared early PN to the delayed start of enteral nutrition. They showed when early PN was used there was reduced mortality when compared to the delayed starting of EN. Patients who received PN had increased infections.
- **Pediatric Guidelines**
 - If EN is not possible, PN should be started within
 - 1-3 days in infants
 - 4-5 days in older children
 - Meta-analysis identified one trial in pediatric burn patients and concluded no difference when EN was started within 24 hrs compared to ≥ 48 hrs; therefore data insufficient!

Simpson et al. *Intensive Care Med.* 2005;31(1):12-23.

ASPEN et al. *J Parenter Enteral Nutr.* 2002 Jan-Feb;26(1 Suppl):1SA-138SA.

Joffe et al. *Cochrane Database Syst Rev.* 2009;2.

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Simpson F., Doig GS. Parenteral vs. enteral nutrition in the critically ill patient: a meta-analysis of trials using the intention to treat principle. *Intensive Care Med.* 2005;31(1):12-23.

ASPEN Board of Directors and the Clinical Guidelines Task Force. Guidelines for the use of parenteral and enteral nutrition in adult and pediatric patients. *J Parenter Enteral Nutr.* 2002 Jan-Feb;26(1 Suppl):1SA-138SA. No abstract available. Erratum in: *J Parenter Enteral Nutr.* 2002 Mar-Apr;26(2):144.

Joffe A et al. Nutritional support for critically ill children. *Cochrane Database Syst Rev.* 2009;2.

Parenteral Nutrition – Indications

- Very low birth weight infants (birth weight < 1500 g)
- Inability to tolerate enteral feeds e.g. paralytic ileus, chemotherapy, radiation enteritis
- Small bowel obstruction
- Radiation enteritis
- Gastrointestinal fistula
- Hemodynamic instability with high risk of mesenteric ischemia (e.g., NEC in preterm infants, ECMO, shock, acute critical illness)
- Conditions associated with intestinal failure e.g., short bowel syndrome, diarrhea with irreversible malabsorption, pseudo-obstruction, intestinal epithelial disorders (microvillus inclusion disease, tufting enteropathy)

Parenteral Nutrition - Route of Administration

- Central versus peripheral venous access
 - Defined by where the tip of the catheter is positioned
- Central
 - Tip is positioned in the superior or inferior vena cava or right atrium
 - Types: peripherally inserted central catheter (PICC), tunneled and non-tunneled central catheters, umbilical venous catheter, implanted port
- Peripheral
 - Tip is not positioned in the superior or inferior vena cava or right atrium
 - Type: peripheral intravenous catheter
- Intradialytic PN

Fuhrman. *Nutr Clin Pract*. 2009;24(4):470-80
Brewer. *Am J Kidney Dis*. 1999;33:205-207.
ASPEN et al. *J Parenter Enteral Nutr*. 2002;26(1 Suppl):1SA-138SA.


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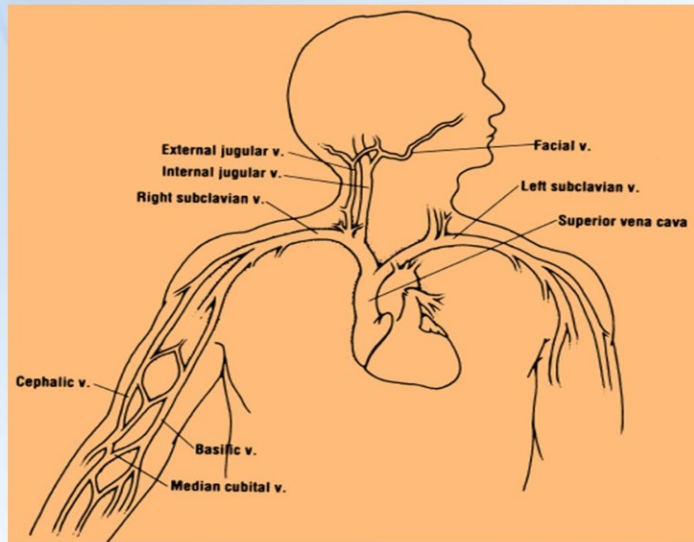
The best location for the tip of a central catheter is at the junction of the SVC and IVC with the right atrium. The danger of placing lines far into the right atrium relates to the possibility of perforation of the heart especially in very small neonates. Patients with renal failure are very fluid restricted thereby limiting the amount of PN calories that can be delivered. Altering the composition of the dialysis solution is a way to provide additional calories and nutrition.

Fuhrman MP. Intradialytic parenteral nutrition and intraperitoneal nutrition. *Nutr Clin Pract*. 2009; 24 (4):470-480

Brewer ED. Pediatric experience with intradialytic parenteral nutrition and supplemental tube feeding. *Am J Kidney Dis*. 1999;33:205-207.

ASPEN Board of Directors and the Clinical Guidelines Task Force. Guidelines for the use of parenteral and enteral nutrition in adult and pediatric patients. *J Parenter Enteral Nutr*. 2002 Jan-Feb;26(1 Suppl):1SA-138SA. No abstract available. Erratum in: *J Parenter Enteral Nutr*. 2002 Mar-Apr;26(2):144.

Parenteral Nutrition - Peripheral vs. Central



Mirtallo et al. *J Parenter Enteral Nutr.* 2004;28(6):S39-70.


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The best location for the tip of a central catheter is at the junction of the SVC and IVC with the right atrium. The danger of placing lines far into the right atrium relates to the possibility of perforation of the heart especially in very small neonates. Patients with renal failure are very fluid restricted thereby limiting the amount of PN calories that can be delivered. Altering the composition of the dialysis solution is a way to provide additional calories and nutrition.

Fuhrman MP. Intradialytic parenteral nutrition and intraperitoneal nutrition. *Nutr Clin Pract.* 2009; 24 (4):470-480

Brewer ED. Pediatric experience with intradialytic parenteral nutrition and supplemental tube feeding. *Am J Kidney Dis.* 1999;33:205-207.

ASPEN Board of Directors and the Clinical Guidelines Task Force. Guidelines for the use of parenteral and enteral nutrition in adult and pediatric patients. *J Parenter Enteral Nutr.* 2002 Jan-Feb;26(1 Suppl):1SA-138SA. No abstract available. Erratum in: *J Parenter Enteral Nutr.* 2002 Mar-Apr;26(2):144.

Parenteral Nutrition - Peripheral vs. Central

Peripheral PN

- Used for <2 weeks
- Patient has no fluid restriction and nutrient needs can be met
- Osmolality 900-1000 mOsmol/L *
 - Maximum 10-12.5% dextrose

Central PN

- Used for >2 weeks
- Patient is fluid restricted and nutrient needs cannot be met by peripheral PN
- Peripheral access limited
- Can use hypertonic solutions

* Mirtallo et al. *J Parenter Enteral Nutr.* 2004;28(6):S39-70.

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PN solutions containing 900 mosmol, according to ASPEN recommendation, or more should be given centrally. In adult patients 1800 mosmol is the maximum osmolality that should be used.

Some institutions may choose D10 or D12.5 based on osmolality or internal guidelines.

Mirtallo J, Canada T, Johnson D, et al. Safe practices for parenteral nutrition. *J Parenter Enteral Nutr.* 2004 Nov-Dec;28(6):S39-70.

Isaacs et al. Parenteral Nutrition of Adults with 900-milliosmolar solution via peripheral vein. *Am J Clin Nutr* 1977; 30:552-559.

Parenteral Nutrition - Central Venous Access Pediatric Issues

- Tunneled and non-tunneled catheters
- The more lumens the greater the risk of infection
- Impregnated catheters useful in the short-term
 - Can be impregnated with antibiotics or antiseptics
 - May prevent catheter-related infection
 - May cause allergic reactions
- Removal in the case of sepsis may not be an option (especially for neonates or SBS)
- Line needs to be secured



Permission from Dr. NK Mittal

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Scales K. *Br J Nurs*. 2010;19(2):88-92.

Non-tunneled catheters are easy to place, used only for the short term, should not be exchanged over a guidewire, are at high risk for infections and cannot be repaired. Tunneled catheters are meant for long-term usage, when plan for duration is greater than one month, require minimal care, requires the operating room or interventional radiology suite for placement and removal, have less infection risk and can be repaired. Picture shows an example of securing device for young children with central lines.

Scales K. Central venous access devices. Part 1: devices for acute care. *Br J Nurs*. 2010 Jan 28-Feb 10;19(2):88-92.

Pediatric Nutrition Support Core Curriculum. Editor: Mark Corkins, MD, CNSP. American Society for Parenteral and Enteral Nutrition (ASPEN), 2010.

Parenteral Nutrition - Administration

- Type of solution
 - 2-in-1: dextrose and amino acids
 - 3-in-1: dextrose, amino acids and lipids
- Filters

0.22 micron filters	1.2 micron filters
Remove most pathogenic bacteria	Removes only <i>Candida</i> and large lipid droplets
Used only with 2-in-1 solutions; Lipid solutions are sheared by the smaller filters	Can be used with 3-in-1 solutions
Never remove a filter!	





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Traditionally PN solutions are 2-in-1 solutions with the IV lipid administered separately. This is still the solution of choice in many institutions since it allows for the easy identification of precipitates and for increased electrolyte administration. The 3-in-1 solutions are usually administered at home for ease of care, are being used in some pediatric institutions, and result in reduced nursing time.

Filters are placed in line between the PN solution and the patient and are very important.

Components of PN

- Non-protein energy
 - Carbohydrates (dextrose)
 - Fat (lipid)
- Protein (amino acids)
- Electrolytes
- Minerals, vitamins, trace elements
- Water
- Miscellaneous: heparin, medications (e.g. ranitidine)




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Examples of other additives to PN include vitamin K, cysteine, carnitine, and insulin.

Components of PN - Macronutrient Guidelines

	A.A.P.		A.S.P.E.N.	
	Weight	Daily Recommendation	Weight / Age	Daily Recommendation
Protein	10-20 kg	1-2.5 g/kg	>10 kg or 1-10 yrs	1-2 g/kg
	>20 kg	0.8-2 g/kg	11-17 yrs	0.8-1.5 g/kg
Energy / Caloric	10-20 kg	60-90 kcal/kg	>1-7 yrs	75-90 kcal/kg
	>20 kg	30-75 kcal/kg	>7-12 yrs	50-75 kcal/kg
			>12-18 yrs	30-50 kcal/kg
Fluid	>10-20 kg = 1000 mL + 50 mL/kg >10 kg			
	>20 kg = 1500 mL + 20 mL/kg >20 kg			
Carbohydrates (Dextrose)	10-20 kg	8-28 g/kg	Carbohydrates should comprise 40% to 60% of total caloric intake.	
	>20 kg	5-20 g/kg		
IV Fat Emulsion	>10kg	1-3 g/kg	The minimum fat requirement is determined by essential fatty acid need, and the daily maximum is 50% to 60% of energy.	

Kleinman RE. *Pediatric Nutrition Handbook 6th Edition* 2009:519-540.

Forchielli ML, Miller SJ. *The ASPEN Nutrition Support Practice Manual* 2005:38-53.

Pediatric Nutrition Support Core Curriculum. Editor: M Corkins. ASPEN, 2010.



These are suggested macronutrient guidelines from AAP and ASPEN however there are other ways to calculate energy needs using accepted equations.

Usually the IV fat emulsion is 20% however 10 and 30% solutions are available; 30% are usually used in 3-in-1 solutions and 10% solutions are infrequently used.
20%

Kleinman RE. *Pediatric Nutrition Handbook 6th Edition* 2009:519-540.

Forchielli ML, Miller SJ. *The ASPEN Nutrition Support Practice Manual* 2005:38-53.

Pediatric Nutrition Support Core Curriculum. Editor: Mark Corkins, MD, CNSP.

American Society for Parenteral and Enteral Nutrition (ASPEN), 2010.

Components of PN - Dextrose

- Major source of non-protein calories is D-glucose
- Typically provide 40 - 55% of caloric intake
- Monohydrate form provides 3.4 kcal/g
- Stepwise increase to allow appropriate response of endogenous insulin preventing glucosuria & osmotic diuresis
- Glucose increases osmolality (risk of phlebitis)

 **Dextrose**
A Health Care Brand
 **CDME**  **NESPONSIA**
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Carbohydrate content of PN is provided by dextrose. Carbohydrates provide calories and are important for glucose homeostasis.

Stepwise increase by 0.5 - 1 mg/kg/min/day in extremely low birth weight infants (<1000 g) because of high risk for glucose intolerance.

Minimum Carbohydrate Requirements for Age

Age	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

Kalhan et al. *Eur J Clin Nutr*. 1999;53:S94-100.

Koletzko et al. *J Pediatr Gastroenterol Nutr*. 2005;41(Suppl 2):S1-87.

Pediatric Nutrition Support Core Curriculum. Editor: M. Corkins. ASPEN, 2010.



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

Kalhan SC, Kilic I. Carbohydrate as nutrient in the infant and child: range of acceptable intake. *Eur J Clin Nutr*. 1999;53 Suppl 1:S94-100.

Koletzko B, Goulet O, Hunt J, Krohn K, Shamir R; Guidelines on Paediatric Parenteral Nutrition of the European Society of Paediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN) and the European Society for Clinical Nutrition and Metabolism (ESPEN), Supported by the European Society of Paediatric Research (ESPR). *J Pediatr Gastroenterol Nutr*. 2005 Nov;41 Suppl 2:S1-87.

Pediatric Nutrition Support Core Curriculum. Editor: Mark Corkins. American Society for Parenteral and Enteral Nutrition (ASPEN), 2010.

Estimation of Glucose Infusion Rate (GIR)

- GIR varies with the age of the patient
- Need 3 - 4 mg/kg/min to meet glucose utilization needs and to maintain normal blood glucose levels
- Maximal glucose oxidation rate under most circumstances 7 - 13 mg/kg/min
 - Above this rate, fat synthesis significantly increases leading to increased RQ (CO_2/O_2)
 - In presence of pulmonary disease, large energy intake may lead to CO_2 retention
 - Maximal glucose oxidation rate occurs with the following GIR
 - neonates and infants: 12.5 mg/kg/min
 - children & adolescents: 6 mg/kg/min
- GIR (mg/kg/min) = $\frac{\text{Dextrose(g/dL)} * \text{Infusion Rate(ml/hr)} * 0.167}{\text{wt (kg)}}$

OR use an online calculator at:

<http://www-users.med.cornell.edu/~spon/picu/calc/glucinfr.htm>

or <http://www.nicutools.org/> (choose "glucose delivery" from list of calculators)

Bresson et al. *Pediatr Res.* 1989; 25(6):645-8. Jones et al. *J Pediatr Surg.* 1993;28:1121.

Yunis et al. *J Pediatr.* 1989;115:127. Samor et al. *Handbook of Pediatric Nutrition* 3rd Ed. 2005: 533.

Koletzko et al. *J Pediatr Gastroenterol Nutr.* 2005;41(Suppl 2):S1-87.



Web based calculators allow calculation of total GIR from multiple infusions with various dextrose concentrations (e.g. dextrose containing rider fluid + PN + dextrose medication carriers).

Neonates need 5 - 6 mg/kg/min while adults glucose needs can be met with 1 - 2 mg/kg/min.

Bresson JL, Narcy P, Putet G et al. Energy substrate utilization in infants receiving total parenteral nutrition with different glucose to fat ratios. *Pediatr Res.* 1989 Jun;25(6):645-8.

Jones MO, Pierro A, Hammond P, Nunn A, Lloyd DA. Glucose utilization in the surgical newborn infant receiving total parenteral nutrition. *J Pediatr Surg.* 1993 Sep;28(9):1121-5.

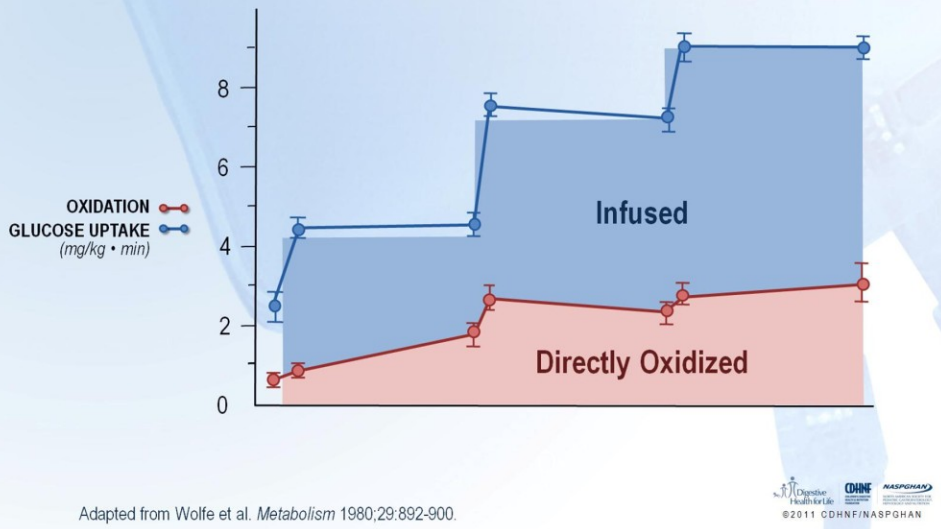
Yunis KA, Oh W. Effects of intravenous glucose loading on oxygen consumption, carbon dioxide production, and resting energy expenditure in infants with bronchopulmonary dysplasia. *J Pediatr.* 1989 Jul;115(1):127-32.

Cox JH and Melbardis IM. (2005). Parenteral Nutrition. In PQ Samor & K King(Eds.), *Handbook of Pediatric Nutrition*, 3rd ed. (page 533). Sudbury, MA: Jones and Bartlett Publishers.

Koletzko B, Goulet O, Hunt J, Krohn K, Shamir R; Guidelines on Paediatric Parenteral Nutrition of the European Society of Paediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN) and the European Society for Clinical Nutrition and Metabolism (ESPEN), Supported by the European Society of Paediatric Research (ESPR). *J Pediatr*

Gastroenterol Nutr. 2005 Nov;41 Suppl 2:S1-87.

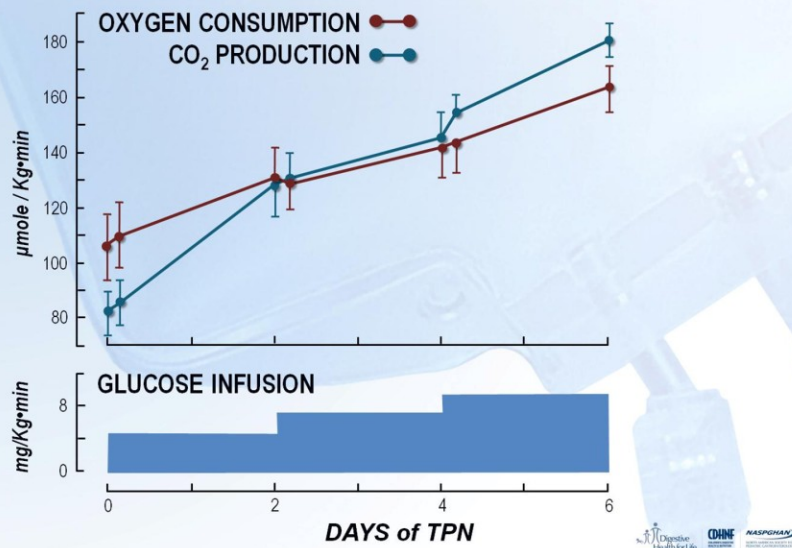
Glucose Oxidation is Limited - I



Metabolic study in adults: as the glucose infusion rate is increased, the rate of oxidation begins to plateau. Above this point, glucose is being increasingly converted to fat.

Wolfe RR, O'Donnell TF Jr, Stone MD, et al. Investigation of factors determining the optimal glucose infusion rate in total parenteral nutrition. *Metabolism*. 1980 Sep;29(9):892-900.

Glucose Oxidation is Limited - II



Adapted from Wolfe et al. *Metabolism* 1980;29:892-900.


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Components of PN - Protein

- Functions of protein
 - Provides structure (e.g., muscle)
 - Provides function (e.g., enzymes, transport proteins)
 - Acts as a nitrogen donor to other compounds (e.g., nucleic acids, carnitine, taurine)
- Protein should not serve as an energy source
- Protein requirements vary by age and disease state
- Infants
 - Infants need conditional amino acids like histidine, taurine and cysteine because of immature synthetic abilities
 - Infant amino acid solutions are based on the serum amino acid pattern seen in breastfed infants
- Excess protein intake leads to hyperazotemia

Shulman et al. *J Pediatr Gastroenterol Nutr.* 2003;36:587-607.

Kleinman RE. *Pediatric Nutrition Handbook 6th Edition* 2009:519-40.

Forchielli et al. *The ASPEN Nutrition Support Practice Manual* 2005:38-53.



Shulman RJ, Phillips S. Parenteral nutrition in infants and children. *J Pediatr Gastroenterol Nutr.* 2003 May;36(5):587-607.
Kleinman RE. *Pediatric Nutrition Handbook 6th Edition* 2009:519-540.
Forchielli ML, Miller SJ. *The ASPEN Nutrition Support Practice Manual* 2005:38-53.

Examples of Amino Acid Solutions (per 100 mL)

		STANDARD		INFANT	
		Aminosyn® 10%	Novamine® 10%	Premasol™ 10%	TrophAmine® 10%
Essential	Isoleucine	0.72 g	0.6 g	0.82 g	0.82 g
	Leucine	0.94 g	0.73 g	1.4 g	1.4 g
	Lysine	0.72 g	0.58 g	0.82 g	0.82 g
	Methionine	0.40 g	0.40 g	0.34 g	0.34 g
	Phenylalanine	0.44 g	0.56 g	0.48 g	0.48 g
	Threonine	0.52 g	0.42 g	0.42 g	0.42 g
	Tryptophan	0.16 g	0.18 g	0.20 g	0.20 g
Nonessential	Valine	0.8 g	0.58 g	0.78 g	0.78 g
	Aspartic Acid	-	-	0.32 g	0.32 g
	Serine	0.42 g	0.50 g	0.38 g	0.38 g
	Glutamic Acid	-	-	0.50 g	0.50 g
	Alanine	1.28 g	2.07 g	0.54 g	0.54 g
Conditionally Essential	Proline	0.86 g	0.68 g	0.68 g	0.68 g
	Arginine	0.98 g	1.15 g	1.2 g	1.2 g
	Glycine	1.28 g	1.03 g	0.36 g	0.36 g
	Glutamine	-	-	0.50 g	0.50 g
	Taurine	-	-	0.025 g	0.025 g
	Cysteine	-	-	<0.016 g	<0.016 g
	Histidine	0.3 g	0.48 g	0.48 g	0.48 g
Tyrosine	0.044 g	0.04 g	0.24 g	0.24 g	

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These are examples of commonly available amino acid solutions. Solutions vary depending on whether they are for infant or older children and they contain all the amino acids including essential, nonessential and conditionally essential. Taurine and cysteine are present in infant solutions.

Pharmacy Handbook and Formulary, The Children's Hospital of Philadelphia. Hudson, ON: Lexi-Comp Inc, 2006;p569.

Amino Acid Requirements in PN

- Amino acids

	g/kg/day
Preterm	2.5-4.0
Term infant	2.2-3.5
Child: 5-20 kg	1.0-2.5
20-40 kg	1.0-2.0
Adolescent	0.8-2.0 *

*150 g/day maximum

- Increased protein needs

- Malnutrition
- Enteric/urinary protein loss
- Stress
- Drugs (e.g. corticosteroids)
- Burns

Kashyap S. *Curr Opin Pediatr*. 2008;20:132
Denne SC. *Semin Neonatol*. 2001;6:377-82
Shulman et al. *J Pediatr Gastroenterol Nutr*. 2003;36:587-607.


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Kashyap S. Is the early and aggressive administration of protein to very low birth weight infants safe and efficacious? *Curr Opin Pediatr*. 2008 Apr;20(2):132-6.
Denne SC. Protein and energy requirements in preterm infants. *Semin Neonatol*. 2001;6(5):377-82.
Shulman RJ, Phillips S. Parenteral nutrition in infants and children. *J Pediatr Gastroenterol Nutr*. 2003 May;36(5):587-607.
Pediatric Nutrition Support Core Curriculum. Editor: Mark Corkins. American Society for Parenteral and Enteral Nutrition (ASPEN), 2010.

Components of PN - Fat

- Fat
 - Concentrated source of calories
 - In children, only use 20% emulsion (provides 2 kcal/mL)
 - Currently in the U.S., lipid solutions are composed of triglycerides from soybean oil and safflower and emulsified by egg yolk phospholipid
- Minimum of 1-2% of calories from a combinations of linoleic and linolenic acid to meet EFA needs (met with 0.5-1.0 g/kg per day fat)
 - Serum triene:tetraene ratio is reflective of EFA status
 - A triene:tetraene ratio < 0.2 is generally considered to reflect EFA sufficiency
- Infused over 24 hours to maximize tolerance
- Monitor triglycerides to assess tolerance

Pediatric Nutrition Support Core Curriculum. Editor: M. Corkins. ASPEN, 2010.
Shulman et al. *J Pediatr Gastroenterol Nutr.* 2003;36:587-607.
Wolfram et al. *J Parent Ent Nutr.* 1978;2:634


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Fat provides calories and meeting EFA needs.

