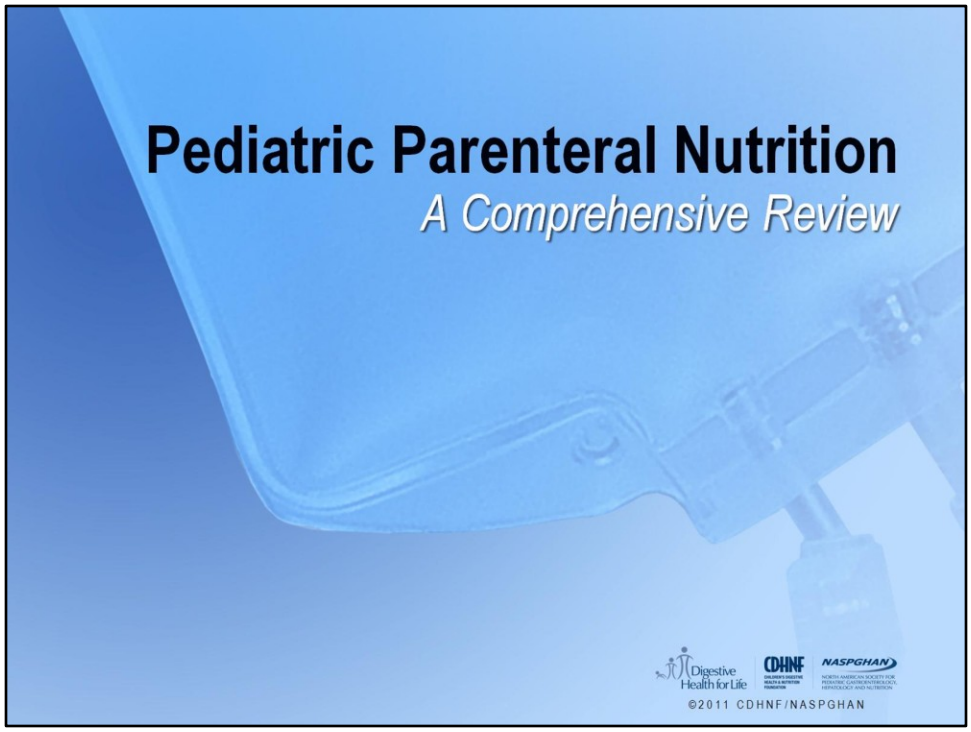
Pediatric Parenteral Nutrition

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

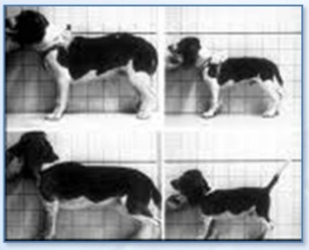
AA	Amino acid
AAP	American Academy of Pediatrics
ASPEN	American Society for Parenteral & Enteral Nutrition
Cr	Chromium
CRP	C-reactive protein
Cu	Copper
DHA	Docosahexaenoic acid
DRI	Dietary Reference Intakes
EN	Enteral nutrition
EFA	Essential fatty acid
EFAD	Essential fatty acid deficiency
GIR	Glucose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