In neonates triglyceride levels upto 200 mg/dL and in older children levels upto 300-400 mg/dL are tolerated.

Fat decreases the osmolality of the PN solution and is a more concentrated form of calories when compared to dextrose and amino acids

Triene:tetraene ratio: If concentrations of the EFA are low, the ω -9 fatty acids are preferentially desaturated and elongated (i.e., 20:3 ω -9) so that the ratio of 20:3 fatty acids to 20:4 ω -6 (arachidonic acid derived from linoleic acid) is increased. Linoleic acid levels are also used to determine EFAD.

Test dose should be used in patients with egg allergy before administration of lipid solutions.

30% emulsions are available, but are used in 3-in-1 solutions only.

Use of IVFE is not contraindicated in patients with pancreatitis.

Pediatric Nutrition Support Core Curriculum. Editor: Mark Corkins. American Society for Parenteral and Enteral Nutrition (ASPEN), 2010.

Shulman RJ, Phillips S. Parenteral nutrition in infants and children. *J Pediatr*

Gastroenterol Nutr. 2003 May;36(5):587-607.

Wolfram G, Eckart J, Walther B, Zöllner N. Factors influencing essential fatty acid requirement in total parenteral nutrition (TPN). J Parenter Enteral Nutr. 1978 Nov;2(5):634-9.

Comparison of Lipid Emulsions*

Fatty Acids	Soy	Fish Oil	SMOF#
Linoleic	50	4	37
Linolenic	9	2	5
Oleic	24	15	55
Eicosapentaenoic	0	20	5
Docosahexaenoic	0	12	5
Arachidonic	0.1	2	1

* Approximate % total fatty acids

Soybean oil, medium chain triglycerides, olive oil and fish oil

<http://www.fresenius-kabi.com/>



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This is the composition of a typical soybean emulsion compared to a fish oil and a SMOF emulsion. Fish oil emulsion is available from the FDA on a compassionate use basis. SMOF is used in Europe but not the USA. Note that DHA levels are highest in the fish oil emulsion.

Fish oil is not routinely available in North America; need IND from FDA. It contains predominately ω -3 fatty acids and approximately 4.4% and 1.8% linoleic and α -linolenic acids by weight of total fatty acids, respectively. Some evidence suggests it may reduce the severity of parenteral nutrition-associated cholestasis. It is unclear whether this is related to composition of the emulsion or reduced dosage of administration. It contains increased eicosapentaenoic and docosahexaenoic acid. In piglets there is a reduced risk for cholestasis which is not explained by difference in membrane fluidity, Na/K ATPase.

Suggested Doses for Lipids

	Starting Dose (g/kg/day)	Maximum Dose (g/kg/day)
Neonate/Infant	1	3
Children	1	2
Adolescent/Adult	0.5	1

Pediatric Nutrition Support Core Curriculum. Editor: M. Corkins. ASPEN, 2010.
ASPEN. *J Parenter Enteral Nutr.* 2002;26(1 Suppl):1SA-138SA

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Pediatric Nutrition Support Core Curriculum. Editor: Mark Corkins. American Society for Parenteral and Enteral Nutrition (ASPEN), 2010.

ASPEN Board of Directors and the Clinical Guidelines Task Force. Guidelines for the use of parenteral and enteral nutrition in adult and pediatric patients. *J Parenter Enteral Nutr.* 2002 Jan-Feb;26(1 Suppl):1SA-138SA.

Components of PN - Micronutrient Guidelines

Daily Electrolyte Requirements	A.A.P.		A.S.P.E.N	
	Infants & Toddlers / Children	Adolescents	Infants / Children	Adolescents & Children >50 kg
Sodium	2-4 mEq/kg	60-150 mEq	2-5 mEq/kg	1-2 mEq/kg
Potassium	2-4 mEq/kg	70-180 mEq	2-4 mEq/kg	1-2 mEq/kg
Calcium	0.45-4 mEq/kg (infants & toddlers)	10-40 mEq	0.5-4 mEq/kg	10-20 mEq/day
	0.45-3.15 mEq/kg (children)			
Phosphorus	0.5-2 mmol/kg	9-30 mmol/day	0.5-2 mmol/kg	10-40 mmol/day
Magnesium	0.25-1 mEq/kg	8-32 mEq	0.3-0.5 mEq/kg	10-30 mEq/day
Chloride	2-4 mEq/kg	60-150 mEq	Chloride / Acetate – As needed to maintain acid-base balance	

Pediatric Nutrition Support Core Curriculum. Editor: M. Corkins. ASPEN, 2010.
 Kleinman RE. *Pediatric Nutrition Handbook 6th Ed* 2009:519-40.
 Sacks et al. *The ASPEN Nutrition Support Practice Manual* 2005:108-17.



- Monitor levels closely and adjust daily in PN if needed. The goal is maintenance of homeostasis; weight based supplementation and altered by disease states.
- Na: Consider acid base balance, and fluids & diuretic therapy prior to adjusting Na in PN
 - K: Consider renal function, diuretic therapy, GI losses, after load reducing agents, Na in PN, insulin, dextrose administration
 - Ca: Consider phosphate level, bone health; elevated Ionized Ca (iCa) levels may be acceptable for certain patients
 - Phos: Consider iCa levels, renal function, bone health
 - Calcium and phosphorus requirements are high in preterm infants

Pediatric Nutrition Support Core Curriculum. Editor: Mark Corkins. American Society for Parenteral and Enteral Nutrition (ASPEN), 2010.

Kleinman RE. *Pediatric Nutrition Handbook 6th Edition*. 2009:519-40.

Sacks GS, Mayhew S, Johnson D. Parenteral Nutrition Implementation and Management. *The A.S.P.E.N. Nutrition Support Practice Manual*. 2005:108-117.

Calcium and Phosphorus

- There are limitations to amounts of Ca and Phos that can be supplied in PN
- Ca and Phos can precipitate depending on the amounts added to the PN solution
- Cysteine lowers pH and may be added to neonate/infant PN (by using TrophAmine[®]) to increase solubility of Ca and Phos

Pediatric Nutrition Support Core Curriculum. Editor: M. Corkins. ASPEN, 2010.
Greene et al. *Am J Clin Nutr.* 1988;48:1324-42

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Curves exist for Ca and Phos solubility and these are based on the type of the AA and pH of the solution. Factors affecting Ca and Phos solubility include temperature, concentration of Ca and Phos, type of AA product and concentration, dextrose concentration, pH of the final solution, cysteine, lighting, and order of the mixing.

Pediatric Nutrition Support Core Curriculum. Editor: Mark Corkins. American Society for Parenteral and Enteral Nutrition (ASPEN), 2010.

Greene HL, Hambidge KM, Schanler R, et al. Guidelines for the use of vitamins, trace elements, calcium, magnesium, and phosphorus in infants and children receiving total parenteral nutrition: report of the Subcommittee on Pediatric Parenteral Nutrient Requirements from the Committee on Clinical Practice Issues of the American Society for Clinical Nutrition. *Am J Clin Nutr.* 1988 Nov;48(5):1324-1342.

Multivitamin Requirements with Examples of some Multivitamin Products

	Preterm (per kg) ⁺	Term infants & children > 1 yr ⁺⁺	MVI Ped [®] (5ml) ⁺⁺⁺	MVI 12 [®] (5 ml) ⁺⁺⁺⁺
Vitamin A, IU	700-1500	2300	2300	3300
Vitamin E, IU	3.5	7	7	10
Vitamin D, IU	40-160	400	400	200
Vitamin K, mg	0.1	0.2	0.2	0
Thiamine, mg	0.2-0.35	1.2	1.2	6
Riboflavin, mg	0.15-0.2	1.4	1.4	3.6
Vitamin B6, mg	0.15-0.2	1	1	6
Niacin, mg	4-6.8	17	17	40
Biotin, mcg	8	20	20	60
Pantothenic acid, mg	1-2	5	5	15
Folate, mcg	56	140	140	600
Vitamin B12, mcg	0.3	1	1	5
Vitamin C, mg	15-25	80	80	200

⁺Tsang RC et al. *Scientific Basis and Practical Guidelines*, 2ndEd 2005; pp.415-16.
⁺⁺ Greene et al. *Am J Clin Nutr*. 1988;48:1324-42.

 CDINE NESPORAS
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Vitamin A is provided as retinol and vitamin E as tocopherol. Note; there is no vitamin K in MVI 12[®] and so it will need to be added at a dose of 0.2 mg. Other vitamins that can be added to PN: Insulin, Levocarnitine, folic acid, hydrochloric acid (only for ECMO patients), cysteine, and Vitamin K.

+ Tsang RC, Uauy R, Koletzko B et al. *Nutrition of the Preterm Infant: Scientific Basis and Practical Guidelines*, 2nd ed. Cincinnati, OH: Digital Educational Publishing, Inc, 2005; pp.415-16.

++ Greene HL, Hambidge KM, Schanler R, et al. Guidelines for the use of vitamins, trace elements, calcium, magnesium, and phosphorus in infants and children receiving total parenteral nutrition: report of the Subcommittee on Pediatric Parenteral Nutrient Requirements from the Committee on Clinical Practice Issues of the American Society for Clinical Nutrition. *Am J Clin Nutr*. 1988 Nov;48(5):1324-42.

+++ http://www.hospira.com/Files/MVI_pediatric_PI.pdf

++++ http://www.hospira.com/Files/MVI-12_PI.pdf

Dosing Recommendations for Pediatric Parenteral Multiple Vitamins *

Manufacturer Recommendations		NAG-AMA Recommendations [◇]	
Weight (kg)	Dose (mL)	Weight (kg)	Dose (mL)
< 1	1.5	< 2.5	2 mL/kg
1-3	3.25	> 2.5	5 mL
> 3	5		

* MVI-Pediatric[®]; assumes normal organ function

◇ Nutrition Advisory Group-American Medical Association

Nutrition Advisory Group AMA. *J Parenter and Enter Nutr.* 1979;3(4):258-262.
Shulman et al. *Pediatric Nutrition Support.* 2007;p273-85.



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The current vitamin preparation for infants and children <11 years of age has not been reformulated since the early 1980s. Preparations used in children older than 11 years of age have been reformulated but should not be used for long periods of time in children <11 years of age to avoid excessive vitamin intakes. The evidence used to support recommendations is not comprehensive and more data is needed. Note that micronutrients may be lost due to adherence to the tubing and due to photodegradation. Note the differences in the recommendations from the manufacturer and the NAG-AMA group.

Multivitamin preparations for parenteral use. A Statement by the nutrition advisory group. American Medical Association Department of Foods and Nutrition 1975. *J Parenter and Enter Nutr.* 1979;3(4):258-262.

Shulman RJ, Philips S. Parenteral nutrition indications, administration and monitoring in Pediatric Nutrition Support. Baker SS, Baker RD, Davis AM. 2007;p273-85.

Components of PN - Trace Elements

Mineral	Multitrace®-4	Multitrace®-4	Multitrace®-5 Concentrate
	(per mL)	(per mL)	(per mL)
	Neonatal	Pediatric	(Adolescent/Adult)
Zinc (as Sulfate)	1.5 mg	1 mg	5 mg
Chromium (as Chloride)	0.85 mcg	1 mcg	10 mcg
Selenium (as Selenious Acid)	none	none	60 mcg
Copper (as Sulfate)	0.1 mg	0.1 mg	1 mg
Manganese (as Sulfate)	25 mcg	25 mcg	0.5 mg

American Regent Product Catalog. <http://www.americanregent.com/>



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There are more than 60 minerals which are integrated into various body processes: chromium, copper, iodine, manganese, molybdenum, selenium, zinc etc. Zinc is often required in larger amounts than suggested. Iron may not be routinely included to PN solutions. Optimal requirements for trace elements for children are unknown. Higher amounts of trace elements are present in PN solutions due to component contamination.

Commercial products contain zinc, copper, chromium, manganese. In patients with
|

Moukarzel A. Chromium in Parenteral Nutrition: Too Little or Too Much? Gastroenterology 2009;137:s18-28.

Components of PN - Iron (Fe)

- Not typically part of standard PN though Fe deficiency is common in patients receiving PN
- Addition of parenteral Fe is controversial because of the potential risk of increased sepsis and because Fe is an oxidant
- Consider in patients who have been NPO for > 2 months
- Avoid Fe in infants until age 2 months because of frequent blood transfusions and the possibility of Fe overload
- Parenteral Fe preparations
 - Fe dextran is the only iron prep that can be given in PN
 - Fe dextran is incompatible with fat emulsions and 3-in-1 solutions
 - Consider daily or weekly dose in bags that do not contain lipid or in 2-in-1 solutions
- Intravenous dose for Fe dextran
 - 0.1 - 0.2 mg/kg per day for infants (age > 2 months) and children
 - 2 - 6 mg per day for older children and adolescents
- Continued monitoring of Fe status is recommended to prevent Fe overload

Khaodhiar et al. *J Parenter Enteral Nutr.* 2002;26(2):114-19.


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Other parenteral Fe preparations include Fe sucrose and Fe tri-phosphates. Fe Dextran is compatible with non-lipid containing PN. Due to the recent black box warnings, may want to consider administration of Fe Dextran under supervision, at least initially. When Fe Dextran infusions are used to treat Fe deficient anemia, a test dose is always administered and the patients closely monitored for allergic reaction.

Other causes of anemia in patients on PN are anemia of chronic disease, Zn and Cu deficiency, vitamin E and B12 deficiency, folic acid deficiency, and hemolysis and occult blood loss. In general oral route is preferred over parenteral route for treatment of Fe deficiency anemia.

In a retrospective adult study of 55 patients treated with home PN for more than 6 months, 30/55 (55%) had evidence of Fe deficiency anemia (10/30 at time of start of PN and 20/30 between 2-97 months after start of PN (mean age 28 months). Loss from GI tract was most prominent reason.

Khaodhiar L, Keane-Ellison M, Tawa NE, et al. Iron deficiency anemia in patients receiving home total parenteral nutrition. *J Parenter Enteral Nutr.* 2002 Mar-Apr;26(2):114-119.

Components of PN - Zinc (Zn)

- Zn is an important trace element especially in growth and wound healing
- Signs of Zn deficiency
 - Dermatitis, alopecia, diarrhea, immune deficiency
 - *Mimics acrodermatitis enteropathica*
- Zn excreted mainly in feces
 - Increased needs in diarrhea, hypercatabolic states, ostomy losses, mucositis, and chest tube losses
- Measure of Zn status
 - Serum Zn is a poor measure but is the only measure clinically available
 - A low alkaline phosphatase may suggest Zn deficiency but this is not diagnostic
- Can increase intake in PN to 1.5 - 2 times usual dose in conditions associated with increased needs



Acknowledgement to dermnetnz.org

Report of WHO/ UNICEF/ IAEA/ IZINCG. *Food Nutr Bull.* 2007;28:S399-S400.

Woolf et al. *Dig Dis Sci.* 1987;32(1):8-15.

Prasad et al. *J Lab Clin Med.* 1963;61:537-49.

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Zn is essential in the structural integrity of proteins, which regulate gene expression, and to nuclear binding proteins that act as transcription factors. It is a component of more than 250 metalloenzymes including alcohol, lactate and pyruvate dehydrogenases, alkaline phosphatase, and DNA and RNA polymerases. Zn losses may be high in proximal enterocutaneous fistulas.

Executive summary. Recommendations for indicators of population zinc status. Report of WHO/ UNICEF/ IAEA/ IZINCG Interagency meeting on zinc status indicators. *Food Nutr Bull.* 2007;28:S399-S400.

Standing Committee on the Scientific Evaluation of Dietary Reference Intakes, Food and Nutrition Board, and Institute of Medicine, Dietary reference intakes for vitamin A, vitamin K, arsenic, boron, chromium, copper, iodine, iron, molybdenum, nickel, silicon, vanadium and zinc, National Academy of Sciences, Washington, DC (2001).

Prasad AS, Miale A Jr, Farid Z, et al. Zinc metabolism in patients with the syndrome of iron deficiency anemia, hepatosplenomegaly, dwarfism, and hypogonadism. *J Lab Clin Med.* 1963 Apr;61:537-49.

Woolf GM, Miller C, Kurian R, Jeejeebhoy KN. Nutritional absorption in short bowel syndrome. Evaluation of fluid, calorie, and divalent cation requirements. *Dig Dis Sci.* 1987;32(1):8-15.

Components of PN - Copper (Cu)

- Cu deficiency is rare except in patients with cholestasis when the dose is adjusted
 - Risk factors: malabsorption, prematurity, and severe malnutrition
 - Can present with anemia (hypochromic, microcytic), leukopenia, neutropenia, bone abnormalities
- Biliary tract is the predominant route for Cu excretion
 - Patients with cholestasis have decreased Cu excretion; maybe at increased risk for toxicity
- Patients with diarrhea have increased Cu needs
- Important to note that elevated Cu level can occur in the absence of significant cholestasis
- Monitoring
 - In addition to checking serum Cu and ceruloplasmin levels, clinical picture should be used to assess status
 - Assess levels periodically

Pediatric Nutrition Support Core Curriculum. Editor: M. Corkins. ASPEN, 2010.

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Chronic Cu toxicity is illustrated in Wilson's disease where high levels of Cu occur in the liver, brain, kidney, and other organs. The disease is manifested as cirrhosis of the liver, a variety of neurologic disorders, and renal damage.

Premature infants are at special risk of becoming Cu deficient because Cu accumulates in the fetus during the third trimester.

Marginal Cu deficiency can result in cardiac diseases, arthritis, loss of hair pigmentation, and neurologic abnormalities, mimicking vitamin B12 deficiency.

Cu deficiency should be investigated among patients with pancytopenia in the face of cholestasis.

Pediatric Nutrition Support Core Curriculum. Editor: Mark Corkins. American Society for Parenteral and Enteral Nutrition (ASPEN), 2010.

McMillan NB, Mulroy C, McKay MW, McDonald CM, Jackson WD. Correlation of Cholestasis with Serum Copper and Whole Blood Manganese Levels in Pediatric Patients. *Nutr Clin Pract* 2008;23:161-5.

Leung FY. Trace Elements in Parenteral Micronutrition. *Clin Biochem* 1995;28:561-66.

Hurwitz M, Garcia MG, Poole RL, Kerner JA. Copper Deficiency During Parenteral Nutrition: A Report of Four Pediatric Cases. *Nutr Clinical Prac* 2004;19:305-08.

Halfdanarson TR, Kumar N, Li CY, Phylly RL, Hogan WJ. Haematologic Manifestations of Copper Deficiency. A Retrospective Review. *Eur J Haematol*. 2008 Jun;80(6):523-31

Allen TM, Manoli A 2nd, LaMont RL. Skeletal Changes Associated with Copper Deficiency. *Clin Orthop Relat Res*. 1982 Aug;(168):206-10.

McMillan NB, Mulroy C, McKay MW, McDonald CM, Jackson WD. Correlation of Cholestasis with Serum Copper and Whole Blood Manganese Levels in Pediatric Patients. *Nutr Clin Pract* 2008;23:161-5.

Components of PN - Manganese (Mn)

- Deficiency is virtually unknown in humans
- Various PN components are contaminated with Mn
- Biliary tract is the predominant route for Mn excretion
 - Patients with cholestasis have decreased Mn excretion and may develop Mn toxicity
- Toxicity
 - Symptoms include insomnia, headache, increased forgetfulness, anxiety and a Parkinson's disease-like illness
 - Best assessed by an MRI scan of the brain (manganese accumulates in the basal ganglia)
- Monitoring
 - Regular monitoring of patients receiving fixed doses of Mn over prolonged periods is recommended
 - Erythrocyte or whole-blood Mn concentrations

Hardy et al. *Curr Opin Clin Nutr Metab Care*. 2008;11:289-96.

Koletzko et al. *J Pediatr Gastroenterol Nutr*. 2005;41:S1-S87.

Fell et al. *Lancet* 1996;347:1218-21.

Kafritsa et al. *Arch Dis Child*. 1998;79:263-65.


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No Recommended Daily Allowance for Mn and published guidelines range from 1µg/kg/d to maximum of 40-100 µg/kg/day for patients > 40 kg. There is an increased risk for Mn toxicity in setting of hepatobiliary impairment and removal of Mn decreases accumulation of Mn in basal ganglia. Excessive doses of Mn are associated with cholestasis and can lead to CNS symptoms – insomnia, headache, increased forgetfulness, anxiety, rapid hand movements, and loss of coordination (Parkinson's-like illness). Regular monitoring of patients receiving fixed doses of Mn over prolonged periods is recommended. Erythrocyte or whole-blood Mn concentrations appear to be

the most accurate and reproducible results.

Hardy IJ, Gillanders L, Hardy G. Is Manganese an Essential Supplement for Parenteral Nutrition? *Curr Opin Clin Nutr MetabCare* 2008;11:289-296.

Koletzko B, Goulet O, Hunt J, et al. Guidelines on Paediatric Parenteral Nutrition of the European Society Of Paediatric Gastroenterology, Hepatology, and Nutrition and the European Society for Clinical Nutrition and Metabolism supported by the European Society of Paediatric Research. *J Pediatr Gastroenterol Nutr* 2005;41:S1-S87.

Fell JM, Reynolds AP, Meadows N et al. Manganese Toxicity in Children Receiving Long Term Parenteral Nutrition. *Lancet* 1996;347:1218-21.

Kafritsa Y, Fell J, Bynevelt M, Taylor W, Milla P. Long-term Outcome of Brain Manganese Deposition in Patients on Home Parenteral Nutrition. *Arch Dis Child* 1998;79:263-65.

Components of PN - Selenium (Se)

- Se deficiency can develop within 6 weeks of Se-free PN
 - Can cause cardiomyopathy, growth retardation, pseudo-albinism, white fingernails, and skin disorder
 - Suggested that patients be supplemented if on exclusive PN for >4 weeks
- Toxicity is rare
 - Can cause nausea, diarrhea, irritability, fatigue, peripheral neuropathy, hair loss, nail changes
- Total plasma selenium
 - Most widely used test of Se status
 - Fairly accurate
 - In the presence of systemic inflammation, levels decrease
- In patients with impaired renal function, remove Se from PN and monitor levels

Pediatric Nutrition Support Core Curriculum. Editor: M. Corkins. ASPEN, 2010.

Masumoto et al. *Nutrition* 2007;23:782-87.

Kanekura et al. *Clin Exp Dermatol*. 2005;30:346-48.



It has been suggested that one should supplement if the patient is on exclusive pediatric PN for >4 weeks.

Experimental Se deficiency causes hypothyroidism.

Pediatric Nutrition Support Core Curriculum. Editor: Mark Corkins. American Society for Parenteral and Enteral Nutrition (ASPEN), 2010.

Rotruck JT, Pope AL, Ganther HE et al. Selenium: Biochemical Role as a Component of Glutathione Peroxidase. *Science* 1973;179:588-90.

Berry MJ, Banu L, Larson PR. Type 1 Iodothyronine Deiodinase is a Selenocysteine-containing Enzyme. *Nature* 1991;349:438-40.

Masumoto K, Ngata K, Higashi M et al. Clinical Features of Selenium Deficiency in Infants Receiving Long-term Nutritional Support. *Nutrition* 2007;23:782-87.

Vinton NE, Dahlstrom KA, Stroble CT, Ament ME. Macrocytosis and

Pseudoalbinism: Manifestations of Selenium Deficiency. *J Pediatr* 1987;111:711-17.

Kanekura T, Yotsumoto S, Maeno N, et al. Selenium Deficiency: Report of a Case. *Clin Exp Dermatol* 2005;30:346-48.

Components of PN - Chromium (Cr)

- Excreted by the kidneys
 - Dose must be decreased in patients with renal failure
- Cr deficiency
 - Can cause glucose intolerance which can be reversed with daily chromium supplementation
 - Best method for diagnosing Cr deficiency is to demonstrate insulin resistance that improves with Cr supplementation and reappears after the supplement is withdrawn
- Cr is a contaminant in PN solutions
 - Contaminants can increase the amount delivered by 10–100%
 - This alone is likely sufficient to prevent chromium deficiency
- Consider monitoring serum Cr concentrations and HgbA_{1c} regularly in patients receiving long-term PN

Pediatric Nutrition Support Core Curriculum. Editor: M. Corkins. ASPEN, 2010.
Moukarzel A. *Gastroenterol.* 2009;137:s18-28.
Howard et al. *J Parenter Enteral Nutr.* 2007;31(5):388-96.

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Changes in purification methods for PN solutions could lead to insufficient concentrations of Cr. If Cr were simply a contaminant, the amount of contamination in the body would increase with time. People still question whether or not Cr should be added to PN.

Chronic PN patients are at risk for Cr toxicity and evidence suggests that Cr should not be supplemented in these patients.

Pediatric Nutrition Support Core Curriculum. Editor: Mark Corkins. American Society for Parenteral and Enteral Nutrition (ASPEN), 2010.

Moukarzel A. Chromium in Parenteral Nutrition: Too Little or Too Much? *Gastroenterology* 2009;137:s18-28.

Howard L, Ashley C, Lyon D, et al. Autopsy tissue trace elements in 8 long-term parenteral nutrition patients who received the current U.S. Food and Drug Administration formulation. *J Parenter Enteral Nutr.* 2007;31(5):388-96.

Vincent JB. The Bioinorganic Chemistry of Chromium. *Polyhedron* 2001;20:1-26.

Stearns DM. Is Chromium a Trace Essential Metal? *Biofactors* 2000;11:149-62.

Components of PN - Miscellaneous

- Heparin 0.5 - 1 Unit/mL
 - May be added to prevent thrombophlebitis
 - Stimulates lipoprotein lipase and improves triglyceride clearance
- Insulin
 - May be used in patients with hyperglycemia
- Ranitidine
 - Compatible with PN when required
- Iodine
 - Not typically added to PN solutions
 - Currently may need to be added because of decreased use of iodine containing topical antiseptics.
- Be aware of compatibility issues with additives
 - Consult with your pharmacist


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In the past there was adequate skin absorption of iodine from topical antiseptics BUT this may no longer be true with decreased use of topical antiseptics. Other possible additives include carnitine, cysteine, and insulin. For drug interaction and compatibility of medications, refer to the ASPEN core curriculum.

Pediatric Nutrition Support Core Curriculum. Editor: Mark Corkins. American Society for Parenteral and Enteral Nutrition (ASPEN), 2010.

Components of PN - Designing a Regimen

- Estimate energy needs
 - Based on age of patient, disease state, severity of illness, activity level and need for catch-up growth
- Calculate fluid needs
- Estimate protein needs
- Obtain baseline laboratory values of serum electrolytes, minerals and triglycerides
- Start with 10% dextrose solution
- Can start with intravenous lipid at lowest end of dose range and make sure triglyceride levels are within acceptable levels when increasing dose
- Advance regimen to goal caloric and fat intake based on laboratory testing and other clinical evidence

Pediatric Nutrition Support Core Curriculum. Editor: M. Corkins. ASPEN, 2010.



The concentration of the dextrose solutions used at the initiation of PN depends on the patient's serum glucose level, glucose content of currently administered fluids, type of catheter through which the PN solution will be administered and desired GIR.

In general, can add goal protein except in the case of renal insufficiency or failure. Dextrose concentration can be advanced by 1 – 5% per day depending on the age of the infant, GIR, serum glucose levels and clinical status. IV lipid can be advanced by 0.5 – 1.0 g/kg per day depending on triglyceride levels.

The ideal non-protein calorie to nitrogen ratio or NPC:N ratio reflects the balance in the PN regimen between the non protein calorie (fat and carbohydrate) and protein calories. In stable patients that ratio should be 150-250:1. This ratio may be less in critically ill patients or higher in renal failure patients. If an elevated BUN cannot be explained by changes in renal function, medications, bleeding or dehydration, then the ratio should be examined.

Pediatric Nutrition Support Core Curriculum. Editor: Mark Corkins. American Society for Parenteral and Enteral Nutrition (ASPEN), 2010.

Wesley JR, Coran AG. Intravenous nutrition for the pediatric patient. *Semin Pediatr Surg.* 1992;1:212-30.

Components of PN - Macronutrient Guidelines

	A.A.P.		A.S.P.E.N.	
	Weight	Daily Recommendation	Weight / Age	Daily Recommendation
Protein	10-20 kg	1-2.5 g/kg	>10 kg or 1-10 yrs	1-2 g/kg
	>20 kg	0.8-2 g/kg	11-17 yrs	0.8-1.5 g/kg
Energy / Caloric	10-20 kg	60-90 kcal/kg	>1-7 yrs	75-90 kcal/kg
	>20 kg	30-75 kcal/kg	>7-12 yrs	50-75 kcal/kg
Fluid	>10-20 kg = 1000 mL + 50 mL/kg >10 kg			
	>20 kg = 1500 mL + 20 mL/kg >20 kg			
Carbohydrates (Dextrose)	10-20 kg	8-28 g/kg	Carbohydrates should comprise 40% to 60% of total caloric intake.	
	>20 kg	5-20 g/kg		
IV Fat Emulsion	>10kg	1-3 g/kg	The minimum fat requirement is determined by essential fatty acid need, and the daily maximum is 50% to 60% of energy.	

Kleinman RE. *Pediatric Nutrition Handbook 6th Edition* 2009:519-540.

Forchielli ML, Miller SJ. *The ASPEN Nutrition Support Practice Manual* 2005:38-53.



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Fluid requirements can also be calculated using body surface area.

Kleinman RE. *Pediatric Nutrition Handbook 6th Edition* 2009:519-540.

Forchielli ML, Miller SJ. *The ASPEN Nutrition Support Practice Manual* 2005:38-53.

Components of PN - Energy Requirements

- Common methods to calculate calorie needs include World Health Organization (WHO) and Dietary Reference Intake (DRI) equations
 - DRI equations provide guidelines from birth - adulthood with a need to use activity/adjustment factors
 - WHO equations provide guidelines from 1 year – adulthood
 - Energy prediction equations should be used as starting guidelines and PN caloric intake adjusted based on response to therapy
- Energy needs
 - In the first year of life are expressed in kcal/kg/d
 - Beyond the first year of life are expressed as kcal/kg per day or kcal per day
- Measure energy expenditure using indirect calorimetry when possible
- Birth through 1 year: 80 - 110 kcal/kg per day

Llyod DA. *Nutrition* 1998;14:101-4.

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Can use the suggested guidelines from AAP or ASPEN.

Llyod DA. Energy requirements of surgical newborn infants receiving parenteral nutrition. *Nutrition*. 1998 Jan;14(1):101-4.

Dietary Reference Intake (DRI):

http://fnic.nal.usda.gov/nal_display/index.php?info_center=4&tax_level=2&tax_subject=256&topic_id=1342.

Energy and protein requirements from a WHO technical report series 724, 1985: <http://www.fao.org/docrep/003/aa040e/aa040e00.HTM>.

Components of PN - Minerals & Acid-Base Balance

- Determining starting doses
 - Use accepted guidelines
 - Consider baseline electrolyte and mineral levels
 - Consider other sources of electrolyte and minerals (intravenous fluids, other sources of electrolytes and minerals)
- Check labs within 24 hours of initiation of PN and adjust levels accordingly
 - Consider other additional electrolyte and mineral supplements patient received and adjust PN dosages accordingly
- Acid-base abnormalities can be treated by addition or removal of sodium or potassium acetate
 - Acetate = bicarbonate precursor
 - Bicarbonate contraindicated in PN
 - Ca/Phos precipitation
 - high Na load

Pediatric Nutrition Support Core Curriculum. Editor: M. Corkins. ASPEN, 2010.

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There are maximum amounts of electrolytes that can be added to the PN solutions based on solubility and risk of precipitation.

Pediatric Nutrition Support Core Curriculum. Editor: Mark Corkins. American Society for Parenteral and Enteral Nutrition (ASPEN), 2010.

Parenteral Nutrition – Cycling PN

- Daily administration of PN over a period of time which is < 24 hrs e.g., 8 - 22 hrs cycle; average 10 - 12 hrs
- Pre-requisite
 - stable regimen
 - ability to handle large volume of fluid and nutrients over a short amount of time
 - The smaller the infant the less tolerant they may be of the cycle
- Putative benefits
 - decreased hepatic steatosis
 - allows for a more normal daytime routine
 - increases mobility of the patient
- Wean PN rate for the last hour by decreasing the rate by 50%. Consider starting the PN solution at 50% of the goal rate for first hour.
- Check serum glucose 30 - 45 minutes after stopping PN with every change in length of cycle. Monitor for glucosuria during cycle.

Slicker et al. *Nutr in Clin Pract.* 2009;24(4):481-86.
Werlin et al. *J Pediatr.* 1994;124:441-44.


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Patients do not need a dextrose rider during hours when they are not receiving PN. There is no true minimum weight to start cycling, but patients should be able to maintain normal glucose values while off PN solution and this is usually around a weight of 5 kg. A potential **disadvantage of cycling PN is an increased risk of line infection.**

Slicker J, Vermilyea S. Pediatric parenteral nutrition: putting the microscope on micronutrients and micronutrients. *Nutr in Clin Pract.* 2009; 24(4):481-486
Werlin SL, Wyatt D, Camitta B. Effect of abrupt discontinuation of high glucose infusion rates during parenteral nutrition. *J Pediatr* 1994; 124:441-444.

Parenteral Nutrition - Transitioning to Enteral Feeds

- Enteral feeds should be started as soon as possible in trophic amounts (<20% of goal calories/volume)
- Once enteral feeds are tolerated, PN volume is weaned as feeds are increased
- Goal fluid volume for feeds may not result in goal caloric intake and enteral feeds may need to be concentrated to achieve goal caloric intake
- Cycling PN during the transition to enteral feeds is useful: in infants and young children, continuous feeds will help with maintenance of normal serum glucose levels and tolerance of cycled regimen

Trophic feeds are considered any volume of feed that is less than 20% of goal.

Parenteral Nutrition - Monitoring

- Growth
 - Weight
 - Length/height
 - Head circumference
- Laboratory
 - Electrolytes/minerals
 - Triglycerides
 - Liver and renal function
 - Hemoglobin
 - Trace element, carnitine and vitamin levels

Szeszycki et al. The aspen pediatric nut support core curriculum. 2010;1st edition:460-76.
Mascarenhas et al. Pediatric Gastrointestinal Disease. 2010;4th edition:964-77.

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Consider measuring carnitine (ester/free ratio) levels in patients who are NPO for a significant amount of time, as indicated. Some clinicians feel that measuring carnitine levels is not helpful.

Szeszycki EN, Cruse WN, Strup M. Evaluation and monitoring of Pediatric patient receiving specialized nutrition support. The aspen pediatric nut support core curriculum. Corkins MC Editor. 2010;1st edition:460-76.

Mascarenhas MR, Wallace E. Parenteral Nutrition. Pediatric Gastrointestinal Disease. Wyllie R, Hyams JS, Kay M Editors. 2010;4th edition;p964-77.

Parenteral Nutrition - Monitoring

	Initial	With Every Change in PN	Weekly until Stable	Monthly as indicated
Electrolytes	✓	✓	✓	
Glucose	✓	✓	✓	
Calcium	✓	✓	✓	
BUN	✓	✓	✓	
Creatinine	✓	✓	✓	
Magnesium	✓	✓	✓	
Phosphorus	✓	✓	✓	
ALT	✓		✓	
AST	✓		✓	
Alkaline phosphatase	✓		✓	
Total protein	✓		✓	
Albumin	✓		✓	
GGT	✓		✓	
Prealbumin	✓		✓	
Triglycerides	✓	✓	✓	
Conjugated bilirubin	✓		✓	
CBC	✓		✓	✓
Iron studies				✓
Trace elements				✓
Vitamins				✓



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Consider checking iCa in patients with low albumin levels.

Consider measuring carnitine levels in patients who are NPO for a significant amount of time, as indicated. Some clinicians feel that measuring carnitine levels is not helpful.

Thyroid function can be checked (TSH) at baseline, if indicated, and yearly.

Consider checking prothrombin time weekly, and then monthly.

Consider measuring urine Na levels to assess adequacy of Na intake especially in patients with SBS and growth problems.

During PN initiation it is customary to follow serum electrolytes closely.

Pediatric Nutrition Support Core Curriculum. Editor: Mark Corkins. American Society for Parenteral and Enteral Nutrition (ASPEN), 2010.

Parenteral Nutrition - Complications

- Infectious
- Mechanical
 - Infusate-related
 - Catheter-related
 - Occlusions
- Metabolic
 - Electrolyte-, mineral-, trace element- and vitamin-related
 - PN-Associated Liver Disease (PNALD)
 - Bone disease
 - Overfeeding and underfeeding
 - Refeeding syndrome
 - Allergy
 - Miscellaneous e.g. nephropathy

Pediatric Nutrition Support Core Curriculum. Editor: M. Corkins. ASPEN, 2010.

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Overfeeding leads to increased fat synthesis with an increase in RQ (CO_2/O_2), leading to CO_2 retention. Excessive CHO intake leads to hypercarbia, hypertriglyceridemia, hyperinsulinemia.

Patients on chronic PN, especially HPN, are at risk for nephropathy. This may be related to subclinical renal damage from components of PN, cumulative drug toxicity from nephrotoxic antibiotics used to treat central line infections.

Pediatric Nutrition Support Core Curriculum. Editor: Mark Corkins. American Society for Parenteral and Enteral Nutrition (ASPEN), 2010.

Moukarzel AA, Ament ME, Buchman A, Dahlstrom KA, Vargas J. Renal function of children receiving long-term parenteral nutrition. *J Pediatr.* 1991 Dec;119(6):864-8.

Buchman AL, Moukarzel A, Ament ME, Gornbein J, Goodson B, Carlson C, Hawkins RA. Serious renal impairment is associated with long-term parenteral nutrition. *J Parenter Enteral Nutr.* 1993 Sep-Oct;17(5):438-44.

Parenteral Nutrition - Infectious Complications I

- Bacterial and fungal causes
- Infection vs. colonization (22% of all hubs)
- Causes
 - Colonization
 - inside catheter or hub
 - outside of the subcutaneous catheter
 - in fibrin sleeve
 - in subcutaneous tract
 - Contamination
 - from blood seeding
 - skin contamination along the catheter tract
 - non-sterile entries into the line
 - contaminated PN solutions
- Risk of sepsis is reported at 1.5 episodes a year in home PN patients

Pediatric Nutrition Support Core Curriculum. Editor: M. Corkins, ASPEN, 2010.
Schmidt-Sommerfeld et al. *J Parenter Enteral Nutr.* 1990;14:148-51


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Central line associated blood stream infections (CLABSI) or Catheter related blood stream infection (CRBSI); both terms have been used to describe infections associated with central line venous catheters.

The infection may be situated within the catheter, within the tunneled portion of the catheter and surrounding tissue, or at the exit site.

Need to differentiate between a central line infection and colonization. About 22% of all hubs are colonized with bacteria.

Infections may be hard to recognise as some patients may be febrile only during PN infusions or when the central line is flushed. A white blood cell count may be normal in circumstances where the infection is at the exit site.

Pediatric Nutrition Support Core Curriculum. Editor: Mark Corkins. American Society for Parenteral and Enteral Nutrition (ASPEN), 2010.

Schmidt-Sommerfeld E, Snyder G, Rossi TM, et al. Catheter-related complications in 35 children and adolescents with gastrointestinal disease on home parenteral nutrition. *J Parenter Enteral Nutr.* 1990;14:148-51.

Parenteral Nutrition - Infectious Complications II

- Prevention
 - Hand hygiene
 - Sterile technique during placement
 - Use line only for PN and not for blood draws
 - Dressing changes per protocol
 - Tubing changes for dextrose AA solutions and IV lipid
 - Avoid multi-lumen catheters
 - Avoid catheters in groin/diaper area
 - Inadequate pediatric data on the benefits of antibiotic and ethanol locks and antibiotic-impregnated catheters

Pediatric Nutrition Support Core Curriculum. Editor: M. Corkins. ASPEN, 2010.

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The recommendations are that the tubing for lipids be changed every 12-24 hours and the dextrose tubing be changed every 72 hours unless it is a 3-in-1 solution.

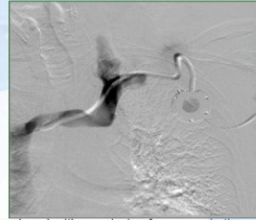
Pediatric Nutrition Support Core Curriculum. Editor: Mark Corkins. American Society for Parenteral and Enteral Nutrition (ASPEN), 2010.

Parenteral Nutrition - Mechanical Complications

- Catheter-related
 - Pneumothorax
 - Hematoma
 - Hemothorax
 - Malposition
 - Venous and intracardiac thrombosis
 - Air embolism
 - Catheter blockage / migration
 - Transient arrhythmias, perforation of the heart
 - Superior vena cava syndrome
- Infusate-related
 - Extravasation into local tissues, pericardium, peritoneum, thorax, mediastinum, liver and scalp

Parenteral Nutrition - Catheter Occlusions

- Most common non-infectious complication of central venous catheters
- Thrombotic vs. non-thrombotic
 - Resistance to flushing and aspiration
 - Non-thrombotic: precipitate due to medication, Ca/Phos, lipid, and minerals
 - Treatment: thrombolytic or specific agents i.e., alcohol for lipid precipitates
- Fibrin sleeve at distal catheter tip
 - Can flush easily but difficulty in aspiration
 - Treatment: thrombolytic therapy



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Non-thrombotic occlusions are caused by calcium phosphate precipitates, medication precipitates, lipid residue, or mineral precipitates. Thrombotic catheter occlusions are usually treated with thrombolytics. The use of 0.1N hydrochloric acid is most effective for clearing catheter occlusions due to precipitation of calcium-phosphate. For catheter occlusions due to precipitates associated with medications in the high pH range such as tobramycin and phenytoin, sodium bicarbonate 1mEq/mL has been anecdotally reported to be effective. 70% ethanol is the most effective solvent to dissolve lipid residue. NaOH may be used to dissolve mineral precipitates.

Picture insert is of an occluded line.

Parenteral Nutrition Lipids & Essential Fatty Acid Deficiency (EFAD)

- EFAD can be seen within days of fat-free PN in neonates
- Deficiency is cumulative
- Can cause
 - decreased growth
 - skin and hair changes
 - increased susceptibility to infection,
 - poor wound healing
 - alterations in platelet function
- To avoid EFAD need minimum of
 - 2% to 4% of the total caloric intake as linoleic acid
 - 0.25% to 0.5% of total caloric intake as alpha linolenic acid
 - Met with minimum of 0.5g/kg per day IVFE
- Diagnosis: triene:tetraene ratio > 0.2 or linoleic acid levels
- In premature infants EFAD can be prevented by supplying 0.6 to 0.8 g/kg per day IVFE



Uauy et al. *Semin Perinatol*. 1989;13:118-30.


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This is a picture of a child with EFAD on the left, and on the right after he was successfully treated.

Uauy R, et al. Essential fatty acid metabolism and requirements during development. *Semin Perinatol* 1989;13:118-30.

Parenteral Nutrition - Refeeding Syndrome

- Definition
 - Severe fluid and electrolyte shifts (especially Phos and K) in malnourished patients undergoing rapid nutritional rehabilitation either enterally or parenterally. Can be avoided by supplementation with Phos, Mg and K.
- Risk Factors
 - Chronic malnutrition, anorexia nervosa, morbid obesity with massive weight loss, patients not fed for 7-10 days with evidence of stress and depletion
- Clinical
 - Low serum Phos, Mg, and K levels, acute respiratory and circulatory collapse
- Treatment
 - Start with providing 50-75% estimated energy needs or give current intake.
 - Increase kcals by 10-20% daily until goal reached; monitor labs, vital signs, fluids.
 - Provide adequate protein.

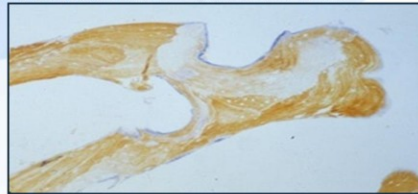
Fuentebella et al. *Pediatr Clin North Am.* 2009;56(5):1201-10.

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Fuentebella J, Kerner JA. Refeeding syndrome. *Pediatr Clin North Am* 2009; 56(5):1201-10

Parenteral Nutrition – Aluminum

- Contaminant of PN ingredients
- Accumulates in bone
- Developmental delay in preterm infants
- High levels of aluminum present in Ca, Phos, heparin, albumin solutions, and some antibiotics
- 2004 FDA mandate to report amounts in commercial products
- Can be measured in blood



Gura. *Nutrition* 2010;26(6):585-94.
Poole et al. *J Parenter Enteral Nutr.* 2008;32(3):242-46.

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This is a slide of a bone and the blue staining represents aluminum deposition.

Gura KM. Aluminum contamination in products used in parenteral nutrition: has anything changed? *Nutrition* 2010 Jun;26(6):585-94.

Poole R, Hintz S, Mackenzie NI, et al. Aluminum Exposure From Pediatric Parenteral Nutrition: Meeting the New FDA Regulation. *J Parenter Enteral Nutr.* 2008;32(3):242-46.

Parenteral Nutrition - Adverse Reactions

- Extremely rare
- Less than 20 cases of parenteral nutrition reactions reported in the literature among adults and children
 - Nearly half with history of malignancy
 - 15% with history of medication or food allergies
- Reported causes
 - Site prep: Chlorhexidine
 - Bottle stoppers; Latex
 - Lipid emulsion
 - Amino acid solution
 - Multivitamins
 - Fe Dextran

Wynn et al. *J Perinatol* 2007;27:586-8.
Scolapio et al. *J Parent Enter Nutr.* 2005;29:451-3.


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Sulfite are added to crystalline amino acid products to diminish amino acid oxidation. Acute and delayed sensitivity reactions can occur after ingestion of sulfite-containing foods and other products. Bisulfite reacts with disulfide bonds to alter protein structure/configuration thus potentially affecting antigenicity. Evidence for this includes the fact that bisulfite and sulfur dioxide can precipitate asthmatic attacks and that bisulfite additives can interact with other components (lipids) and cause sensitization.

Butylated hydroxyanisole (BHA) and Butylated hydroxytoluene (BHT) are added to Pediatric MVI[®] as preservatives. Oral BHA and BHT are associated with allergy symptoms. Polysorbate emulsifiers are added to E-Ferol parenteral solutions. Polyethoxylated castor oil is added to Cremophor MVI[®] preparations.

Allergic reactions to soy are common but are more prevalent in Japan than in the USA, and relates to soy-based lipid emulsions. In general the allergy is usually attributed to soy protein and therefore a reaction to soy oil is less likely. Patients can have frequent reactions to other legumes (peanut, lentils, garbanzo beans, peas). There are 15 different proteins that can be potential antigens though P34 protein responsible for 75% of reactions. There is a higher risk to those with egg allergy.

Wynn RJ, Boneberg A, Lakshminrusimha S. Unexpected Source of Latex Sensitization in a Neonatal Intensive Care Unit. *J Perinatol* 2007;27:586-8.
Scolapio JS, Ferrone M, Gilham RA. Urticaria Associated with Parenteral Nutrition. *J Parenter Enter*

Nutr. 2005;29:451-3.

Wu SF, Chen W. Hypersensitivity to Vitamin Preparation in Parenteral Nutrition: Report of 1 case. Acta Paediatr Taiwan 2002;43:285-7.

Levy M, Dupuis LL. Parenteral Nutrition Hypersensitivity. J Parenter Enteral Nutr 1990;14:213-5.

Bullock L, Etchason E, Fitzgerald JF, Mcguire WA. Case Report of an Allergic Reaction to Parenteral Nutrition in a Pediatric Patient. J Parenter Enteral Nutr 1990;14:98-100.

Nikaido S, Tanaka M, Yamoto M et al. Anaphylactoid Shock Caused by Chlorhexidine Gluconate. Masui 1998;47:330-4.

Udall JN, Richardson DS. Allergic Reactions to Parenteral Nutrition Solutions. Nutr Support Serv 1986;6:20-22.

Parenteral Nutrition - Metabolic Bone Disease I

- Extensively described in adults
 - Decreased bone mineral density
 - Osteoporosis
 - Bone pain and fractures
- Has been described in children weaned from PN
- Etiology
 - Underlying disease-related and PN-related mechanisms
 - Altered vitamin D intake
 - Phosphorus, nitrogen and energy imbalance
 - Aluminum contamination (FDA now requires reporting of aluminum content in all PN additives)

Seidner DL. *J Parenter Enter Nutr*. 2002;26(5):S37-S42.


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The etiology of metabolic bone disease seen in patients on chronic PN is unclear and probably multifactorial. It may be related to altered vitamin D metabolism, Cu and vitamin K deficiency, and aluminum toxicity. Clinically patients present with bone pain (back pain) and pathologic fractures. Aluminum toxicity is known to occur in the brain, bone and liver causing bone pain, metabolic bone disease, osteoporosis, patchy osteomalacia, reduced bone apposition and fracturing osteomalacia, encephalopathy and impaired neurological development. However Advenier et al showed in 10 children (av age 8 year) on PN for an average of 6.5 years, elevated aluminum levels with no associated symptoms.

Seidner DL. Parenteral nutrition-associated metabolic bone disease. *JPEN* 2002; 26(5):S37-S42

Advenier E, Landry C, Colomb V, et al. Aluminum contamination of parenteral nutrition and aluminum loading in children on long-term parenteral nutrition. *J Pediatr Gastroenterol Nutr*. 2003 Apr;36(4):448-53.

Dellert SF, Farrell MK, Specker BL, Heubi JE. Bone mineral content in children with short bowel syndrome after discontinuation of parental nutrition. *J Pediatr*. 1998; 132(3 Pt 1):516-9.

Leonberg BL, Chuang E, Eicher P, Tershakovec AM, Leonard L, Stallings VA. Long-term growth and development in children after home parental nutrition. *J Pediatr*. 1998 Mar; 132(3 Pt 1):461-6.

Nousia-Arvanitakis S, Angelopoulou-Sakadami N, Metroliou K. Complications associated with total parenteral nutrition in infants with short bowel syndrome. *Hepatogastroenterology*. 1992 Apr;39(2):169-72.

Parenteral Nutrition - Metabolic Bone Disease II

- In children on Home PN
 - Regular measurements
 - plasma Ca and Phos
 - parathyroid hormone and vitamin D
 - urinary Ca
 - serum alkaline phosphatase
 - Aluminum contamination of PN solutions should be kept to a minimum
 - Regular assessment of bone mineralization should be performed
- Treatment
 - Adequate Ca, Phos, Mg and vitamin D
 - Weight bearing exercise
 - Change medications (such as diuretics), if possible
 - Referral to a bone specialist

Seidner DL. *J Parenter Enter Nutr.* 2002;26(5):S37-S42.

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Bone specialist: physician with experience treating pediatric patients with bone disease, often endocrinologist.

The workup for patients with metabolic bone disease include parathormone, vitamin D levels (25 hydroxy and 1,25hydroxy), alkaline phoshatase, alkaline phosphatase

isoenzymes including bone specific alkaline phosphatase, serum Phos, Ca, Mg and Cu levels, and urine Ca, creatinine and Phos levels.

Seidner DL. Parenteral nutrition-associated metabolic bone disease. JPEN 2002; 26(5):S37-S42

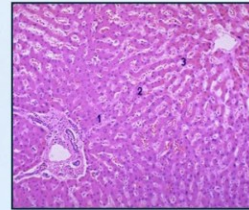
Koletzko B, Goulet O, Hunt J, Krohn K, Shamir R; Guidelines on Paediatric Parenteral Nutrition of the European Society of Paediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN) and the European Society for Clinical Nutrition and Metabolism (ESPEN), Supported by the European Society of Paediatric Research (ESPR). J

Pediatr Gastroenterol Nutr. 2005
Nov;41 Suppl 2:S1-87.

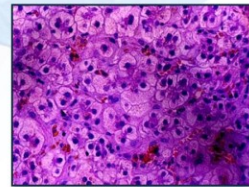
Parenteral Nutrition - Liver Disease I

- Well described complication of PN
- Develops in 40 – 60% of neonates; ~15% in children
- Variable degree of injury
 - Mild: mild cholestasis, gall stones, hepatic steatosis
 - Severe: can result in cirrhosis and liver failure
- Pathogenesis:
 - Multifactorial
 - Prolonged duration of PN
 - Lack of enteral feeding
 - Prematurity and low birth weight
 - Early and recurrent sepsis
 - Length of bowel remnant
 - Reduced enterohepatic circulation
 - Deficiency or toxicity of components of PN solutions (excess glucose, excess energy, AA content, Mn, Cu, and fat emulsions)

Normal Liver



Cholestasis



Ovchinsky N. *J Parent & Enteral Nutr.* 2010;34(5):472-73.


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Treatment considered decreasing IV fat emulsion, start EN if only trophic, wean PN or adjust PN components.

Ovchinsky N. conjugated bile acid as potential early markers of parenteral nutrition associated liver disease. *JPEN* 2010;34(5):472-473

Parenteral Nutrition - Liver Disease II

Treatment

- Provide maximal tolerated EN
- Provide cyclical PN as soon as possible
- Consider and treat small bowel bacterial overgrowth
- Consider reducing intravenous lipids to 1g/kg per day, if conjugated bilirubin rises with no other explanation
 - Consider fish-oil based lipids, if the above strategy fails
- If transaminases, alkaline phosphatase or conjugated bilirubin continue to increase, consider commencing ursodeoxycholic acid

Gura et al. *Pediatrics* 2008;121(3):e678-86.
Koletzko et al. *J Pediatr Gastroenterol Nutr.* 2005;41(Suppl 2):S1-87.

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Ursodeoxycholic acid is often used but limited data on its effectiveness.

Koletzko B, Goulet O, Hunt J, Krohn K, Shamir R; Guidelines on Paediatric Parenteral Nutrition of the European Society of Paediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN) and the European Society for Clinical Nutrition and Metabolism (ESPEN), Supported by the European Society of Paediatric Research (ESPR). *J Pediatr Gastroenterol Nutr.* 2005 Nov;41 Suppl 2:S1-87.

Gura KM, Lee S, Valim C, et al. Safety and efficacy of a fish-oil-based fat emulsion in the treatment of parenteral nutrition-associated liver disease. *Pediatrics.* 2008 Mar;121(3):e678-86.

Parenteral Nutrition - Liver Disease III

- Consider early referral to an experienced liver-intestinal transplant or intestinal rehabilitation program for children with a poor prognosis or if on PN > 3 months and one or more of the following:
 - Serum conjugated bilirubin > 3 mg/dL
 - Platelet count < 100,000/uL
 - PT > 15 sec
 - PTT > 40 sec
 - Hepatic fibrosis
 - Concerns about central venous access

Koletzko et al. *J Pediatr Gastroenterol Nutr.* 2005;41(Suppl 2):S1-87
Selvaggi et al. *Transplantation* 2005;79:1639–43.
Mittal et al. *Pediatr Clin N Am.* 2003:1419–33.


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Mittal NK, Tzakis AG, Kato T, et al. Current status of small bowel transplantation in children: update 2003. *Pediatr Clin N Am.* 50 (2003):1419– 1433.

Selvaggi G, Gyamfi A, Kato T, Gelman B, Aggarwal S, Begliomini B, Bennett J, Nishida S, Tzakis AG. Analysis of Vascular Access in Intestinal Transplant Recipients Using the Miami Classification from the VIIIth International Small Bowel Transplant Symposium. *Transplantation* 2005;79: 1639–1643.

Koletzko B, Goulet O, Hunt J, Krohn K, Shamir R; Guidelines on Paediatric Parenteral Nutrition of the European Society of Paediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN) and the European Society for Clinical Nutrition and Metabolism (ESPEN), Supported by the European Society of Paediatric Research (ESPR). *J Pediatr Gastroenterol Nutr.* 2005 Nov;41 Suppl 2:S1-87.

Parenteral Nutrition - Conclusions

- PN can be lifesaving in patients with limited tolerance of enteral nutrition
- Development of a PN regimen should take into account the age and clinical condition of the patient
- The practitioner must be aware of the risks of PN
- Monitoring is key to successful therapy



Neonatal Parenteral Nutrition

Neonatal PN

- Early initiation of nutrition is critical for the neonate.
- PN should be initiated in infants who are not likely to achieve total enteral nutrition within the first week of life.
- Trial of aggressive PN on the first day of life (versus later start)
 - Fewer infections
 - Neonates more likely to be > 10th percentile for weight at discharge
- Protein is required to decrease or prevent catabolism, especially in infants who are ill.
- Early delivery of amino acids improves glucose tolerance.

Wilson et al. *Arch Dis Child Fetal Neonatal Educ.* 1997;77:F4-11.

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Wilson DC, Cairns P, Halliday HL, et al. Randomised controlled trial of an aggressive nutritional regimen in sick very low birth weight infants. *Arch Dis Child Fetal Neonatal Ed.* 1997 Jul;77(1):F4-11.

Neonatal PN - Indications

- Inability to start or advance feeds within first 1 - 2 days for preterm or VLBW infants; or within 3 - 5 days for term infants
- Necrotizing Enterocolitis (NEC)
- Functional immaturity of the gastrointestinal tract or gestational age at birth < 30 - 32 weeks
 - Use while advancing enteral feeds
- Unrepaired congenital gastrointestinal anomalies
 - Gastroschisis, bowel atresias, omphalocele, cystic fibrosis with meconium ileus, Hirschsprung's disease, ileus
- Short Bowel Syndrome
- Increased risk of NEC due to impaired gastrointestinal perfusion
 - Patent ductus arteriosus, hypotension, indomethacin therapy, etc.

Carlson. *ADA Pocket Guide to Neonatal Nutrition* 2009:29-30.


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Carlson SJ, "Parenteral Nutrition" in *ADA Pocket Guide to Neonatal Nutrition*;29-30.

Neonatal PN - “Starter PN”

- A standardized PN solution
 - Contains amino acids, dextrose, and calcium; no other electrolytes
- May allow more convenient and cost-effective timely initiation of PN
- Can be used as a bridge until a more complete PN solution can be ordered
- These solutions are often started in the delivery room or upon admission to the NICU
- Usually run at a maximum of 60 - 80 mL/kg per day
- Additional intravenous fluids may be ordered separately to provide electrolytes when needed.

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Example Starter PN

- Dextrose 7.5% **OR** 10 %
- Trophamine 4%
- Calcium gluconate 2000 mg/L (9 mEq/L)
- Heparin 0.5 units/mL
- Total volume: 250 mL
- Rate: 60 mL/kg/day

Neonatal PN - Goals

- Primary goals
 - To provide adequate energy and protein to prevent negative energy and nitrogen balance
 - To prevent essential fatty acid deficiency
 - To support normal growth and development
 - To decrease morbidity

Neonatal PN - Calculations

- Use birth weight for calculations until birth weight regained. Thereafter, daily weight is used in calculations
- Use an estimated dry weight for calculations when indicated
- Monitoring growth is essential
 - Daily weight
 - Weekly length and head circumference

Neonatal PN - Daily Energy Requirements

- Variety of methods and recommendations exist.

Preterm infants	90-120 kcal/kg/d
Term infants	
0-6 months	85-105 kcal/kg per day
6-12 months	80-100 kcal/kg per day

- Must consider clinical condition of the infant
- Minimal requirement to prevent catabolism is at least 40 kcal/kg per day and 2 g/kg per day protein.
- Collaboration with Registered Dietitian who specializes in neonates and/or PharmD is an important part of care of the neonate

Mirtallo et al. *J Parenter Enteral Nutr.* 2004;28(6):S55-S57.


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Mirtallo J, Canada T, Johnson D, et al. Safe practices for parenteral nutrition. Task Force for the Revision of Safe Practices for Parenteral Nutrition. *J Parenter Enteral Nutr.* 2004 Nov-Dec;28(6):S39-70. Erratum in: *J Parenter Enteral Nutr.* 2006 Mar-Apr;30(2):177.

Neonatal PN - Fluid Requirements

- Establish total fluid limit or allowance
 - Usually started at 80-100 mL/kg per day or at current stable fluid intake
 - Must consider fluids supplied parenterally, orally and enterally, other infusions, and additional fluid losses (e.g. diarrhea).
- Subtract intravenous fluids and other drips/flushes to calculate amount remaining for PN and lipid emulsion
 - Generally need at least 30 mL/kg per day to allow compounding
 - Amount of substrates that can be compounded into the PN solution is dependent on the fluid volume
 - lower fluid volume = less room for substrates

Two options for calculation of PN volume for infants who are also receiving enteral feeds:

- (a) determine the total volume of the day's enteral feedings; then order the remainder of fluid and component needs as PN. This will require daily recalculation of parenteral composition, or
- (b) order the PN solution as if the infant were NPO, but only administer the amount of PN needed to supply the volume NOT provided

by enteral feedings. The parenteral nutrition composition will vary minimally. The cost of the unused solution is negligible; be aware that the patient will only get a percentage of the micronutrients in the PN bag.

Parenteral Nutrition Guidelines for Newborn Infants. Available from:
<http://www.metrohealth.org/documents/patient%20services/neonatology/Nutrition%20Pathway%20Parenteral%20Nutritio%20Guidelines.pdf>

Neonatal PN - Dextrose

- Initiate based on current glucose infusion rate (GIR)
 - Advance GIR daily by 1-3mg/kg/min until caloric goal met
 - Must consider recent blood glucose levels and assess limitations
- Alternate method
 - Start with 10-12.5% dextrose, or 2.5-5% higher than current intravenous fluids
 - Advance by 2.5-5% per day to goal (requires central access) if serum glucose levels are acceptable
- Need minimum 5 – 6 mg/kg/min to meet brain's energy needs
- Fat synthesis occurs with rates > 12.5 mg/kg/min in infants
 - May aid in increasing low fat mass of VLDW infant however fat synthesis significantly increases Respiratory Quotient so that overfeeding in presence of pulmonary disease can potentially lead to CO₂ retention
- Published guidelines suggest maximum GIR of 12-15 mg/kg/min for infants. However, GIR's in excess of this range are often well tolerated

Yunis et al. *J Pediatr.* 1989 Jul;115(1):127-32.
Bresson et al. *Pediatr Res.* 1989;25(6):645-8.
Cox et al. *Handbook of Pediatric Nutrition*, 3rd Ed., 2005;p533.


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Smaller preterm infants are prone to hyperglycemia and may require a limited GIR or insulin to attain normal glucose levels. The maximum dextrose concentration depends on tolerance and access. A higher GIR is required to compensate for calories when lipids are restricted (e.g. cholestasis prevention, hypertriglyceridemia). Consider **advancing GIR daily by 0.5 - 1 mg/kg/min per day for VLBW premies; 1 - 1.5 mg/kg/min per day for term infants.**

Yunis KA, Oh W. Effects of intravenous glucose loading on oxygen consumption, carbon dioxide production, and resting energy expenditure in infants with bronchopulmonary dysplasia. *J Pediatr.* 1989 Jul;115(1):127-32.

Bresson JL, Narcy P, Putet G et al. Energy substrate utilization in infants receiving total parenteral nutrition with different glucose to fat ratios. *Pediatr Res.* 1989 Jun;25(6):645-8.

Cox JH and Melbardis IM. (2005). Parenteral Nutrition. In PQ Samor & K King(Eds.), *Handbook of Pediatric Nutrition, 3rd ed.* (page 533). Sudbury, MA: Jones and Bartlett Publishers.

Koletzko B, Goulet O, Hunt J, Krohn K, Shamir R; Guidelines on Paediatric Parenteral Nutrition of the European Society of Paediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN) and the European Society for Clinical Nutrition and Metabolism (ESPEN), Supported by the European Society of Paediatric Research (ESPR). *J Pediatr Gastroenterol Nutr.* 2005 Nov;41 Suppl 2:S1-87.

Neonatal PN - Amino Acid Solutions for Infants (per 100 mL)

		INFANT		
		Premasol™ 10%	TrophAmine® 10%	Aminosyn® PF 10%
Essential	Isoleucine	0.82 g	0.82 g	0.76 g
	Leucine	1.4 g	1.4 g	1.2 g
	Lysine	0.82 g	0.82 g	0.68 g
	Methionine	0.34 g	0.34 g	0.18 g
	Phenylalanine	0.48 g	0.48 g	0.43 g
	Threonine	0.42 g	0.42 g	0.51 g
	Tryptophan	0.20 g	0.20 g	0.18 g
	Valine	0.78 g	0.78 g	0.67 g
Nonessential	Aspartic Acid	0.32 g	0.32 g	0.53 g
	Serine	0.38 g	0.38 g	0.49 g
	Glutamic Acid	0.50 g	0.50 g	0.82 g
	Alanine	0.54 g	0.54 g	0.69 g
	Proline	0.68 g	0.68 g	0.81 g
Conditionally Essential	Arginine	1.2 g	1.2 g	1.2 g
	Glycine	0.36 g	0.36 g	0.39 g
	Glutamine	0.50 g	0.50 g	0.82 g
	Taurine	0.025 g	0.025 g	0.07 g
	Cysteine	<0.016 g	<0.016 g	-
	Histidine	0.48 g	0.48 g	0.31 g
	Tyrosine	0.24 g	0.24 g	0.04g



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These are examples of amino acids solutions used in infants. Solutions contain all the amino acids including essential, nonessential and conditionally essential. Taurine and cysteine are present.

Please ensure that you check the specific product websites regarding updates.

Neonatal PN - Protein

- Protein requirements

Preterm infants	3 -3.5 g/kg/d
Term infants	
0-6 months	2.5-3 g/kg per day
6-12 months	2-2.5 g/kg per day

- Generally start amino acids at 2-3 g/kg per day
- Traditional step-wise advance of protein
 - No benefit and may be associated with a negative nitrogen balance due to delay in reaching target protein intakes
- Higher protein intakes up to a maximum of 4 g/kg per day should be considered for infants with protein losses or healing needs. (e.g. extremely low birth weight infants, chest tube losses, wound dehiscence, etc.)

Tsang et al. *Nutrition of the Preterm Infant*. 2nd Edition 2005:4176-418.

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Tsang et al eds. Nutrition of the preterm infant: scientific basis and practical guidelines. *Nutrition of the Preterm Infant: Scientific Basis and Practical Guidelines*. Digital Educational Publishing Inc: Cincinnati, OH;2005:4176-418.

Neonatal PN - Lipid

- Provides essential fatty acids
- Concentrated source of calories (20% solution = 2 kcal/mL)
- 20% emulsion is preferable
 - Lower volume requirement
 - Improved triglyceride clearance over 10% emulsion
- May prolong integrity of peripheral intravenous line due to low osmolarity
- Lipid emulsions in the US are either based on soybean oil or a combination of safflower and soybean oil

Neonatal PN Lipids & Essential Fatty Acid Deficiency (EFAD)

- EFAD can be seen within days of fat-free PN in neonates
- Deficiency is cumulative
- Can cause
 - decreased growth
 - skin and hair changes
 - increased susceptibility to infection,
 - poor wound healing
 - alterations in platelet function
- To avoid EFAD need minimum of
 - 2% to 4% of the total caloric intake as linoleic acid
 - 0.25% to 0.5% of total caloric intake as alpha linolenic acid
 - Met with minimum of 0.5g/kg per day IVFE
- Diagnosis: triene:tetraene ratio > 0.2 or linoleic acid levels
- In premature infants EFAD can be prevented by supplying 0.6 to 0.8 g/kg per day IVFE



Uauy et al. *Semin Perinatol*. 1989;13:118-30.


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This is a picture of a child with EFAD on the left, and on the right after he was successfully treated.

Uauy R, et al. Essential fatty acid metabolism and requirements during development. *Semin Perinatol* 1989;13:118-30.

Neonatal PN - Lipid Infusion & Clearance

- Most commonly infused over 20 - 24 hrs
- Maximum infusion rate is 0.15 g/kg/hr
- Poor lipid clearance may be seen with immaturity, infection, stress, liver disease, corticosteroids, or malnutrition.
- No conclusive evidence for restriction of IVFE in infants with unconjugated hyperbilirubinemia
- Provided as a separate infusion from dextrose and amino acid solution to enhance Ca and Phos solubility (not as 3-in-1 solution)

Pediatric Nutrition Support Core Curriculum. Editor: Mark Corkins. ASPEN, 2010.

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The hang time for lipids is 24 hours for central venous catheters and 12 hours for peripheral catheters.

Pediatric Nutrition Support Core Curriculum. Editor: Mark Corkins. American Society for Parenteral and Enteral Nutrition (ASPEN), 2010.

CDC website: <http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5110a3.htm>

Neonatal PN - Lipid Initiation & Dosing

- Usually initiated at 1-2 g/kg per day
- Increased by 0.5-1 g/kg per day
- Maximum of 3 g/kg per day
- Consider limiting to 1g/kg per day in neonate on long-term PN for prevention/treatment of cholestasis
- Adjust lipid dose based on clinical status

Brans et al. *Am J Dis Child*. 1988;142(2):145-52.

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Evidence emerging for restriction of IVFE to prevent or treat PN associated cholestasis. Alternate lipid forms not commercially available in the US (e.g. Omegaven) are utilized for prevention and treatment of PN associated cholestasis,

Brans YW, Andrew DS, Carrillo DW, et al. Tolerance of fat emulsions in very-low-birth-weight neonates. *Am J Dis Child*. 1988 Feb;142(2):145-52.

Neonatal PN - Heparin

- Prophylactic to prevent thrombosis
- Reduces formation of fibrin sheath around 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)

Birch et al. *Arch Dis Child Fetal Neonatal Ed.* 2010 Jul;95(4):F252-7.

Uslu et al. *J Perinatol.* 2010 [Epub].

Kerner JA. "Parenteral Nutrition" in *Nutrition in Pediatrics 3rd Edition*, 2003:969.

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Kerner JA. (2003). Parenteral Nutrition. In Walker, Watkins, & Duggan(Eds.), *Nutrition in Pediatrics, 3rd ed.* (p 969). Hamilton, Ontario: BC Decker, Inc.

Birch P, Ogden S, Hewson M. A randomised, controlled trial of heparin in total parenteral nutrition to prevent sepsis associated with neonatal long lines: the Heparin in Long Line Total Parenteral Nutrition (HILLTOP) trial.

Arch Dis Child Fetal Neonatal Ed. 2010 Jul;95(4):F252-7. Epub 2010 Jun 7.

Randolph AG, Cook DJ, Gonzales CA, Andrew M. Benefit of heparin in central venous and pulmonary artery catheters: a meta-analysis of randomized controlled trials. *Chest* 1998 Jan;113(1):165-71.

Uslu S, Ozdemir H, Comert S, Bolat F, Nuhoglu A. The effect of low-dose heparin on maintaining peripherally inserted percutaneous central venous catheters in neonates. *J Perinatol.* 2010 Apr 8. [Epub ahead of print]

Neonatal PN - Carnitine

- May aid triglyceride clearance
 - Facilitates transport of fatty acids across mitochondrial membrane
- Conditionally essential in the preterm infant
- Serum levels decrease when carnitine is not added to PN
- Conflicting studies regarding benefit
- Consider supplementation
 - Extremely low birth weight premature infants
 - Children on long-term PN (> 2 weeks)
 - Hypertriglyceridemia
 - Significant liver disease
- Frequently used dose is 10 – 20 mg/kg per day

Pediatric Nutrition Support Core Curriculum. Editor: M. Corkins. ASPEN, 2010.
Borum. *Gastroenterol.* 2009;137(5 Suppl):S129-34.
Crill et al. *Nutr Clin Pract.* 2007;22:204-213.


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Other published guidelines suggest a frequently used pharmacological intravenous dosage of 10 – 20 mg/kg/day with a maximum dosage of 100 mg/day. However, these dosages are much higher than typical dietary intake and several studies suggest better results with lower doses. Negative effects were exhibited with doses of 48 mg/kg/d in parenterally fed preterm neonates.

The adult dose is 2-5 mg/kg/day. Some institutions may use a dose 10 mg/kg/day for maintenance and a dose of 20 mg/kg/day if deficiency exists. Dose can be adjusted based on levels.

Dose can be adjusted based on levels (ester/free ratio)

Pediatric Nutrition Support Core Curriculum. Editor: Mark Corkins. American Society for Parenteral and Enteral Nutrition (ASPEN), 2010.

Borum PR. Carnitine in parenteral nutrition. *Gastroenterol.* 2009 Nov;137(5 Suppl):S129-34.

Crill CM, et al. The use of carnitine in pediatric nutrition. *Nutrition in Clinical Practice.* 2007 Apr; 22:204-213.

Borum PR. (1997). Carnitine. In TG Baumgartner (Ed.), *Clinical Guide to Parenteral Nutrition, 3rd ed.* (p. 629-643). Deerfield, IL: Fujisawa USA, Inc.

Neonatal PN - Electrolytes

- Individualized based on laboratory analyses.
- Adjust daily if needed.
- Must ensure proper conversion to institution-specific dosing units (e.g. mEq/L vs. mEq/kg; mmol/kg vs. mEq/kg)
- PN electrolyte content markedly above/below normal ranges may be required
 - Prolonged diarrhea or emesis
 - Increased ostomy output
 - Diuretics and other medications
 - Renal insufficiency

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The patient may be getting electrolytes from other sources e.g. umbilical arterial catheter, arterial lines, medications, fluid and electrolyte boluses. Calculation of daily intake should take into consideration these factors and what the patient has received in the last 24 hours.

Consider measuring urine Na levels to assess adequacy of Na intake especially in patients with SBS and growth problems.

During PN initiation it is customary to follow serum electrolytes closely.

Neonatal PN Daily Electrolyte & Mineral Requirements*

	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.

Kleinman. *Pediatric Nutrition Handbook 6th Ed.* 2009:519-40.



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These are suggested daily electrolyte and mineral requirements. Usually start at the lower end of the dose range.

Acetate should be used to correct acidosis and Na or K salt may be used based on serum electrolyte levels.

Kleinman RE. *Pediatric Nutrition Handbook 6th Edition* 2009:519-540.

Pharmacy Handbook and Formulary, The Children's Hospital of Philadelphia. Hudson, ON: Lexi-Comp Inc, 2006;p.571.

Neonatal PN – Electrolytes; Acid/Base Balance

- Chloride: provided as Na chloride, K chloride, and as part of cysteine hydrochloride. Occasionally added as HCl in ECMO patients.
- 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 et al. *Am J Health Syst Pharm*. 2007;64:730–739.
Bohrer et al. *J Parenter Enteral Nutr*. 2002;26:382–389.

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Some practitioners may feel that these differences in Al content are not significant and do not warrant selection of K acetate over Na acetate.

Smith BS, Kothari H, Hayes BD, *et al*. Effect of additive selection on calculated aluminum content of parenteral nutrient solutions. *Am J Health Syst Pharm* 2007; 64:730–739.

Bohrer D, do Nascimento PC, Binotto R, *et al*. Contribution of the raw material to the aluminum contamination in parenterals. *J Parenter Enteral Nutr* 2002; 26:382–389.

Bishop NJ, Morley R, Day JP, *et al*. Aluminum neurotoxicity in preterm infants receiving intravenous feeding solutions. *N Engl J Med* 1997; 336:1557–1561.

Neonatal PN - Calcium & 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 in those receiving long-term PN.
 - Monitor serum levels closely
 - Adjust Ca and Phos daily in PN if needed
 - 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)
- Use products with lowest aluminum content when possible (Na Phos contains 28,000 mcg/L; K Phos contains 51,000 mcg/L)
- Ca and Phos in PN are based on both recommended intakes and ratios of these nutrients, and on compounding limits of solubility.

Groh-Wargo et al. *Nutritional Care for High Risk Newborns*. Precept Press, Inc. 2000.
Porcelli et al. *J Am Coll Nutr*. 1997 Jun;16(3):283-7.

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Factors affecting calcium and phosphorus solubility in PN include the following: absolute amounts of calcium and phosphorus, form of calcium salt (calcium gluconate allows improved solubility), order of mixing, pH of the solution (acidic pH allows improved solubility), temperature, amino acid content and composition, dextrose concentration and presence of other additives. Check with your pharmacist or use computer software available to assist with determination of calcium and phosphorus solubility.

Pediatric Nutrition Support Core Curriculum. Editor: Mark Corkins. American Society for Parenteral and Enteral Nutrition (ASPEN), 2010.

Groh-Wargo, S, Thompson, M, Cox J, (Eds). *Nutritional care for high-risk newborns*. Chicago, IL: Precept Press, Inc., 2000.

Pelegano JF, Rowe JC, Carey DE, et al. [Effect of calcium/phosphorus ratio on mineral retention in parenterally fed premature infants. *J Pediatr Gastroenterol Nutr* 1991;12:351-5.](#)

Porcelli PJ, Block SM. Increased parenteral nutrition calcium and phosphorus for very-low-birth-weight infants using computer software assisted ordering. *J Am Coll Nutr*. 1997 Jun;16(3):283-7.

Neonatal PN Calcium/Phosphorus Solubility & Cysteine

- Cysteine is considered to be an essential amino acid for preterm infants
- Can be added to PN solution
- Lowers pH of the solution allowing increased solubility of Ca and Phos
- Dosing recommendation is 40 mg cysteine per g of TrophAmine®
- Addition of cysteine may necessitate supplementation with acetate in preterm infants and possibly other patients prone to acidosis

Shulman et al. *J Pediatr Gastroenterol Nutr.* 2003;36:587-607.

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Shulman RJ, Phillips S. Parenteral nutrition in infants and children. *J Pediatr Gastroenterol Nutr.* 2003 May;36(5):587-607.

Neonatal PN - Multivitamins

- Comprehensive scientific data not yet available to delineate optimal amounts
- Cannot use adult preparations despite periodic nationwide shortages of parenteral vitamin products in infants <1500 g due to propylene glycol and polysorbate additives
- Current vitamin formulations
 - Content of water-soluble vitamins may be too high
 - Content of fat-soluble vitamins may be too low
 - Vitamin A adheres to the plastic tubing, so delivery to infant is compromised
- Susceptible to photodegradation and oxidization

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

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Use of adult preparations for infants <1500 g may present a danger due to the infant's inability to metabolize propylene glycol and polysorbate additives.

Greene HL, Hambidge KM, Schanler R, et al. Guidelines for the use of vitamins, trace elements, calcium, magnesium, and phosphorus in infants and children receiving total parenteral nutrition: report of the Subcommittee on Pediatric Parenteral Nutrient Requirements from the Committee on Clinical Practice Issues of the American Society for Clinical Nutrition. *Am J Clin Nutr.* 1988 Nov;48(5):1324-42.

Neonatal PN - Photodegradation & Oxidation

- Oxygen causes degradation of vitamins in PN.
 - Oxygen originates from filling process, air remaining in the bag after filling, and permeation through the bag wall
 - Degradation reduced with use of new multilayered bags and careful oxygen monitoring during filling process.
- Light exposure generates peroxide/free radical formation in PN solutions.
 - Both dextrose and AA solutions containing vitamins and IV lipids are prone to peroxidation.
 - Covering PN bags and IV tubing with aluminum foil or light protective covers or use of tinted bags and tubing reduces photodegradation.

Berger. *Gastroenterol.* 2009;137(5 Suppl):S71.

Levin. *Pharmaceutical Considerations (2000) In Nutritional Care for High-Risk Newborns*, Rev. 3rd Ed.

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Vitamin C is especially prone to degradation by oxygen. Only 35% of vitamin C remained after 24 hrs when stored at 4°C; only 15% remained after 24 hrs when stored at 21°C. Light exposure from phototherapy results in exposure of the neonate to peroxidation products.

Berger MM. Vitamin C requirements in parenteral nutrition. *Gastroenterol.* 2009 Nov;137(5 Suppl):S71.

Levin MI and Kyllonen SS. (2000). Parenteral Nutrition: Pharmaceutical Considerations. In S Groh-Wargo, M Thompson, J Cox(Eds.), *Nutritional Care for High-Risk Newborns*, Rev. 3rd ed. (p. 187). Chicago, IL: Precept Press, Inc.

Neonatal PN

Examples of Multivitamin Pediatric Products

MVI® Pediatric	INFUVITE® Pediatric
5 mL	2 vial system (4 mL 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 Vitamin B6: 1 mg Vitamin B12: 1 mcg Biotin 20 mcg Folic acid 140 mcg.	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 >3kg: 100% of the standard dose (5 mL) Infants 1-3kg: 65% of the dose (3.25 mL) Infants <1kg: 30% of the dose (1.5 mL)	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_pediatic_PL.pdf
http://www.infuvite.com/PDF/infuvite_Packagelnsert.pdf



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Neonatal PN - 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 wt (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
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

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

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

In 1988 Greene et al reviewed the use of vitamins in infants and children on PN. They compared the current recommendations at that time to what they considered was their best estimate for new formulations.

Greene HL, Hambidge KM, Schanler R, et al. Guidelines for the use of vitamins, trace elements, calcium, magnesium, and phosphorus in infants and children receiving total parenteral nutrition: report of the Subcommittee on Pediatric Parenteral Nutrient Requirements from the Committee on Clinical Practice Issues of the American Society for Clinical Nutrition. *Am J Clin Nutr*. 1988 Nov;48(5):1324-42.
BA, Graham PJ. Vitamin A supplementation for preventing morbidity and mortality in very low birth weight infants. *Cochrane Database Syst Rev* 2000;(2):CD000501.

Neonatal PN - Trace Element Recommendations

- Only through the use of individualized trace element products can recommended intakes of trace elements be achieved.

Trace Element	Preterm neonates * < 3kg (mcg/kg /d)	Term neonates * 3-10 kg (mcg/kg/d)
Zinc	400	50-250
Copper	20	20
Manganese	1	1
Chromium	0.05-0.2	0.2
Selenium	1.5-2	2
*Assumes normal age-related organ function and normal losses.		

Moukarzel A. *Gastroenterol.* 2009;137:s18-28.
Mirtallo et al. *J Parenter Enteral Nutr.* 2004;28(6):S55-S57.

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There are more than 60 minerals which are integrated into various body processes: chromium, copper, iodine, manganese, molybdenum, selenium, zinc etc. Zinc is often required in larger amounts than suggested. Iron may not be routinely included to PN solutions. Optimal requirements for trace elements for children are unknown. Higher amounts of trace elements are present in PN solutions due to component contamination.

Commercial products contain zinc, copper, chromium, manganese. In patients with
|

Moukarzel A. Chromium in Parenteral Nutrition: Too Little or Too Much? *Gastroenterol.* 2009;137:s18-28.

Mirtallo J, Canada T, Johnson D, et al. Safe practices for parenteral nutrition. Task Force for the Revision of Safe Practices for Parenteral Nutrition. *J Parenter Enteral*

Nutr. 2004 Nov-Dec;28(6):S39-70. Erratum in: J Parenter Enteral Nutr. 2006 Mar-Apr;30(2):177.

Neonatal PN - Zinc (Zn)

- Zn is an important trace element especially in growth and wound healing
- Signs of Zn deficiency
 - Dermatitis, alopecia, diarrhea, immune deficiency
 - Mimics acrodermatitis enteropathica
- Zn excreted mainly in feces
 - Increased needs in diarrhea, hypercatabolic states, ostomy losses, mucositis, and chest tube losses
- Measure of Zn status
 - Serum Zn is a poor measure but is the only measure clinically available
 - A low alkaline phosphatase may suggest Zn deficiency but this is not diagnostic
- Can increase intake in PN to 1.5-2 times usual dose in conditions associated with increased needs



Acknowledgement to dermnetnz.org

Report of WHO/ UNICEF/ IAEA/ IZINCG. *Food Nutr Bull* 2007;28:S399-S400.
Prasad et al. *J Lab Clin Med*. 1963;61:537-49.


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Zinc is essential to the structural integrity of proteins, which regulate gene expression, and to nuclear binding proteins that act as transcription factors. It is a component of more than 250 metalloenzymes including alcohol, lactate and pyruvate dehydrogenases, alkaline phosphatase, and DNA and RNA polymerases.

Executive summary. Recommendations for indicators of population zinc status. Report of WHO/ UNICEF/ IAEA/ IZINCG Interagency meeting on zinc status indicators. *Food Nutr Bull*, 2007;28:S399-S400.

Standing Committee on the Scientific Evaluation of Dietary Reference Intakes, Food and Nutrition Board, and Institute of Medicine, Dietary reference intakes for vitamin A, vitamin K, arsenic, boron, chromium, copper, iodine, iron, molybdenum, nickel, silicon, vanadium and zinc, National Academy of Sciences, Washington, DC (2001).

Prasad AS, Miale A Jr, Farid Z, et al. Zinc metabolism in patients with the syndrome of iron deficiency anemia, hepatosplenomegaly, dwarfism, and hypogonadism. *J Lab Clin Med*. 1963 Apr;61:537-49.

Neonatal PN – Copper (Cu)

- Decrease or omit with cholestasis (risk for toxicity due to biliary excretion of Cu)
 - Case reports of deficiency when decreased or omitted in PN
 - Premature infants are at special risk of becoming Cu deficient because Cu accumulates in the fetus during the third trimester
 - Consider checking Cu and ceruloplasmin levels (and using clinical circumstances) to guide dose adjustments, especially with cholestasis

Hurwitz et al. *Nutr Clin Pract*. 2004;19:305-8.
Shike. *Gastroenterol*. 2009;137:S13-S17.
Frem et al. *J Parent Enter Nutr*. 2010;50:650-54.


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Hurwitz M, Garcia MG, Poole RL, et al. Copper Deficiency. *Gastroenterology*. 2009 Nov;137(5 Suppl):S13-7.

Shike M. Copper in parenteral nutrition. *Nutr Clin Pract*. 2004 Jun;19(3):305-8.

Frem J, Sarson Y, Sternberg T, et al. Copper supplementation in parenteral nutrition of cholestatic infants. *J Pediatr Gastroenterol Nutr*. 2010 Jun;50(6):650-4.

Neonatal PN – Manganese (Mn)

- Deficiency is virtually unknown in humans.
- Contaminant of PN solutions
 - Likely adequate to meet needs without additional supplementation.
- Omit from PN with cholestasis (risk for toxicity due to biliary excretion of Mn).
- When using a commercial multiple trace element product, excessive intake of Mn can occur when recommended doses of Zn are given.
- Risk for neurotoxicity with excessive intake

Hardy G. *Gastroenterol.* 2009;137:S29-S35.

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Hardy G. Manganese in parenteral nutrition: who, when, and why should we supplement? *Gastroenterology*. 2009 Nov;137(5 Suppl):S29-35. Review.

Neonatal PN – Selenium (Se) & Chromium (Cr)

- Selenium:
 - Should be provided to all patients at initiation of PN
 - Omit in patients with renal disease
 - Increased requirement with oxidative stress, critical illness, 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)
- Chromium:
 - Recent data suggests need to lower the recommended amount of Cr in PN.
 - Omit in patients with renal disease

Shenkin A. *Gastroenterol.* 2009;137:S61-S69.
Moukarzel A. *Gastroenterol.* 2009;137:S18-S28.


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Shenkin A. Selenium in intravenous nutrition. *Gastroenterology*. 2009 Nov;137(5 Suppl):S61-9.

Moukarzel A. Chromium in parenteral nutrition: too little or too much? *Gastroenterology*. 2009 Nov;137(5 Suppl):S18-28. Review.

Neonatal PN – Iron (Fe)

- Parenteral formulation: Fe Dextran
- Controversial; not recommended as a routine additive
- 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 per day for infants > 2 months of age or those with Fe deficiency

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

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Other parenteral Fe preparations include Fe sucrose and Fe tri-phosphates. Fe Dextran is compatible with non-lipid containing PN. Due to the recent black box warnings, may want to consider administration of Fe Dextran under supervision, at least initially. When Fe Dextran infusions are used to treat Fe deficient anemia, a test dose is always administered and the patients closely monitored for allergic reaction.

Other causes of anemia in patients on PN are anemia of chronic disease, Zn and Cu deficiency, vitamin E and B12 deficiency, folic acid deficiency, and hemolysis and occult blood loss. In general oral route is preferred over parenteral route for treatment of Fe deficiency anemia

In a retrospective adult study of 55 patients treated with home PN for more than 6 months, 30/55 (55%) had evidence of Fe deficiency anemia (10/30 at time of start of PN and 20/30 between 2-97 months after start of PN (mean age 28 months). Loss from GI tract was most prominent reason.

Greene HL, Hambidge KM, Schanler R, et al. Guidelines for the use of vitamins, trace elements, calcium, magnesium, and phosphorus in infants and children receiving total parenteral nutrition: report of the Subcommittee on Pediatric Parenteral

Nutrient Requirements from the Committee on Clinical Practice Issues of the American Society for Clinical Nutrition. *Am J Clin Nutr.* 1988 Nov;48(5):1324-42.

Neonatal PN - Monitoring

	Initial	With Every Change in PN	Weekly until Stable	Monthly/ as indicated
Electrolytes	✓	✓	✓	
Glucose	✓	✓	✓	
Calcium	✓	✓	✓	
BUN	✓	✓	✓	
Creatinine	✓	✓	✓	
Magnesium	✓	✓	✓	
Phosphorus	✓	✓	✓	
ALT	✓		✓	
AST	✓		✓	
Alkaline phosphatase	✓		✓	
Total protein	✓		✓	
Albumin	✓		✓	
GGT	✓		✓	
Prealbumin	✓		✓	
Triglycerides	✓	✓	✓	
Conjugated bilirubin	✓		✓	
CBC	✓		✓	✓
Iron studies				✓
Trace elements				✓
Vitamins				✓



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Consider checking iCa in patients with low albumin levels.

Consider measuring carnitine levels in patients who are NPO for a significant amount of time, as indicated. Some clinicians feel that measuring carnitine levels is not helpful.

Thyroid function can be checked (TSH) at baseline, if indicated, and yearly.

Consider checking prothrombin time weekly, and then monthly.

Neonatal PN - Monitoring Triglycerides

- Serum triglyceride levels are often used to monitor clearance of intravenous fat emulsion
 - Levels less than 200 mg/dL are acceptable
 - Consider checking the level prior to start of intravenous fat emulsion and after any increase in rate of the emulsion
 - With decline in overall clinical status
 - Monitor every 1 - 2 weeks once the patient is on a stable regimen

Forget et al. *Acta Paediatr Scand*. 1975;64:377-84.

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Forget PP, Fernandes J, Begemann PH. Utilization of fat emulsion during total parenteral nutrition in children. *Acta Paediatr Scand* 1975;64:377-84.

Neonatal PN - Discontinuing Parenteral Nutrition

- When adequate hydration is attained from enteral or oral feedings
- When the infant is
 - Tolerating enteral feedings
 - Receiving ≤ 25 mL/kg per day of PN
- The rate of dextrose administration should be tapered to prevent rebound hypoglycemia

The background of the slide is a light blue, semi-transparent image of medical equipment, likely a drip chamber or part of an IV stand, with various tubes and connectors visible. The text is centered over this background.

Parenteral Nutrition For The Specialized Patient

Parenteral Nutrition – Specialized Patient

- Critical Illness
- Inflammatory Bowel Disease (IBD)
- Short Bowel Syndrome (SBS)
- Liver
- Renal
- Oncology
- Metabolic

Critical Illness - Enteral Nutrition

A functional gut should always be used for enteral nutrition, including in critical illness

Benefits	Limitations
Reduce gut atrophy	More likely to underfeed
Improve gut motility	Contraindications: nonfunctional gut; anatomical disruption, obstruction, ischemia, peritonitis; Severe shock states
Reduced infections (enhanced gut immune function and avoidance of translocation)	Frequent interruptions for fasting for diagnostic and other procedures limit efficacy, especially in malnourished patients
Cost effective	Risk of aspiration
Less likely to overfeed	

Braunschweig et al. *Amer J Clin Nutr*. 2001;74(4):534-42.

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Some experts believe that gut atrophy does not occur in humans. Bacterial translocation due to gut atrophy or PN has not been conclusively demonstrated in human and when it has been shown it was not clinically meaningful (personal communication, A. Buchman)

Braunschweig CL, et al. Enteral compared with parenteral nutrition: a meta-analysis. *Amer J Clin Nutr*. 2001;74(4):534-42.

Critical Illness - Timing

- Timing of nutrition may be as or more important than route
 - A meta-analysis in adults compared early PN to the delayed start of enteral nutrition. They showed when early PN was used there was reduced mortality when compared to the delayed starting of EN. Patients who received PN had increased infections.
- Pediatric Guidelines
 - If enteral nutrition not possible, parenteral nutrition should start within
 - 1-3 days in infants
 - 4-5 days in older children
 - Meta-analysis identified one trial in pediatric burn patients and concluded no difference when enteral nutrition was started within 24 hr compared to ≥ 48 hr: therefore data insufficient to make firm recommendations

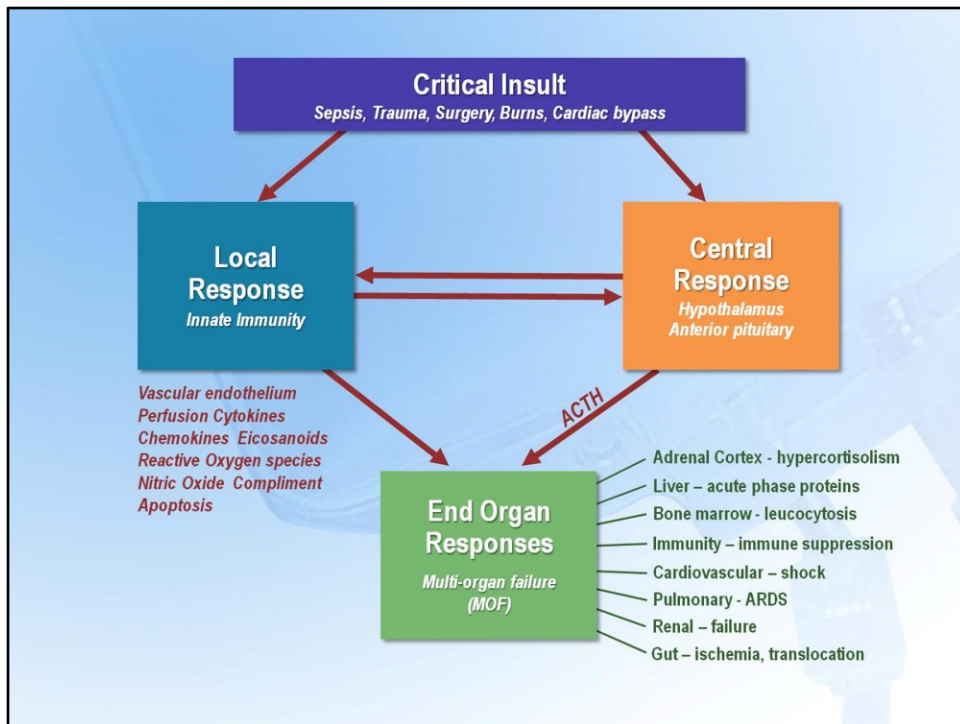
Simpson et al. *Intens Care Med*. 2005;31(1):12-23.
ASPEN et al. *J Parenter Enteral Nutr*. 2002;26(1 Suppl):1SA-138SA.
Joffe et al. *Cochrane Database Syst Rev*. 2009;15(2):CD005144.

 CDHNE ASPEN NASPHAN
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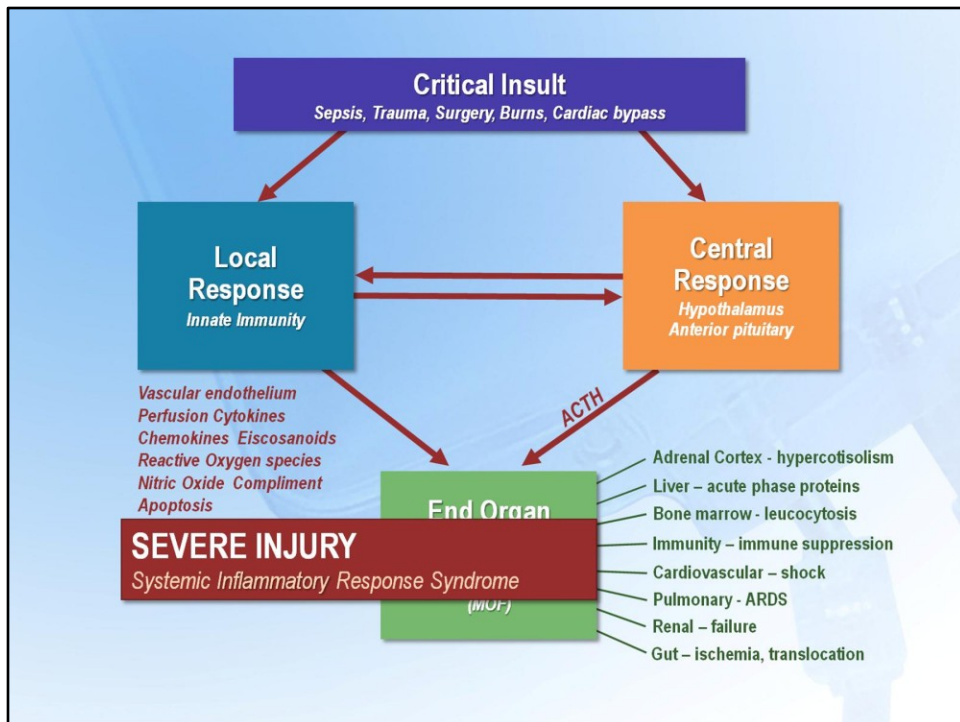
Simpson F, Doig GS. Parenteral vs. enteral nutrition in the critically ill patient: a meta-analysis of trials using the intention to treat principle. *Intens Care Med* 2005; 31(1):12-23.

ASPEN Board of Directors and the Clinical Guidelines Task Force. Guidelines for the use of parenteral and enteral nutrition in adult and pediatric patients. *J Parenter Enteral Nutr*. 2002;26(1 Suppl):1SA-138SA. Erratum in: *J Parenter Enteral Nutr* 2002;26(2):144.

Joffe A, et al. Nutritional support for critically ill children. *Cochrane Database Syst Rev*. 2009 Apr 15;(2):CD005144.



Severe injury is associated with a constellation of signs and symptoms commonly known as the systemic inflammatory response syndrome (SIRS). This syndrome reflects the metabolic response to injury at a central (neuroendocrine) level and at a local tissue (at the site of injury) level that leads to end organ damage from the release of systemically active mediators. The injury can be burns, surgery or trauma. The mediators include cytokines, chemokines, nitric oxide and fatty acid derived eicosonoids. End organ damage can be severe and present as multi-organ failure.



Severe injury is associated with a constellation of signs and symptoms commonly known as the systemic inflammatory response syndrome (SIRS). This syndrome reflects the metabolic response to injury at a central (neuroendocrine) level and at a local tissue (at the site of injury) level that leads to end organ damage from the release of systemically active mediators. The injury can be burns, surgery or trauma. The mediators include cytokines, chemokines, nitric oxide and fatty acid derived eicosonoids. End organ damage can be severe and present as multi-organ failure.

Critical Illness Systemic Inflammatory Response Syndrome

- Pre-resuscitative ebb phase (hours)
 - Hypometabolic phase
- Hypermetabolic flow phase (days)
 - But resting energy expenditure is often reduced
 - patients are typically ventilated and sedated
 - children cannot grow during this phase
- Recovery phase (weeks)
 - Hypermetabolism can persist for a month (e.g. the 'chronic' PICU patients with progressive malnutrition)
 - Children can grow during this phase

Chwals. *Curr Opin in Pediatr.* 1994; 6(3):334-40.


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This data is from a review based largely on opinion and clinical experience.

The hypometabolic phase often lasts a day and is dominated by the neuroendocrine response to injury initiated through the ACTH - cortisol - catecholamine pathways as well as the acute vascular responses to injury that presents as acute shock. Tissue, including gut ischemia predominates in this phase. This hypometabolic phase is diminished due to brain death and hypometabolism dominates independent of tissue injury.

The subsequent hypermetabolic phase last days and is dominated by the production of cytokine, endotoxin and reactive oxygen metabolites which are produced in response to injury, inflammation and often sepsis. Tissue reperfusion occurs at this stage.

The mediators of the recovery phase often set up competing pro-inflammatory and anti-inflammatory (compensatory anti-inflammatory response syndrome or CARS) or immune suppressing pathways, leading to considerable complexity in this system and how the patient presents (early or late multi-organ failure).

Furthermore the entire process is made more complex by 'secondary hits' e.g. need for surgery and sepsis. The patient is at high risk given reduced gut function and

bacterial translocation and decreased immune function.

Chwals WJ. The metabolic response to surgery in neonates. *Curr Opin Pediatr.* 1994;6(3):334-40.

Critical Illness - Intermediary Metabolism

- Hyperglycemia
- Hypertriglyceridemia
- High free fatty acid levels
- High lactate levels
- Disturbed normal energy substrate balance
 - Mobilizes both substrates at once

Wolfe et al. *World J Surg.* 2000; 24(6): 639-47.


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In healthy states our normal response to **fasting** is first to mobilize glycogen stores from the liver. Amino acids are used for gluconeogenesis as glycogen is depleted and as glucose is quickly depleted as a fuel, triglycerides are mobilized from adipose tissue. These mobilized *free fatty acids predominate as the fuel source in fasting*. Multiple hormones are involved including glucagon and growth hormone. Conversely our normal response to **feeding** is insulin release resulting in glucose uptake, oxidation and glycogen production. Triglycerides are stored in adipose tissue. *Glucose is the primary fuel source*.

In critical illness both glucose and fatty acids are mobilized as a fuel source. At the same time as an aberrant metabolic response dominated by stress hormone (cortisol and catecholamines), cytokine release and insulin and growth hormone resistance occurs. Muscle protein breakdown provides amino acids for gluconeogenesis and acute phase and immune proteins. Glycogen breakdown and increased glucose uptake leads to rapid release of lactate. Glucose feeding leads to hyperglycemia and lipolysis is not suppressed so that simultaneously there is an increased free fatty acid production and hence triglycerides from their hepatic conversion. This situation makes the individual vulnerable to overfeeding.

Wolfe RR, Martini WZ. Changes in intermediary metabolism in severe surgical illness. *World J Surg.* 2000;24(6):639-47.

Critical Illness – Risk of Overfeeding

- Risk of overfeeding (non-protein)
 - Glucose
 - Increase in morbidity and mortality with sepsis related to hyperglycemia
 - ↑CO₂ production - difficulty weaning ventilator
 - Excess glucose is converted to fat (lipogenesis) - fatty liver
 - Fat
 - Lipid overload syndrome (↓lipoprotein lipase function)
 - Hepatic steatosis
 - May impair response to sepsis

Srinivasan et al. *Pediatr Crit Care Med*. 2004;5(4):329-36.
Alaeeen et al. *J Pediatr Surg*. 2006;41(1):239-44.


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Aberrant intermediary metabolism leads to excess energy substrates and so providing more non-protein energy may only increase the potential risks of hyperglycemia and excess free fatty acids and hence triglycerides.

High glucose levels in children with critical illness are associated with more mortality, length of stay and ventilator days, particularly given concomitant sepsis. Poor diabetic control is also associated with poor wound healing and sepsis and supports the role of elevated circulating glucose in critical illness. Further support from in vitro work showing increased extracellular glucose contributes to impaired immune (particularly neutrophil function) and anti-oxidant defences (stimulates generation of reactive oxidant species). Excess glucose undergoes oxidation, increasing VCO₂ and this can increase work of breathing and will increase lipogenesis: excess fat, stored in the liver as steatosis.

Lipoprotein lipase dysfunction in critical illness places patients at increased risk of lipid overload syndrome from parenteral lipid. Excess lipid delivery in the face of poor lipid clearance contributes also to hepatic steatosis and concerns over sepsis, given pro-inflammatory lipid pathways.

Some experts believe that while there is theoretical risk of increased PCO₂ with overfeeding, there is limited data to indicate prolonged ventilator weaning. Fat overload syndrome occurs when patients get very high doses of intravenous lipid. This can occur when the dextrose amino acid solution and IV fat emulsion administration rates are interchanged and the patient gets a very high dose, or

sometimes a total daily dose, of IV fat emulsion over a short period of time. Clinically the patient will have an elevated triglyceride level tachypnea, hypoxia, thrombocytopenia. Therapy for the fat overload syndrome is supportive. The risk for pancreatitis occurs with elevated triglyceride levels of greater than 1000 mg/dL.

Srinivasan V. et al. Association of timing, duration, and intensity of hyperglycemia with intensive care unit mortality in critically ill children. *Pediatr Crit Care Med* 2004;5(4):329-36.

Alaedeem DI, Walsh MC, and Chwals WJ. Total parenteral nutrition-associated hyperglycemia correlates with prolonged mechanical ventilation and hospital stay in septic infants. *J Pediatr Surgery* 2006;41(1):239-44.

Critical Illness - Implications for PN Support II

- Risk of underfeeding
- Worsening malnutrition during ICU stay
- Increased metabolism will become relevant during recovery phase
 - Increased further with onset of enteral nutrition
 - Protein & energy required for tissue repair
 - Eventual recovery of growth potential

Hulst. *Clin Nutr.* 2004;23(2):223-32.
Hulst. *Clin Nutr.* 2004; 23(6):1381-89.


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The critical care patient is also at risk of not meeting intended nutrient delivery due to the following reasons:

- 1) frequent interruptions from fasting for procedures or investigations
- 2) limitations in fluid delivery and need for fluid restriction
- 3) delayed introduction of caloric feeding and the difficulties in accurately predicting calorie requirements (predicting energy requirements).

Pediatric patients admitted to intensive care are known to frequently have baseline malnutrition. The combination of a catabolic state with critical illness and the risk of underfeeding along with a cumulative energy deficit promote worsening of that underlying malnutrition during the ICU stay.

Specifically as patients enter the recovery phase of the systemic inflammatory response and when they begin enteral feeding, they are at risk of not having calorie delivery increased to meet the requirements for tissue repair, re-emerging growth potential and increased thermic effect of food.

Hulst J, et al. Malnutrition in critically ill children: from admission to 6 months after discharge. *Clin Nutr.* 2004;23(2):223-32.

Hulst JM, et al. The effect of cumulative energy and protein deficiency on anthropometric parameters in a pediatric ICU population. *Clin Nutr.* 2004;23(6):1381-9.

Critical Illness - Protein & Energy Reserves

- At least 20% of children admitted to intensive care are malnourished
- Protein loss is not reflected in weight loss
- Complications of muscle wasting
 - Prolonged ventilation
 - Acquired pneumonia
 - Prolonged length of stay and rehabilitation
 - Increased mortality
- Protein stores are critical
 - 20% loss of protein stores critically impairs muscle function

Hulst et al. *Clin Nutr.* 2004;23(2):223-32.

Plank et al. *Ann Surg.* 1998;228(2):146-58.

Pollack et al. *J Parent & Enteral Nutr.* 1985;9(3):309-13.

Windsor et al. *Brit J Surg.* 1988;75(9):880-2.


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Malnutrition is common in children admitted to PICU (Hulst et al) and worsens over the length of stay.

The main prognostic factor is loss of lean mass – associated most importantly with increased mortality (Pollack et al).

Critical Illness - Body Composition I

- Maintenance of lean body mass during critical illness is ideal – but is it possible?
 - Adults with multi-organ failure have muscle wasting regardless of nutrition support!
 - If wasted at the initiation of nutrition support, they will have the most benefit from the intervention
 - Metabolic studies in adults show that PN reduces but does not eliminate catabolism

Hill et al. *J Parenter Enter Nutr.* 1992;16(3):197-218.
Green et al. *Nutrition* 1995;11(6):739-46.
Shaw et al. *Ann Surg.* 1987;205(3):288-94.


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Hill GL. Body composition research: implications for the practice of clinical nutrition. *J Parenter Enteral Nutr.* 1992;16(3):197-218.
Green CJ, et al. Energy and nitrogen balance and changes in midupper-arm circumference with multiple organ failure. *Nutrition* 1995;11(6):739-46.
Shaw JH, Wildbore M, Wolfe RR. Whole body protein kinetics in severely septic patients. The response to glucose infusion and total parenteral nutrition. *Ann Surg.* 1987;205(3):288-94.

Critical Illness - Body Composition II

- Protein stores more limited in infants & children and limited further when malnourished at admission
- Children in ICU with cumulative energy and protein deficits have muscle wasting which is correlated with decreased mid-upper arm circumference
- Monitoring anthropometry (at least body weight) is necessary to deliver adequate parenteral nutrition in critical illness

Hulst et al. *Clin Nutr.* 2004;23(2):223-32.
Hulst et al. *Clin Nutr.* 2004;23(6):1381-9.

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These investigators have shown that one quarter of children admitted to ICU are likely to have malnutrition based on anthropometric measurements and these same measurements worsen during intensive care stay directly correlated with the length of stay.

Critical Illness – Energy Requirements

- Increased energy requirements are not typically seen in critical care patients due to:
 - Inactivity / muscle paralysis / sedatives / coma
 - Lack of enteral feeding
- Notable exceptions
 - Burns: increased energy requirements
 - Head injury: specific hypermetabolic response to head injury makes prediction of energy requirements very difficult

Chiolero et al. *Nutrition*. 1997; 13(Suppl 9):45-51.
Chwals et al. *J Pediatr Surg*. 1995; 30(8):1161-64.
Verhoeven et al. *Inten Care Med*. 1998; 24(5):464-68.
Foley et al. *J Neurotrauma*. 2008; 25:1415-31.


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We used to think that hypermetabolic patients required more energy however this is not the case! Factors to explain this are documented on this slide and these include: 1) neuro-protection through cooling, 2) lack of thermic effect of enteral feeding, and 3) use of drugs like sedatives, beta blockers and morphine.

There is a notable individual variability in REE that is difficult to predict. In general however we can now state that burns is one of the few clinical situations with a significant increase in REE. Few drugs – again a notable exception being catecholamines - will increase REE in the ICU setting.

In addition while head trauma patients are often paralyzed and sedated, they have a specific hypermetabolic response (driven by central hormonal aberrations in the systemic inflammatory response) that may lead to increased REE and in this population measurement of EE, rather than use of prediction equations may be particularly important.

Chioléro R, Revelly JP, Tappy L. Energy metabolism in sepsis and injury. *Nutrition*. 1997 Sep;13(9 Suppl):45S-51S.

Chwals WJ, Letton RW, Jamie A, et al. Stratification of injury severity using energy expenditure response in surgical infants. *J Pediatr Surg*. 1995;30(8):1161-4.

Verhoeven JJ, Hazelzet JA, van der Voort E, et al. Comparison of measured and predicted energy expenditure in mechanically ventilated children. *Intensive Care*

Med. 1998;24(5):464-8.

Foley N, Marshall S, Pikul J, et al. Hypermetabolism following moderate to severe traumatic acute brain injury: a systematic review. *J Neurotrauma*. 2008;25(12):1415-31.

Critical Illness - Resting Energy Expenditure I

- Predictive equations for energy are limited in accuracy in critical illness however they are still used
- Modified use of predictive equations
 - In ICU and post-operatively predictive equations tend to overestimate REE (**do not** add stress factors)
 - Energy requirements are safest when 0.8 -1.2 times the predicted REE if calorimetry not available

Chiolero et al. *Nutrition*. 1997;13(Suppl 9):45-51.
Chwals et al. *J Pediatr Surg*. 1995; 30(8):1161-64.
Verhoeven et al. *Intens Care Med*. 1998; 24(5):464-68.


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More information can be found on energy expenditure via the following references:

Chioléro R, Revelly JP, Tappy L. Energy metabolism in sepsis and injury. *Nutrition*. 1997;13(9 Suppl):45S-51S.

Chwals WJ, Letton RW, Jamie A, et al. Stratification of injury severity using energy expenditure response in surgical infants. *J Pediatr Surg*. 1995;30(8):1161-4.

Verhoeven JJ, Hazelzet JA, van der Voort E, et al. Comparison of measured and predicted energy expenditure in mechanically ventilated children. *Intens Care Med*. 1998;24(5):464-8.

Critical Illness - Resting Energy Expenditure II

- Selective use of Indirect calorimetry
 - Increases the accuracy of energy prediction
 - Respiratory quotient may help predict risk of over- and under-feeding
 - Practical limitation
- Measure individual energy requirement (calorimetry when possible) to deliver adequate parenteral nutrition in critical illness

Verhoeven et al. *Intens Care Med.* 1998;24(5):464-8.

Chwals et al. *J SurgRes.* 1988;44(5):467-72.

Hulst et al. *Nutrition.* 2005;21(2):192-8.

Joosten et al. *Crit Care Med.* 2000;28(8):3014-8.


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Verhoeven JJ, et al. Comparison of measured and predicted energy expenditure in mechanically ventilated children. *Intens Care Med* 1998;24(5):464-8.

Chwals WJ, et al. Measured energy expenditure in critically ill infants and young children. *Journal of Surgical Research* 1988;44(5):467-72.

Hulst JM, et al. Adequate feeding and the usefulness of the respiratory quotient in critically ill children. *Nutrition* 2005;21(2):192-8.

Joosten KF, et al. Accuracy of an indirect calorimeter for mechanically ventilated infants and children: the influence of low rates of gas exchange and varying FIO₂. *Crit Care Med* 2000;28(8):3014-8.

Critical Illness - Parenteral Protein Needs

- Both protein breakdown & synthesis are increased in critical illness
 - Negative nitrogen balance results
- Protein supply is critical – but often underestimated
 - Bedside tools to evaluate nitrogen balance limited (especially in renal impairment)
 - may consider 6 - 24 hour urine nitrogen collection
 - Monitor anthropometrics
 - Increased requirement in burns, gastrointestinal losses, open wounds, continuous renal replacement therapy

Maxvold et al. *Crit Care Med.* 2000;28(4):1161-65.
Lopez et al. *J Parent Enter Nutr.* 1986;10(12):517-13.
Bodamer et al. *Eur J Pediatr.* 1997;156(Suppl1):59-61.
Zappitelli et al. *Crit Care Med.* 2008;36(12):3239-45.


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Protein turnover is increased in critical illness, but in general a negative nitrogen balance results as protein breakdown is increased over synthesis

Maxvold NJ, Smoyer WE, Custer JR, et al. Amino acid loss and nitrogen balance in critically ill children with acute renal failure: a prospective comparison between classic hemofiltration and hemofiltration with dialysis. *Crit Care Med.* 2000;28(4):1161-5.

Lopez AM, Wolfsdorf J, Raszynski, A et al. Estimation of Nitrogen Balance Based on a Six-Hour Urine Collection in Infants. *J Parenter Enteral Nutr.* 1986;10: 517-18.

Bodamer OA, Leonard JV, Tasker RC, et al. Protein turnover in critically ill children. *Eur J Pediatr.* 1997;156 Suppl 1:S59-61.

Zappitelli M, Goldstein SL, Symons JM, et al. Protein and calorie prescription for children and young adults receiving continuous renal replacement therapy: a report from the Prospective Pediatric Continuous Renal Replacement Therapy Registry Group. *Crit Care Med.* 2008;36(12):3239-45.

Critical Illness - Specific Amino Acids I

- Glutamine
 - Non-essential amino acid
 - Conditionally essential in sepsis, trauma, burns
 - Low amounts in PN due to solubility concerns
 - Current published recommendations for adults with trauma and burns
 - Meta-analysis highlights reporting bias
 - Pediatric trials inconclusive

Windle. *J Burn Care & Res.* 2006;27(6):764-72.
Kreymann. *Curr Opin Clin Nutr & Metabol Care.* 2008;11(2):156-9.
Heyland et al. *J Parenter Enteral Nutr.* 2003;27(5):355-73.
Avenell. *Proceed Nutr Societ.* 2006;65(3):236-41.


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Glutamine is not commercially available in the USA. Some experts consider its use investigational since it is not FDA approved.

Windle EM. Glutamine supplementation in critical illness: evidence, recommendations, and implications for clinical practice in burn care. *J Burn Care & Res* 2006;27(6):764-72.

Kreymann KG. Early nutrition support in critical care: a European perspective. *Curr Opin Clin Nutr & Metabol Care* 2008;11(2):156-9.

Heyland DK et al. Canadian clinical practice guidelines for nutrition support in mechanically ventilated, critically ill adult patients. *J Parenter & Enteral Nutr* 2003;27(5):355-73.

Avenell A. Glutamine in critical care: current evidence from systematic reviews. *Proceed Nutr Societ* 2006;65(3):236-41.

Notable Pediatric trials:

Albers MJ et al., Glutamine supplementation of parenteral nutrition does not improve intestinal permeability, nitrogen balance, or outcome in newborns and infants undergoing digestive-tract surgery: results from a double-blind, randomized, controlled trial. *Ann Surgery* 2005;241(4):599-606.

Poindexter BB et al. Parenteral glutamine supplementation does not reduce the risk of mortality or late-onset sepsis in extremely low birth weight infants. *Pediatrics* 2004;113(5):1209-15.

Grover Z, Tubman R, and McGuire W. Glutamine supplementation for young infants with severe gastrointestinal disease. Cochrane Database Syst Rev. 2007 Jan 24;(1):CD005947.

Critical Illness - Specific Amino Acids II

- Arginine
 - Non-essential amino acid, essential in neonates, conditionally essential in stress
 - Ammonia detoxification, nitric oxide synthesis
 - Endogenous arginine production is dependent on gut metabolism
 - Expect low plasma levels in fasting states
 - No pediatric data
 - Role as 'immunonutrient' limited by lack of data & confounding factors in studies

Marik et al. *Intensive Care Med.* 2008;34(11):1980-90.


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Marik PE and Zaloga GP. Immunonutrition in critically ill patients: a systematic review and analysis of the literature. *Intensive Care Med.* 2008;34(11):1980-90.

Critical Illness - Parenteral Glucose

- Avoidance of parenteral glucose overfeeding is important during critical illness
- Insulin therapy for tight glucose control in adults controversial; risk of hypoglycemia
- Pediatric data limited
 - Poor risk/benefit ratio
 - Hypoglycemia is common and so monitoring is important
 - Avoid dextrose delivery (include **all** intravenous sources)
 - > 15 mg/kg/min in preterm infants
 - > 12 mg/kg/min term infants and children
 - > 8 mg/kg/min adolescent

Wiener et al. *JAMA*. 2008;300(8):933-44.

Vlasselaers et al. *Lancet*. 2009;373(9663):547-56.

Preissig et al. *Pediatr Crit Care Med*. 2008;9(6):581-8.

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Wiener RS, Wiener DC, and Larson RJ. Benefits and risks of tight glucose control in critically ill adults: a meta-analysis.[Erratum appears in *JAMA*. 2009 Mar 4;301(9):936]. *JAMA* 2008;300(8):933-44.

Vlasselaers D et al. Intensive insulin therapy for patients in paediatric intensive care: a prospective, randomized controlled study. *Lancet*. 2009;373(9663):547-56.

Preissig CM et al. A protocolized approach to identify and manage hyperglycemia in a pediatric critical care unit. *Pediatr Crit Care Med*. 2008;9(6):581-8.

Critical Illness - Parenteral Lipid I

Benefits	Risks
Concentrated source of calories	Predominant n-6 content of soy lipid may promote both inflammation & peroxidation
Isotonic	Decreased lipid clearance in stress & sepsis <ul style="list-style-type: none">•Hyperlipidemia•Fatty liver•Lipid overload syndrome
Prevent EFAD	Soy based lipids are low in AA and devoid of DHA, important in infant development
Reduced risk of metabolic complications related to excessive hypertonic dextrose infusion	Soy based lipids contain phytosterols

It has been suggested that phytosterols content of IV lipid may be related to PNALD.

Critical Illness - Parenteral Lipid II

- Evidence for adverse effect of soy lipid in critically ill adults
 - Meta-analysis (26 trials, 2211 adult patients) use of lipids might increase complications (P=0.09)
- Evidence limited for adverse effect of soy lipid in pediatric population
 - Case control data suggest lipids may increase sepsis rates, especially in critically ill neonates

Heyland et al. *JAMA*. 1998;280(23):2013-9.

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Heyland DK et al. Total parenteral nutrition in the critically ill patient: a meta-analysis. *JAMA*. 1998;280(23):2013-9.

Critical Illness - Parenteral Lipid III

- Benefits of lipid in the critically ill
 - PN without lipid will increase de novo lipogenesis & CO₂ production, more than PN with lipid
 - Increased glucose infusion rate will decrease fat oxidation
- Judicious use of lipid is important for critically ill infants and children; caution is required during acute stress and sepsis

Tappy et al. *Crit Care Med.* 1998;26(5):860-7.
Nordenstrom et al. *Ann Surg.* 1983;198(6):725-35.

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Tappy L et al. Effects of isoenergetic glucose-based or lipid-based parenteral nutrition on glucose metabolism, de novo lipogenesis, and respiratory gas exchanges in critically ill patients. *Crit Care Med.* 1998;26(5):860-7.

Nordenstrom J et al. Free fatty acid mobilization and oxidation during total parenteral nutrition in trauma and infection. *Ann Surg.* 1983;198(6):725-35.

Critical Illness - Micronutrients

- Important role for adequate supply of trace elements and vitamins in oxidant defense
- Monitor & ensure adequate supply (especially burns, gastrointestinal losses and continuous renal replacement therapy)
 - Se
 - Zn
 - Cu
 - Thiamine (vitamin B₁)
 - Vitamin C

Dylewski et al. *J Trauma*. 2010;69(3):584-8.
Corcoran et al. *Anaesth Intens Care*. 2009;37(5):740-7.
Mehta et al. *Pediatr Clin North Am*. 2009;56(5):1143-60.


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Dylewski ML, Bender JC, Smith AM, et al. The selenium status of pediatric patients with burn injuries. *J Trauma* 2010;69(3):584-8; discussion 588.

Corcoran TB, O'Neill MP, Webb SA, et al. Inflammation, vitamin deficiencies and organ failure in critically ill patients. *Anaesth Intens Care*. 2009;37(5):740-7.

Mehta NM, Duggan CP. Nutritional deficiencies during critical illness. *Pediatr Clin North Am*. 2009;56(5):1143-60.

Specific Conditions - ECMO

- REE not readily predictable leading to risk of overfeeding
- PN historically was used because of concern of decreased splanchnic perfusion with feeding
- But enteral nutrition not contraindicated; can be safe alternative
 - See ASPEN Guidelines for nutrition support for neonates supported by ECMO
 - Risk for hyperbilirubinemia with ECMO

Jaksic et al. *J Pediatr Surg*. 2010;34(3):247-53.
Jaksic et al. *J Parenter Enter Nutr*. 2001;36(1):63-7.


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ASPEN Clinical guidelines: nutrition support of neonates supported with extracorporeal membrane oxygenation. Jaksic T, Hull MA, Modi BP, Ching YA, George D, Compher C; American Society for Parenteral and Enteral Nutrition (A.S.P.E.N.) Board of Directors. Children's Hospital Boston, Harvard Medical School, Boston, MA, USA. *JPEN J Parenter Enteral Nutr*, 2010, May-Jun;34(3):247-53.

Jaksic T, et al. Do critically ill surgical neonates have increased energy expenditure? *J Parenter Enter Nutr*. 2001;36(1):63-7.

Keshen, et al. Stable isotopic quantification of protein metabolism and energy expenditure in neonates on and post extracorporeal life support. *J Pediatr Surg*. 1997;32(7):958-963.

Jaksic T, et al. Nutrition support of neonates supported with extracorporeal membrane oxygenation. *J Pediatr Surgery* 2010;34(3):247-53.

Other references of interest:

Pettignano R, et al. Total enteral nutrition versus total parenteral nutrition during pediatric extracorporeal membrane oxygenation. *Crit Care Med*. 1998;26(2):358-63.

Wertheim HF, et al. The incidence of septic complications in newborns on extracorporeal membrane oxygenation is not affected by feeding route. *J Pediatr Surg*. 2001;36(10):1485-9.

Specific Conditions - Chylothorax

- Common indication for parenteral nutrition in critical care (especially post cardiac surgery)
- Parenteral lipid is not contraindicated
- Availability and efficacy of enriched MCT enteral formulas should limit need for parenteral nutrition support
- Replace chest tube losses
 - Protein
 - Electrolytes
 - Zn

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Chest tube losses can include high amounts of protein and electrolytes, especially Na, Zn, and fat. Need to monitor patient for EFAD if chest tube losses are prolonged

Specific Conditions Gastrointestinal Surgery & Ostomies

- Attention to fluid and electrolyte losses
- Measure or estimate electrolyte content of losses.
Approximate losses are as follows:
 - Sodium 50 - 150 mM/L (hence chloride)
 - Bicarbonate 15 - 30 mM/L
 - Potassium 5 - 10 mM/L
- Monitor
 - Urinary sodium (hyperaldosteronism / fluid losses)
 - Specific electrolytes such as magnesium

Woolf et al. Dig Dis Sci. 1987;32(1):8-15.

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Zn losses are high from ostomies and proximal enterocutaneous fistulas.

Woolf GM, Miller C, Kurian R, et al. Nutritional absorption in short bowel syndrome. Evaluation of fluid, calorie, and divalent cation requirements. Dig Dis Sci. 1987;32(1):8-15.

IBD - Considerations for Use of PN

- Intolerance to enteral feeds
- Restricted enteral intake/severe perianal disease
- Fistulas, perforation and intra-abdominal abscesses
- Toxic megacolon
- Intestinal obstruction
- Perioperative nutrition rehabilitation
- Short bowel syndrome
- Unable to sustain growth on enteral feeds

IBD - Nutritional Considerations

- Energy needs vary based on patient's disease and nutritional status
- Prediction equations provide only guidance
- Protein needs
 - In general, needs are similar to those for healthy children
 - Patients with diarrhea, malabsorption, fistulas, and malnutrition may require increased protein
- Zn
 - Needs may be increased if there is malnutrition, diarrhea, high output stomas, and SBS
- Fe
 - Fe deficiency is more common in IBD due to decreased intake and increased losses; more common in Crohn's disease compared to ulcerative colitis.
- Fluid
 - Needs should be individualized
- Vitamin D deficiencies can occur
 - Measure levels taking into account the time of year and location of the patient
 - Supplement as required.

Pediatric Nutrition Support Core Curriculum. Editor: M. Corkins. ASPEN, 2010.
Wiskin et al. *Clin Nutr.* 2009;28(6):652-6.
Azcue et al. *Gut.* 1997;41(2):203-8.


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Dietary studies in patients with IBD namely Crohn's disease have shown decreased intakes of Zn, Cu, Fe, Ca, folic acid, vitamin C and vitamin D when compared to controls and the RDA. Essential fatty acid status may also be altered. Fat soluble vitamin deficiencies and vitamin B12 can occur in patients with ileal disease and/or resection. Lower BMD that is commonly seen in patients with Crohn's disease may be related to vitamin D and K deficiency.

Pediatric Nutrition Support Core Curriculum. Editor: Mark Corkins. American Society for Parenteral and Enteral Nutrition (ASPEN), 2010.

Wiskin AE, Wootton SA, Culliford DJ, Afzal NA, Jackson AA, Beattie RM. Impact of disease activity on resting energy expenditure in children with inflammatory bowel disease. *Clin Nutr.* 2009;28(6):652-6.

Treble TM et al. Essential fatty acid status in paediatric Crohn's disease: relationship with disease activity and nutritional status. *Aliment Pharmacol Ther* 2003; 18(4):433-442.

Schoon EJ et al. Low serum and bone vitamin K status in patients with longstanding Crohn's disease: another pathogenetic factor of osteoporosis in Crohn's disease? *Gut* 2001;48(4):473-477.

Azcue M, Rashid M, Griffiths A, Pencharz PB. Energy expenditure and body composition in children with Crohn's disease: effect of enteral nutrition and

treatment with prednisolone. *Gut*. 1997 Aug;41(2):203-8.

Geerling BJ et al. Comprehensive nutritional status in patients with long-standing Crohn's disease currently in remission. *Am J Clin Nutr* 1998; 67(5): 919-926.

Thomas AG, Taylor F, Miller V. Dietary intake and nutritional treatment in childhood Crohn's disease. *J Pediatr Gastroenterol Nutr*, 1993; 17(1):75-81.

Driscoll RH et al. Vitamin D deficiency and disease in patients with Crohn's disease. *Gastroenterol* 1982;83(6):1252-1258.

Kirchner et al. Reversal of growth retardation in Crohn's disease with therapy emphasizing oral nutritional restitution. *Gastroenterol* 1981; 80(1):10-15.

SBS/Intestinal Failure Nutritional Considerations I

- PN should be used to meet energy needs when EN is insufficient or cannot be tolerated
- Start trophic enteral feeds when possible and advance as tolerated
- Cycle PN regimen when possible
- Energy needs to be provided for treatment of malnutrition and to promote normal growth
 - Prediction equations may be helpful but the patient's response is the best guide to adjusting caloric intake
 - Avoid overfeeding and provide adequate calorie intake for normal linear growth

Pediatric Nutrition Support Core Curriculum. Editor: Mark Corkins. American Society for Parenteral and Enteral Nutrition (ASPEN), 2010.

SBS/Intestinal Failure

Nutritional Considerations II

- Increased requirements in patients with gastrointestinal losses
 - Fluid
 - Zn
 - Bicarbonate – needs to be replaced as acetate in PN
 - Na (especially in ileostomies): patients will not grow until adequately supplemented; urine Na measurements can be used to guide Na replacement
 - Fe needs increased due to gastrointestinal blood loss and malabsorption especially if patient has loss of proximal small bowel

Pediatric Nutrition Support Core Curriculum. Editor: Mark Corkins. American Society for Parenteral and Enteral Nutrition (ASPEN), 2010.

SBS/Intestinal Failure Nutritional Considerations III

- Long-term monitoring of growth and micronutrient levels
- For children on long-term PN with, or at risk for, developing PN-associated liver disease
 - Consider limiting IVFE to 1g/kg per day IVFE for long-term PN for prevention/treatment of cholestasis
 - Retrospective evidence emerging for restriction of IVFE to prevent or treat PN associated cholestasis
 - Alternate lipid forms not commercially available in the US (e.g. fish oil, structured lipids and olive oil) are utilized for prevention and treatment of PN associated cholestasis

de Meijer et al. *J Parenter Enteral Nutr.* 2009;33(5):541-7.
Cober et al. *Curr Opin Organ Transplant.* 2010;15(3):330-3.


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Pediatric Nutrition Support Core Curriculum. Editor: Mark Corkins. American Society for Parenteral and Enteral Nutrition (ASPEN), 2010.

de Meijer VE, Gura KM, Le HD, et al. Fish oil-based lipid emulsions prevent and reverse parenteral nutrition-associated liver disease: the Boston experience. *J Parenter Enteral Nutr.* 2009;33(5):541-7.

Cober MP, Teitelbaum DH. Prevention of parenteral nutrition-associated liver disease: lipid minimization. *Curr Opin Organ Transplant.* 2010;15(3):330-3.

Liver Disease – Nutritional Considerations

Restricted nutrients

- Na
 - Administered in small amounts because excess Na intake in the face of hypoalbuminemia contributes to increased ascites
- Cu and Mn
 - If cholestasis is present
- Total fluids
 - Determined by weight and fluid balance
- If encephalopathy present, restrict protein intake and monitor serum ammonia. Use of branch chain containing protein products may be helpful e.g., TrophAmine®
- Adjustment in lipids need to be made in patients with hyperlipidemia

Nutrients requiring supplementation

- Protein: if hypoalbuminemia present
- Fat soluble vitamins D, E and K: if deficient
- Zn: if deficient
- K: if on diuretics

Mager et al. *J Nutr.* 2006;136(1):133-9.

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Mager DR, Wykes LJ, Roberts EA, et al. Branched-Chain Amino Acid Needs in Children with Mild-to-Moderate Chronic Cholestatic Liver Disease. *J Nutr.* 2006;136(1):133-9.

Renal Disease – Considerations for use of PN

- Peritoneal dialysis complicated by ileus or peritonitis
- Critically ill patients on hemodialysis
- Severe malnutrition, intolerance of enteral feeds
- Short bowel syndrome
- Intestinal obstruction (mechanical or pseudo-obstruction)


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Use of PN may be considered in patients with renal disease who have the above conditions.

In patients with acute renal failure, fluid intake is often reduced and the amount of fluid available for PN significantly impacts on caloric intake. Protein intake is often restricted to meet minimum requirements. Electrolyte intake is based on serum levels. Once the patient goes on dialysis, fluid, caloric and protein intake can be increased to better meet needs.

Chronic Renal Disease Recommended Energy And Protein Intakes

Age group	Pre-dialysis		Hemodialysis		Peritoneal dialysis	
	Energy kcal/kg/d	Protein g/kg/d	Energy Kcal/kg/d	Protein g/kg/d	Energy kcal/kg/d	Protein g/kg/d
0-6 m	100-110	2.2	100-110	2.6	100-110	3
6-12 m	95-105	1.5	95-105	1	95-105	2.4
1-3 y	90	1.1	90	1.6	90	2.0
4-10 y	70	0.95	70	1.6	70	1.8-2.0
11-14 y (boys)	55	0.95	55	1.4	55	1.8
11-14 y (girls)	47	0.95	47	1.4	47	1.8
15-18 y (boys)	45	0.85	45	1.3	45	1.5
15-18 y (girls)	40	0.85	40	1.2	40	1.5

National Kidney Foundation. *Am J Kidney Dis.* 2009;53(Suppl 2):S1-S124.



Protein losses are increased in dialysis

Need to meet protein needs but can deal with urea through dialysis, i.e. don't reduce protein requirements

National Kidney Foundation. KDOQI Clinical practice guideline for nutrition in children with CKD: 2008 update. *Am J Kidney Dis.* 2009; 53 (Suppl 2):S1-S124.

Renal Disease – Fluid & Electrolyte Considerations

Restricted nutrients

- Total fluids – determined by dialysis settings
- Na, K, Phos (administered in small amounts because excretion is decreased)
- Deduct dialysate dextrose when calculating glucose infusion rate (GIR)
- Lipids in patients with hyperlipidemia of renal failure
- Limit vitamin C to <100 mg per day in patients with hyperoxaluria

Nutrients requiring supplementation

- Protein
 - Increased losses with dialysis
- Na and alkali
 - Increased losses in 'nonoliguric' renal failure (e.g., congenital hydronephrosis, renal dysplasia)

Oncology - Considerations for Use of PN

- Tumors causing gastrointestinal obstruction
- Severe malnutrition and intolerance of enteral feeds
- Uncontrolled nausea and vomiting
- Severe mucositis and enteritis (especially in stem cell transplant recipients)
- Typhlitis
- Post surgery

Oncology – Nutritional Considerations

- Increased risk for fluid overload post stem cell- and bone marrow-transplant
 - Restrict volume and Na content of PN
- Mucositis
 - Increased protein and Zn requirements
- Increased risk of glucose intolerance secondary to corticosteroids and stress response
- Start parenteral glucose at minimum requirements for age group and thereafter adjust as tolerated
- Do not need supplemental Fe due to frequent transfusion requirements


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Use PN for a short period and then implement NG tube feeds. Type and amount of protein should be modified based on disease.

Pediatric Nutrition Support Core Curriculum. Editor: Mark Corkins. American Society for Parenteral and Enteral Nutrition (ASPEN), 2010.

Inborn Errors of Metabolism – Basic Principles

- PN should be started quickly to prevent catabolism
- General goals of support during metabolic stressors:
 - Promote anabolism
 - Diminish catabolism
- Common metabolic stressors:
 - Trauma
 - Infection
 - Burns
 - Altered mental status
 - Gastrointestinal (pancreatitis, ileus)
- PN should be for short duration and EN started when feasible
- Metabolic parameters should be monitored closely with adjustment of type and amount of protein when necessary

This slide reviews the basic principles of PN support in metabolic disease. The following slides will go over principles of management in select metabolic disorders

Inborn Errors of Metabolism – Phenylketonuria

- Hypercatabolism occurs during stress
 - Parallels the extent of infection/injury
- Goal is prevention of prolonged phenylalanine (PHE) elevation
- Interventions to depress catabolic response
 - PN as bridge to enteral nutrition
 - PHE-free parenteral amino-acid solution with some standard parenteral amino-acids

Acosta. *Nutrition Management of Patients with Inherited Metabolic Disorders* 2010:137.

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Acosta PB. Nutrition Management of Patients with Inherited Metabolic Disorders-
Chapter 5- Phenylketonuria p137.

Inborn Errors of Metabolism

Mitochondrial Disorders

- Avoid exposure to PN if possible
- High-glucose diet is a metabolic challenge for impaired oxidative phosphorylation
 - Glucose oxidation is largely aerobic in the liver
- High lipid/low carbohydrate diet recommended in Complex I deficiency
- Carnitine supplementation is recommended in patients with secondary carnitine deficiency

Munnich et al. *The Online Metabolic & Molecular Bases of Inherited Disease, Chapter 99.*

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Munnich A, Rötig A, Cormier-Daire V, et al. PART 10: DISORDERS OF MITOCHONDRIAL FUNCTION. Chapter 99: Clinical Presentation of Respiratory Chain Deficiency

Management of Acute Crisis in Propionic Acidemia and Methylmalonic Acidemia

- Remove sources of isoleucine (ILE), methionine (MET), threonine (THR), valine (VAL)
- IV glucose and electrolytes: 150 mL/kg; glucose infusion rate: 10 mg/kg/min
 - Treat metabolic acidosis and maintain normal sodium levels
- Add lipids 2-3 g/kg per day to achieve total caloric goal of 120-150 kcal/kg per day (infant)
 - Intravenous L-carnitine 100-300 mg/kg per day to help remove metabolites
- Combination PN (and EN) within 24 - 48 hrs to prevent ILE, MET, THR and VAL deficiency
 - Initiate protein at 0.5 g/kg per day and increase as tolerated not exceeding prescribed amounts
 - Monitor daily plasma amino acids until stable
- Peripheral PN will not provide sufficient energy for anabolism

Kahler et al. *J Pediatr*. 1989;115(2):235-41.
Prietsch et al. *J Inherit Metab Dis*. 2002;25:531-46.
Ney et al. *J Inherit Metab Dis*. 1985;8:132-42.


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Usual crises triggers include infections, fasting, exposure to intact protein loads

(isoleucine, methionine, threonine, valine) Patients need a **LOW-**

protein diet (0.5–1.5 g/kg per day)
or selective reduction in the content
of propionate precursors. Even
though the goal is to minimize the number of attacks
of ketoacidosis one cannot prevent attached and normal development is not possible
in all patients. One needs to minimize fasting because catabolism
increases propionate metabolites.

**Strategies employed during
ketoacidosis include withdrawal of all dietary protein,**

administer parenteral sodium bicarbonate, administration of parenteral glucose to avoid catabolism, and treatment of acute attacks accompanied by hyperammonemia treated with peritoneal dialysis.

TPN has been used to treat critically ill patients and daily monitoring/adjustment of components based upon metabolic parameters is required. In one small series of longer term TPN use, protein intake was started at 0.5 grams/kg/day (propionyl CoA precursors were 0.07 mmol/kg/day), amino acid admixture was adjusted (lysine (diacetate) reduced by 50% to decrease acetate, alanine added to make up) and metabolic status was frequently monitored. This included reduction of glycine concentration reduced by 50% due to oxaluria and adjustment of propionyl precursors based upon metabolic status.

PART 9: ORGANIC ACIDS

Chapter 94: Disorders of Propionate and Methylmalonate Metabolism

Wayne A. Fenton, Roy A. Gravel, David S. Rosenblatt

withdrawing all dietary protein and administering sodium bicarbonate parenterally; glucose is also required to avoid catabolism. Acute attacks, particularly those accompanied by hyperammonemia, have been treated with peritoneal dialysis.²³² Total parenteral nutrition also has been used to treat critically ill patients.²³³

Parenteral nutrition in propionic and methylmalonic acidemia

Stephen G. Kahler, MD, David S. Millington, PhD,

Stephen D. Cederbaum, MD, Jorge Vargas, MD, Laurel D. Bond, RD,

David A. Maltby, MS, Diane S. Gale, BS, and Charles R. Roe, MD (J PEDIATR 1989;115:235-41)

31-month old with propionic acidemia: precursors of propionyl-CoA (isoleucine, valine, methionine, and threonine) were mixed separately from the other amino acids to facilitate dietary changes. In addition, an orally administered L-carnitine supplement, 50 mg (0.31 mmol)/kg every 6 hours, was maintained throughout the hospital stay to enhance the excretion of propionyl-CoA as propionylcarnitine; 3 and daily monitoring of metabolic status was carried out by analysis of urinary organic acids using a gas chromatography-mass spectrometry method to provide information on which dietary adjustments could be based

Kahler SG, Millington DS, Cederbaum SD, Vargas J, Bond LD, Maltby DA, Gale DS, Roe CR. Parenteral nutrition in propionic and methylmalonic acidemia. J Pediatr. 1989

Aug;115(2):235-41.

Prietsch V, Lindner M et al. Emergency Management of Inherited Metabolic Diseases. *J Inherit Metab Dis* 2002;25:531-46.

Ney D, Bay C, Saudubray J-M et al. An Evaluation of Protein Requirements in Methylmalonic Acidaemia. *J Inher Metab Dis* 1985;8:132-42

Inborn Errors of Metabolism

Maple Syrup Urine Disease

- Comatose or Neurologically compromised patients
 - Goal calories
 - Infants: 120 - 140 kcal/kg per day
 - Children: 80 - 100 kcal/kg per day
 - Adults: 40 - 45 kcal/kg per day
 - Add insulin to treat hyperglycemia (need anabolic GIR)
 - Use branch chain amino acid (BCAA)-free solution and monitor plasma amino acids
 - Neonates: give 2.5 - 3 g/kg per day protein
 - Plasma ILE/VAL decrease more rapidly than LEU
 - Add ILE/VAL supplement to PN at lower limits of recommended intake
 - Add LEU when plasma LEU reaches 200µmol/L
 - Normalization of all 3 BCAA usually happens in 48 - 72 hrs
- When able to tolerate enteral feeds start BCAA-free food

Heldt et al. *Mol Genet Metab.* 2005;84:313-16.
Elsas et al. *Modern Health in Nutrition and Disease* 10th Ed. 2005:909-59.
Morton et al. *Pediatrics.* 2002;109:999-1008.
www.childrenshospital.org/newenglandconsortium/NBS/MSUD.html


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In MSUD metabolic issues and toxicity are tied to plasma leucine status. There is little toxicity with increased levels of isoleucine or valine. L1 neutral transporter allows brain uptake of Paa, Trypt, Leu, Meth, Isol, tyr, hist, val, thr and in cases of leucinoses, leucine is taken up by the L1 transporter at the expense of other L-neutral amino acids especially in the brain. The sequelae of BCAA deficiencies include poor growth, anemia, immunodeficiency, dysmyelination/global delays.

Heldt K, Schwahn B, et al. Diagnosis of MSUD by Newborn Screening Allows Early Intervention Without Extraneous Detoxification. *Mol Genet Metab* 2005;84:313-316.

Elsas LJ, Acosta PB. Inherited Metabolic Disease: Amino Acids, Organic Acids and Galactose in Shils ME, Shike M et al. *Modern Health in Nutrition and Disease* 10th Ed. Philadelphia 2005:909-959.

Berry GT, Heidenrich R, et al. Branched Chain Amino Acid Free Parenteral Nutrition in the Treatment of Acute Metabolic Decompensation in Patients with MSUD. *NEJM* 1991;324:175-79.

Morton DH, et al. Diagnosis and Treatment of MSUD: Study of 36 Patients. *Pediatrics* 2002;109:999-1008.

Wendel U, et al. MSUD: Therapeutic Use of Insulin in Catabolic States. *Eur J Pediatr* 1982;139:172-75.

New England Consortium at Children's Hospital Boston. Acute Illness Protocols. www.childrenshospital.org/newenglandconsortium/NBS/MSUD.html

Inborn Errors of Metabolism

Glutaric Aciduria Type 1

- Acute crisis management to prevent encephalopathy
 - Eliminate dietary lysine, tryptophan and total protein for 48 hrs until reduction of organic acidemia
 - Management of infants
 - 10% dextrose and electrolytes 150 mL/kg per day (GIR 10mg/kg/min)
 - Calorie goal : 120-150 kcal/kg per day
 - Lipids: 2 - 3 g/kg per day
 - Oral riboflavin 100 - 200 mg per day with food in 15 - 25 mg portions
 - After stabilized, introduce protein preferably through the enteral route
 - Parenteral protein
 - short term PN: 0.8 g/kg per day
 - long-term PN: use tailored protein solutions

Kolker et al. *J Inherit Metab Disease*. 2004;27:893-902.
Kahler et al. *J Human Genet*. 1988;43:Supp1-A9.

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Kolker S, Greenberg D, et al. Emergency Treatment in Glutaryl Co Dehydrogenase Deficiency. *J Inherit Metab Disease* 2004;27:893-902.

Kahler SG, laofolla AK. Effect of Dietary Alteration and Parenteral Nutrition in Glutaric Aciduria Type 1. *J Human Genet* 1988;43:Supp1- A9.

Inborn Errors of Metabolism

Urea Cycle Disorders

- Principles of nutrition therapy
 - Abundant calories with restricted nitrogen intake and arginine supplementation
 - Activate alternate pathways for nitrogen excretion
 - Monitor closely for catabolic stressors
 - Early consideration of parenteral support, if emesis is present, to diminish catabolic sequelae
 - High parenteral caloric intake
 - goal 80 - 100 cal/kg per day for infants
 - 10% dextrose and intralipid with glucose infusion rate of 6 - 8 mg/kg/min and 1 - 2 g/kg per day fat
 - persistent catabolism use 10 - 35% dextrose along with insulin

Brausilow et al. *NEJM*. 1984;310:1630-4.


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This slide covers the aims of nutritional therapy in patients with urea cycle disorders. The goal should be to restrict nitrogen intake and minimize catabolism as well as activate pathways aside from urea for nitrogen excretion. Arginine, which is downstream in the pathway requires supplementation.

The risk factors for hyperammonemia are birth in neonates and illness, excess protein intake, surgery and catabolic stressors in older patients. Similar to other disorders, the plan is to stop catabolism through the delivery of high caloric intake of glucose and lipids with the addition of insulin if needed to stop the catabolism of glucose.

Brausilow SW, Danney M, Waber LJ, Batshaw M, et al. Treatment of Episodic Hyperammonemia in Children with Inborn Errors of Urea Synthesis. *NEJM* 1984;310:1630-4.



Home Parenteral Nutrition

Home PN - Background

- In the US, children account for 14% of patients on home PN
- All children dependent on long-term PN should be discharged on home PN, if and when
 - they are stable
 - includes stability of the underlying disease, fluid and electrolyte requirements, and reliable central venous access.
 - familial and social criteria are fulfilled
- Should be followed by a team with experience taking care of Home PN patients
- Resource for patients & parents
 - The Oley Foundation <http://www.oley.org/>


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Founded in 1983 by Lyn Howard, MD and her patient, Clarence "Oley" Oldenburg, the Oley Foundation is a national, independent, non-profit 501(c)(3) organization that provides information and psycho-social support to consumers of home parenteral and enteral nutrition, helping them live fuller, richer lives. The Foundation also serves as a resource for consumer's families, homePEN clinicians and industry representatives, and other interested parties.
<http://www.oley.org/>

Koletzko B, Goulet O, Hunt J, Krohn K, Shamir R; Guidelines on Paediatric Parenteral Nutrition of the European Society of Paediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN) and the European Society for Clinical Nutrition and Metabolism (ESPEN), Supported by the European Society of Paediatric Research (ESPR). J Pediatr Gastroenterol Nutr. 2005 Nov;41 Suppl 2:S1-87.

Home PN - Preparation for Discharge I

- Parents/caregivers have to be informed, motivated and able to cope with all medical, emotional and technical problems related to Home PN (HPN)
- Family suitability for HPN must be carefully assessed by a health care team member; may include
 - visiting the home and examining practical details such as space for dedicated refrigerator, electricity, and connected telephone
- The assistance of a social worker is needed before discharge especially if the home environment is inadequate

Koletzko et al. *J Pediatr Gastroenterol Nutr.* 2005;41(Suppl 2):S1-87.

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Koletzko B, Goulet O, Hunt J, Krohn K, Shamir R; Guidelines on Paediatric Parenteral Nutrition of the European Society of Paediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN) and the European Society for Clinical Nutrition and Metabolism (ESPEN), Supported by the European Society of Paediatric Research (ESPR). *J Pediatr Gastroenterol Nutr.* 2005 Nov;41 Suppl 2:S1-87.

Home PN - Preparation for Discharge I (cont'd)

Parents Knowledge	Handling	Catheter & Line	Pump	Child
Current Care	Hand washing technique Preparation of sterile field Drawing up solutions into syringe	Flushing of heparinization Initiation & termination of infusion	Operation Maintenance	Catheter exit site Temperature
Emergency What to do? Who to contact?	Materials missing	Blockage of the line Breakage/split catheter Air in the line	Alarms	Exit site Infection Fever Digestive problem

Koletzko et al. *J Pediatr Gastroenterol Nutr.* 2005;41(Suppl 2):S1-87.



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Koletzko B, Goulet O, Hunt J, Krohn K, Shamir R; Guidelines on Paediatric Parenteral Nutrition of the European Society of Paediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN) and the European Society for Clinical Nutrition and Metabolism (ESPEN), Supported by the European Society of Paediatric Research (ESPR). *J Pediatr Gastroenterol Nutr.* 2005 Nov;41 Suppl 2:S1-87.

Home PN - Preparation for Discharge II

- Parents/caregivers need to be taught to pay meticulous attention to central venous catheter care to prevent central line associated bloodstream infections
 - Hand washing
 - Sterile field preparation
 - Drawing up solutions into syringe
 - Flushing the line
 - Initiation and termination of PN infusion


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Parents/caregivers will be asked to add the multivitamins to the PN solution just prior to it being administered. Other additive that may need to be added include iron and ranitidine.

Home PN - Preparation for Discharge III

- Parents/caregivers also need to be taught to recognize common central venous catheter problems
 - Occlusion
 - Damage
 - Accidental removal
 - Infection e.g., fever
- They should be aware of whom to contact and how to provide first aid
- They should also be able to recognize and manage the symptoms of hypoglycemia and dehydration

Home PN - Central Venous Access

- Tunneled central catheters must be used
- Implanted ports are an acceptable alternative
- Long-term peripherally inserted central catheters (PICC)-lines are not routinely recommended for HPN patients but may be used in special circumstances including short-term HPN

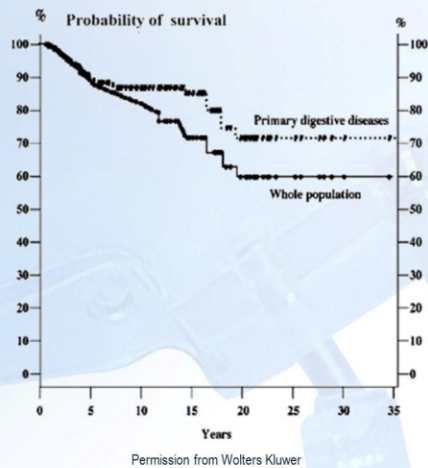
Staun et al. *Clin Nutr.* 2009;28(4):467-79.

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Staun M, Pironi L, Bozzetti F, et al. ESPEN Guidelines on Parenteral Nutrition: Home Parenteral Nutrition (HPN) in adult patients. *Clin Nutr.* 2009 Aug;28(4):467-79.

Home PN - Outcomes

- Retrospective cohort of 302 children
 - 76% with primary digestive disorders
 - 24% with other disorders
- Median duration of HPN was 1.3 years
- The likelihood of death depended on underlying diagnosis
 - 9% of children with primary digestive disorders died
 - more from liver disease or sepsis than their primary disease
 - 38% of children with primary nondigestive diseases died
 - mainly from their primary disease



Colomb et al. *J Pediatr Gastroenterol Nutr.* 2007;44:347-53.

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The survival probabilities at 2, 5, 10, and 15 years were 97%, 89%, 81%, and 72%, respectively. Also the cause of death varied with diagnosis.

In children that died from primary digestive disorders, 24% died from their primary disease and 48% died from liver disease or sepsis.

In children that died from primary non-digestive diseases, 94% died from their primary disease and 6% died from liver disease or sepsis.

Colomb V, Dabbas-Tyan M, Taupin P, et al. Long-term outcome of children receiving home parenteral nutrition: a 20-year single-center experience in 302 patients. *J Pediatr Gastroenterol Nutr.* 2007 ;44:347-53

Home PN – Five Year Prospective Study

- The primary cause of death on HPN
 - Underlying disease-related in patients with HPN duration ≤ 2 years
 - HPN-related in those on HPN duration >2 years
- For children, survival rate was
 - 90.9% for those not transplant eligible (n=44)
 - 90.7% for those eligible for transplant but not transplanted (n=43)
 - 75.0% for those actually transplanted (n=12)
 - Follow up period for those transplanted not clear

Pironi et al. *Gut*. 2011;60(1):17-25.

 DIGESTIVE HEALTH UNIT CDINE NASPOHAN
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Pironi L, Joly F, Forbes A, et al. Long-term follow-up of patients on home parenteral nutrition in Europe: implications for intestinal transplantation. *Gut*. 2011;60(1):17-25.

Home PN - Economics in Patients with SBS

- Billable charges during the first 5 years after onset of SBS exceeded \$1.6 million
 - Costs were highest in the first year
 - Inpatient hospitalization accounted for 80% of all expenses
 - Home care costs were low in the first year and increased every year thereafter as long as the child required home care for care of SBS
 - Mean parental nutrition costs varied between \$80,000 and \$150,000 per year
- Costs vary depending on number of hospitalizations
- Reducing septic episodes reduced costs

Spencer et al. *Am J Clin Nutr.* 2008;88(6):1552-9.

Digestive Health Center
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Spencer AU, Kovacevich D, McKinney-Barnett M, et al. Pediatric short-bowel syndrome: the cost of comprehensive care. *Am J Clin Nutr.* 2008 Dec;88(6):1552-9.

Home PN – Economics

- HPN is approximately 50-75% more “economical” than inpatient hospital care
- The longer a patient survives on HPN, the more cost-effective home treatment becomes.
- HPN in children in the UK led to cost savings of about 2 million Euros in a single year by decreasing the incidence of septic episodes (1/142 days in hospital to 1/567 days at home)

Colomb. *Curr Opin Clin Nutr Metab Care*. 2000;3:237-9.
Puntis. *Nutrition*. 1998;14:809-12.
Richards et al. *Br J Surg*. 1996;83:1226-9.
Melville et al. *J Hosp Infect*. 1997;35:197-205.


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Colomb V. Economic aspects of paediatric home parenteral nutrition. *Curr Opin Clin Nutr Metab Care*. 2000;3(3):237-9.

Puntis JW. The economics of home parenteral nutrition. *Nutrition*. 1998;14(10):809-12.

Richards DM, Irving MH. Cost-utility analysis of home parenteral nutrition. *Br J Surg*. 1996;83(9):1226-9.

Melville CA, Bisset WM, Long S, et al. Counting the cost: hospital versus home central venous catheter survival. *J Hosp Infect*. 1997;35(3):197-205.

Home PN - Long-Term Adequacy

- Nutritional measurements are key to determining adequacy of the PN, patients should demonstrate adequate weight gain and linear growth
- Address developmental delays with appropriate interventions

Home PN – Weaning Parenteral Nutrition

- Every child on HPN with short bowel syndrome should also receive some form of EN support whenever possible
- Continuous tube feeding following the postoperative period significantly increases net macronutrient absorption compared with oral feeding
- The child should also be fed by mouth, as tolerated
- The EN support can be breast milk, protein hydrolysate formula or elemental formula
- If stool/stoma output < 40-50 ml/kg per day, EN can be advanced
- As EN is increased, parenteral support is weaned and ultimately discontinued

Joly et al. *Gastroenterol.* 2009;136(3):824-31.

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EN support should be tailored based on the patient.

Joly F, Dray X, Corcos O, Barbot L, Kapel N, Messing B. Tube feeding improves intestinal absorption in short bowel syndrome patients. *Gastroenterol.* 2009;136(3):824-31.

Pediatric Nutrition Support Core Curriculum. Editor: Mark Corkins. American Society for Parenteral and Enteral Nutrition (ASPEN), 2010.

Home PN - Monitoring I

- Weight
 - Height
 - Head circumference (patients < 3 years age)
 - Clinical examination
 - Diet assessment by a registered dietician
 - Frequency depends on
 - Clinical stability of patient
 - Duration on PN
 - Labs are initially weekly, spread out with demonstrated stability
 - Developmental assessment in younger children
 - Psychosocial functioning
 - Renal function (GFR)
- Every 1-3 months with more frequent monitoring initially

Koletzko et al. *J Pediatr Gastroenterol Nutr.* 2005;41(Suppl 2):S1-87.

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Koletzko B, Goulet O, Hunt J, Krohn K, Shamir R; Guidelines on Paediatric Parenteral Nutrition of the European Society of Paediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN) and the European Society for Clinical Nutrition and Metabolism (ESPEN), Supported by the European Society of Paediatric Research (ESPR). *J Pediatr Gastroenterol Nutr.* 2005 Nov;41 Suppl 2:S1-87.

Home PN - Monitoring II

Parameter	Initial	Follow-up
Electrolytes	Weekly to bi-weekly	Monthly
BUN/creatinine	Weekly to bi-weekly	Monthly
Ca, PO ₄ , Mg	Weekly to bi-weekly	Monthly
Glucose	Weekly to bi-weekly	Monthly
Triglycerides	Weekly to bi-weekly	Monthly
Liver function tests	At 2 weeks	1-3 months
CBC, platelets	Weekly to bi-weekly	1-3 months
Iron indices	As indicated	3-6 months

Baker et al. *Pediatric Nutrition Support*. 2007.
 Koletzko et al. *J Pediatr Gastroenterol Nutr*. 2005;41(Suppl 2):S1-87.



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The above are suggested, however there may be variation in certain populations e.g. adult and adolescents.

Other tests which may be considered include:

- Venous pH: some centres may check
- Prealbumin: can be monitored
- PT/PTT: could be done

Consider measuring urine Na levels to assess adequacy of Na intake especially in patients with SBS and growth problems.

During PN initiation it is customary to follow serum electrolytes closely.

Pediatric Nutrition Support Core Curriculum. Editor: Mark Corkins. American Society for Parenteral and Enteral Nutrition (ASPEN), 2010.

Baker SS, Baker RD, Davis Am. *Pediatric Nutrition Support*. 2007. Jones and Bartlett, Sudbury, MA

Koletzko B, Goulet O, Hunt J, et al. Guidelines on Paediatric Parenteral Nutrition of the European Society of Paediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN) and the European Society for Clinical Nutrition and Metabolism (ESPEN), Supported by the European Society of Paediatric Research (ESPR). *J Pediatr Gastroenterol Nutr*. 2005 Nov;41 Suppl 2:S1-87.

Home PN - Monitoring III

Parameter	Initial	Follow-up
Fat-soluble vitamins (A, D, E, K)	As indicated	6-12 months
Carnitine	As indicated	6-12 months
Riboflavin, folate/vitamin B ₁₂	As indicated	6-12 months
Thyroid function parameters	As indicated	1-3 months
Liver & Biliary tract ultrasound	As indicated	6-12 months
Bone densitometry	As indicated	12 months
Trace elements (Cu, Mn, Se, Zn)	As indicated	6-12 months

Baker et al. *Pediatric Nutrition Support*. 2007.
 Koletzko et al. *J Pediatr Gastroenterol Nutr*. 2005;41(Suppl 2):S1-87.
 Sokol et al. *N Engl J Med*. 1984;310(19):1209-12.
 Horwitt et al. *Ann NY Acad Sci*. 1972;203:223.



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Trace elements

- Mn: follow whole blood levels although ideal may be a MRI of brain
- Zn: serum zinc is not an accurate marker of zinc deficiency
- Cu: serum copper and ceruloplasmin
- Se: serum or whole blood selenium
- Fe: hemoglobin, serum ferritin or iron, transferrin saturation

Fat-soluble vitamins

- Vitamin A: serum vitamin A

- **Vitamin E: serum vitamin E : total lipid ratio**, levels are more accurate if compared with total lipid

levels. In children with liver disease Horwitt et al found a ratio of mg vitamin E / g total serum lipids greater than 0.8 indicated adequate levels.

- Vitamin K adequacy: prothrombin time, PIVKAI
- Vitamin D: 25-hydroxy vitamin D; both 1,25-Dihydroxy- and 25-Hydroxy- vitamin D in renal disease

Some experts believe that carnitine status should only be measured in the neonate.

Pediatric Nutrition Support Core Curriculum. Editor: Mark Corkins. American Society for Parenteral and Enteral Nutrition (ASPEN), 2010.

Baker SS, Baker RD, Davis Am. Pediatric Nutrition Support. 2007. Jones and Bartlett, Sudbury, MA

Koletzko B, Goulet O, Hunt J, et al. Guidelines on Paediatric Parenteral Nutrition of the European Society of Paediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN) and the European Society for Clinical Nutrition and Metabolism (ESPEN), Supported by the European Society of Paediatric Research (ESPR). J Pediatr Gastroenterol Nutr. 2005 Nov;41 Suppl 2:S1-87.

Sokol RJ, Heubi JE, Iannaccone ST, et al. Vitamin E deficiency with normal serum vitamin E concentrations in children with chronic cholestasis. N Engl J Med 1984; 310(19):1209-1212.

Horwitt MK, Harvey CC, Dahm CH and Jr. Searcy MT. Relationship between tocopherol and serum lipid levels for determination of nutritional adequacy. Ann NY Acad Sci 1972; 203:223.

Home PN - Long-Term Complications

- Infectious: central vein catheter associated infection
- Mechanical
- Chronic liver disease, cirrhosis, liver failure
 - PNALD is leading indication for combined liver/ intestinal transplant
- Bone disease
- Trace element deficiencies and excesses
- Loss of PN access sites
- Renal disease

Moukarzel et al. *J Pediatr*. 1991;119(6):864-8.
Buchman et al. *J Parenter Enteral Nutr*. 1993;17(5):438-44.
Lauverjat et al. *Clin Nutr*. 2006 Feb;25(1):75-81.


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Patients at risk for renal disease should have GFR monitored.

Patients on chronic PN, especially HPN, are at risk for nephropathy. This may be related to subclinical renal damage from components of PN, cumulative drug toxicity from nephrotoxic antibiotics used to treat central line infections.

Moukarzel AA, Ament ME, Buchman A, Dahlstrom KA, Vargas J. Renal function of children receiving long-term parenteral nutrition. *J Pediatr*. 1991 Dec;119(6):864-8.
Buchman AL, Moukarzel A, Ament ME, Gornbein J, Goodson B, Carlson C, Hawkins RA. Serious renal impairment is associated with long-term parenteral nutrition. *J Parenter Enteral Nutr*. 1993 Sep-Oct;17(5):438-44.

Lauverjat M, Hadj Aissa A, Vanhems P, Boulétreau P, Fouque D, Chambrier C. Chronic dehydration may impair renal function in patients with chronic intestinal failure on long-term parenteral nutrition. *Clin Nutr*. 2006 Feb;25(1):75-81. Epub 2005 Dec 13.

Home PN - Infectious Complications I

- Bacterial and fungal causes
- Infection vs. colonization (22% of all hubs)
- Causes
 - Colonization
 - inside catheter or hub
 - outside of the subcutaneous catheter
 - in fibrin sleeve
 - in subcutaneous tract
 - Contamination
 - from blood seeding
 - skin contamination along the catheter tract
 - non-sterile entries into the line
 - contaminated PN solutions
- Risk of sepsis is reported at 1.5 episodes a year in home PN patients

Schmidt-Sommerfeld et al. *J Parenter Enteral Nutr.* 1990;14:148-51.

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Need to differentiate between a central line infection and colonization. About 22% of all hubs are colonized with bacteria.

Schmidt-Sommerfeld E, Snyder G, Rossi TM, et al. Catheter-related complications in 35 children and adolescents with gastrointestinal disease on home parenteral nutrition. *J Parenter Enteral Nutr.* 1990;14:148-51.

Home PN - Infectious Complications II

- Prevention
 - Hand hygiene
 - Sterile technique during placement
 - Use line only for PN and not for blood draws
 - Dressing changes per protocol
 - Tubing changes for dextrose AA solutions and IV lipid
 - Avoid multi-lumen catheters
 - Avoid catheters in groin/diaper area
 - Inadequate pediatric data on the benefits of antibiotic and ethanol locks and antibiotic-impregnated catheters

Pediatric Nutrition Support Core Curriculum. Editor: M. Corkins. ASPEN, 2010.

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The recommendations are that the tubing for lipids be changed every 12-24 hours and the dextrose tubing be changed every 72 hours unless it is a 3-in-1 solution.

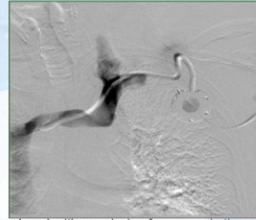
Pediatric Nutrition Support Core Curriculum. Editor: Mark Corkins. American Society for Parenteral and Enteral Nutrition (ASPEN), 2010.

Home PN - Mechanical Complications

- Catheter-related
 - Pneumothorax
 - Hematoma
 - Hemothorax
 - Malposition
 - Venous and intracardiac thrombosis
 - Air embolism
 - Catheter blockage / migration
 - Transient arrhythmias, perforation of the heart
- Infusate-related
 - Extravasation into local tissues, pericardium, peritoneum, thorax, mediastinum, liver and scalp

Home PN - Catheter Occlusions

- Most common non-infectious complication of central venous catheters
- Thrombotic vs. non-thrombotic
 - Resistance to flushing and aspiration
 - Non-thrombotic: precipitate due to medication, Ca/Phos, lipid, and minerals
 - Treatment: thrombolytic or specific agents i.e., alcohol for lipid precipitates
- Fibrin sleeve at distal catheter tip
 - Can flush easily but difficulty in aspiration
 - Treatment: thrombolytic therapy



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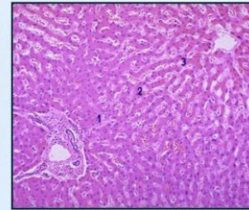
Non-thrombotic occlusions are caused by calcium phosphate precipitates, medication precipitates, lipid residue, or mineral precipitates. Thrombotic catheter occlusions are usually treated with thrombolytics. The use of 0.1N hydrochloric acid is most effective for clearing catheter occlusions due to precipitation of calcium-phosphate. For catheter occlusions due to precipitates associated with medications in the high pH range such as tobramycin and phenytoin, sodium bicarbonate 1mEq/mL has been anecdotally reported to be effective. 70% ethanol is the most effective solvent to dissolve lipid residue. NaOH may be used to dissolve mineral precipitates.

Picture insert is of an occluded line.

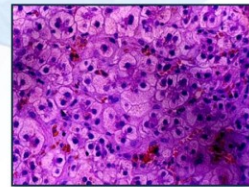
Home PN - Liver Disease I

- Well described complication of PN
- Develops in 40 – 60% of neonates; ~15% in children
- Variable degree of injury
 - Mild: mild cholestasis, gall stones, hepatic steatosis
 - Severe: can result in cirrhosis and liver failure
- Pathogenesis:
 - Multifactorial
 - Prolonged duration of PN
 - Lack of enteral feeding
 - Prematurity and low birth weight
 - Early and recurrent sepsis
 - Length of bowel remnant
 - Reduced enterohepatic circulation
 - Deficiency or toxicity of components of PN solutions (excess glucose, excess energy, AA content, Mn, Cu, and fat emulsions)

Normal Liver



Cholestasis



Ovchinsky N. *J Parent & Enteral Nutr.* 2010;34(5):472-73.


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Treatment considered decreasing IV fat emulsion, start EN if only trophic, wean PN or adjust PN components.

Ovchinsky N. conjugated bile acid as potential early markers of parenteral nutrition associated liver disease. *JPEN* 2010;34(5):472-473

Home PN - Liver Disease II

Treatment

- Provide maximal tolerated EN
- Provide cyclical PN as soon as possible
- Consider and treat small bowel bacterial overgrowth
- Consider reducing intravenous lipids, if conjugated bilirubin rises with no other explanation
 - Consider fish-oil based lipids, if the above strategy fails
- If transaminases, alkaline phosphatase or conjugated bilirubin continue to increase, consider commencing ursodeoxycholic acid

Gura et al. *Pediatrics*. 2008;121(3):e678-86.

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Ursodeoxycholic acid often used but limited data on its effectiveness if given enterally.

Koletzko B, Goulet O, Hunt J, Krohn K, Shamir R; Guidelines on Paediatric Parenteral Nutrition of the European Society of Paediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN) and the European Society for Clinical Nutrition and Metabolism (ESPEN), Supported by the European Society of Paediatric Research (ESPR). *J Pediatr Gastroenterol Nutr*. 2005 Nov;41 Suppl 2:S1-87.

Gura KM, Lee S, Valim C, et al. Safety and efficacy of a fish-oil-based fat emulsion in the treatment of parenteral nutrition-associated liver disease. *Pediatrics*. 2008 Mar;121(3):e678-86.

Home PN - Liver Disease III

- Consider early referral to an experienced liver-intestinal transplant program for children with a poor prognosis or if on PN > 3 months and one or more of the following:
 - Serum conjugated bilirubin > 3 mg/dL
 - Platelet count < 100,000/uL
 - PT > 15 sec
 - PTT > 40 sec
 - Hepatic fibrosis
 - Concerns about central venous access

Mittal et al. *Pediatr Clin N Am*. 2003;1419–33.
Selvaggi et al. *Transplantation*. 2005;79:1639–43.


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Early referral to a transplant or intestinal rehabilitation program may allow for avoidance of a liver transplant.

Mittal NK, Tzakis AG, Kato T, et al. Current status of small bowel transplantation in children: update 2003. *Pediatr Clin N Am*. 50 (2003):1419– 1433.

Selvaggi G, Gyamfi A, Kato T, Gelman B, Aggarwal S, Begliomini B, Bennett J, Nishida S, Tzakis AG. Analysis of Vascular Access in Intestinal Transplant Recipients Using the Miami Classification from the VIIIth International Small Bowel Transplant Symposium. *Transplantation* 2005;79: 1639–1643.

Koletzko B, Goulet O, Hunt J, Krohn K, Shamir R; Guidelines on Paediatric Parenteral Nutrition of the European Society of Paediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN) and the European Society for Clinical Nutrition and Metabolism (ESPEN), Supported by the European Society of Paediatric Research (ESPR). *J Pediatr Gastroenterol Nutr*. 2005 Nov;41 Suppl 2:S1-87.

Home PN - Special Considerations in SBS/Intestinal Failure

- For children on long-term PN with, or at risk for, developing PNALD
 - Consider limiting IVFE to 1g/kg per day IVFE for long-term PN for prevention/treatment of cholestasis
 - Evidence emerging for restriction of IVFE to prevent or treat PN associated cholestasis
 - Alternate lipid forms not commercially available in the US (e.g. fish oil, structured lipids and olive oil) are utilized for prevention and treatment of PN associated cholestasis

de Meijer et al. *J Parenter Enteral Nutr.* 2009;33(5):541-7.
Cober et al. *Curr Opin Organ Transplant.* 2010;15(3):330-3.

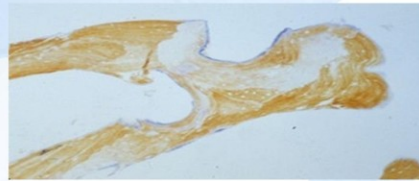

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de Meijer VE, Gura KM, Le HD, et al. Fish oil-based lipid emulsions prevent and reverse parenteral nutrition-associated liver disease: the Boston experience. *J Parenter Enteral Nutr.* 2009;33(5):541-7.

Cober MP, Teitelbaum DH. Prevention of parenteral nutrition-associated liver disease: lipid minimization. *Curr Opin Organ Transplant.* 2010;15(3):330-3.

Home PN – Aluminum

- Contaminant of PN ingredients
- Accumulates in bone
- Developmental delay in preterm infants
- High levels of Al present in Ca, Phos and albumin solutions
- 2004 FDA mandate to report amounts
- Can be measured in blood



Gura. *Nutrition* 2010;26(6):585-94.
Poole et al. *J Parenter Enteral Nutr.* 2008;32(3):242-46.

 CDHNE NASPHAN
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This is a slide of a bone and the blue staining represents Al deposition.

Gura KM. Aluminum contamination in products used in parenteral nutrition: has anything changed? *Nutrition* 2010 Jun; 26(6): 585-94.

Poole R, Hintz S, Mackenzie NI, et al. Aluminum Exposure From Pediatric Parenteral Nutrition: Meeting the New FDA Regulation. *J Parenter Enteral Nutr.* 2008;32(3):242-46.

Home PN - Bone Disease I

- Extensively described in adults
 - Decreased bone mineral density
 - Osteoporosis
 - Bone pain and fractures
- Has been described in children weaned from PN
- Etiology
 - Underlying disease-related and PN-related mechanisms
 - altered vitamin D intake
 - Phos, nitrogen and energy imbalance
 - aluminum contamination (FDA now requires reporting of aluminum content in all PN additives)

Seidner DL. *J Parenter Enter Nutr.* 2002;26(5):S37-S42.


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The etiology of metabolic bone disease seen in patients on chronic PN is unclear and probably multifactorial. It may be related to altered vitamin D metabolism, Cu and vitamin K deficiency, and aluminum toxicity. Clinically patients present with bone pain (back pain) and pathologic fractures. Aluminum toxicity is known to occur in the

brain, bone and liver causing bone pain, metabolic bone disease, osteoporosis, patchy osteomalacia, reduced bone apposition and fracturing osteomalacia, encephalopathy and impaired neurological development. However Advenier et al showed in 10 children (av age 8 year) on PN for an average of 6.5 years, elevated aluminum levels with no associated symptoms.

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Home PN - Bone Disease II

- In children on Home PN
 - Regular measurements
 - plasma calcium and phosphorus
 - parathyroid hormone and vitamin D
 - urinary calcium
 - serum alkaline phosphatase
 - Aluminum contamination of PN solutions should be kept to a minimum
 - Regular assessment of bone mineralization should be performed
- Treatment
 - Adequate calcium, phosphorus, magnesium and vitamin D
 - Weight bearing exercise
 - Change medications (such as diuretics), if possible
 - Consider referral to bone specialist

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