Table of Contents

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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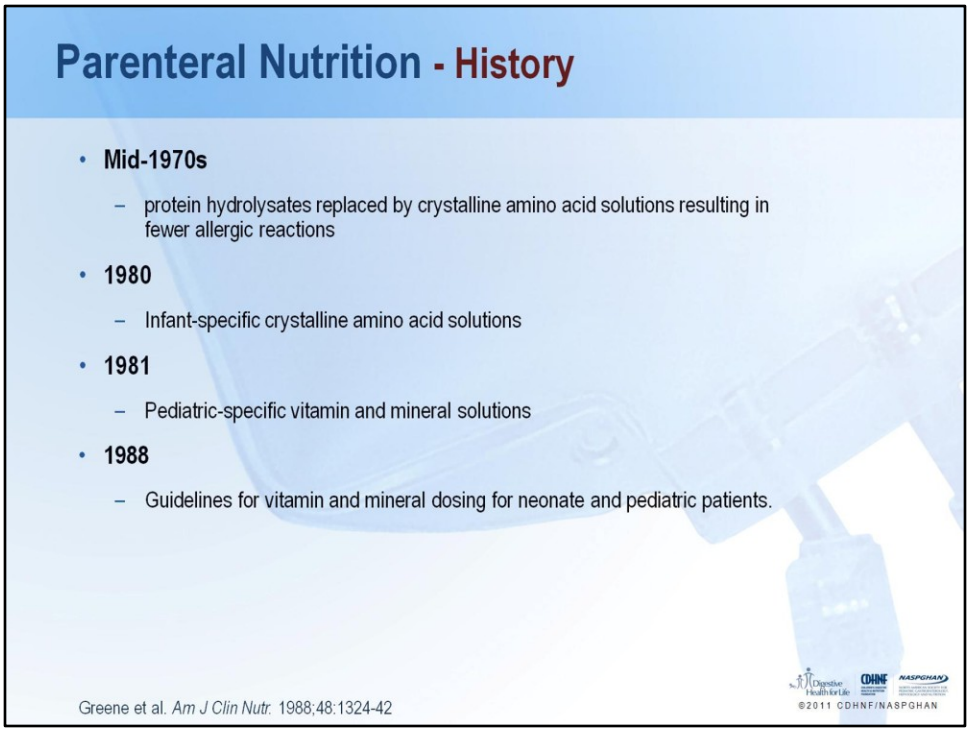
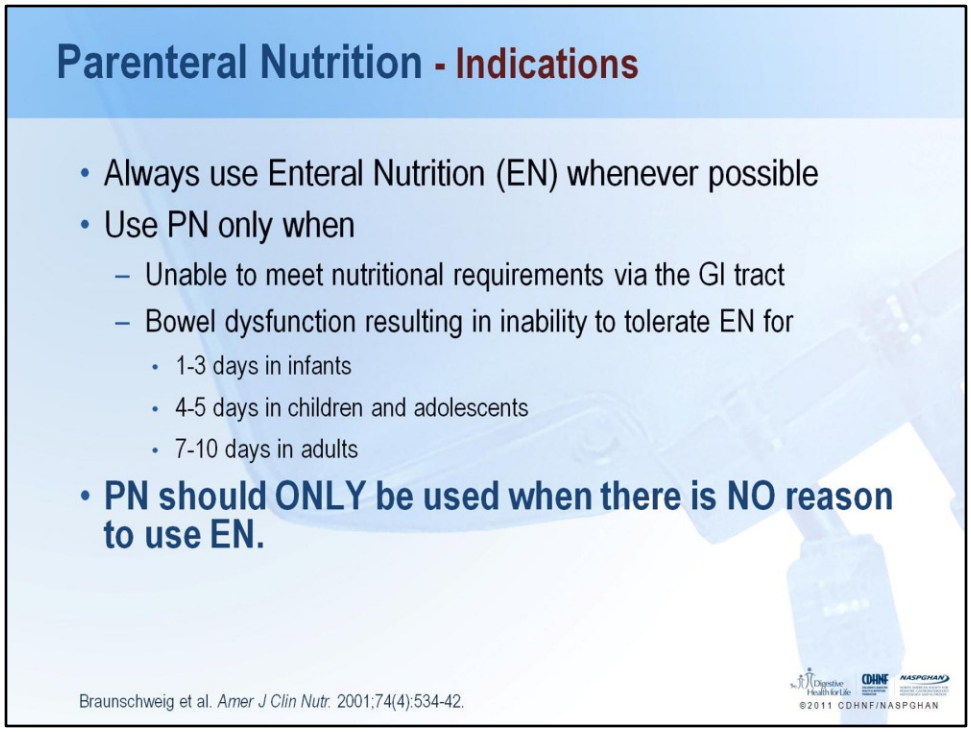
*Dudrick et al. *Surgery* 1968;64:134-142.
Sukarochana et al. Surg Gyn Obstetr. 1965;121:79.
www.nutritioncare.org

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.



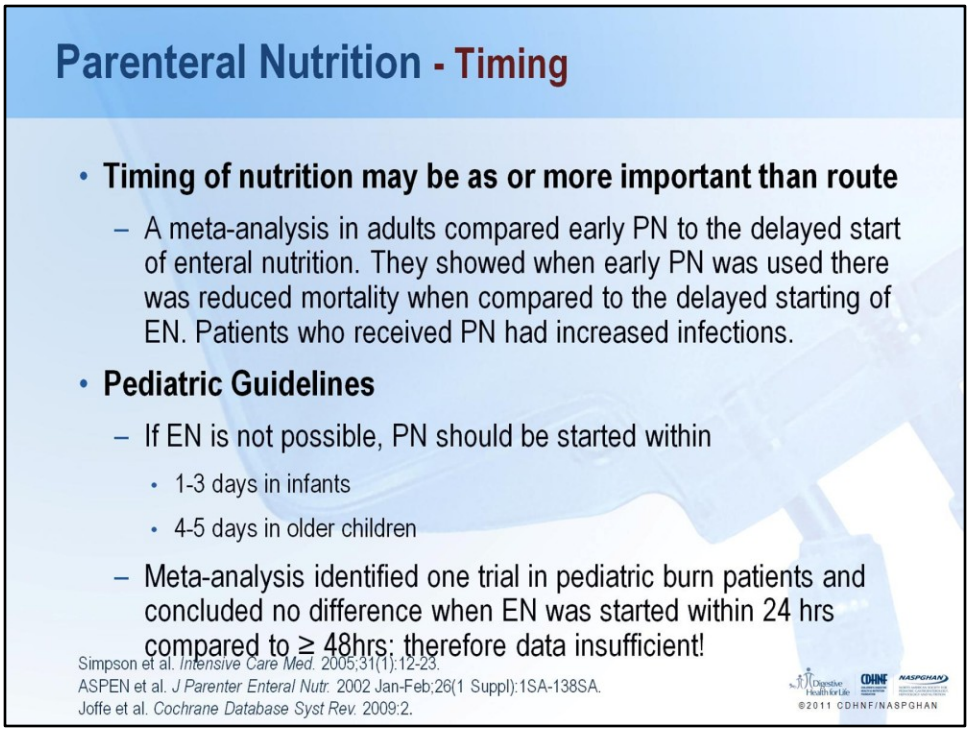
Greene HL, Hambidge KM, Schanler R, et al. Guidelines for the use of vitamins, trace elements, calcium, magnesium, and phosphorus in infants and children receiving total parenteral nutrition: report of the Subcommittee on Pediatric Parenteral Nutrient Requirements from the Committee on Clinical Practice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



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.



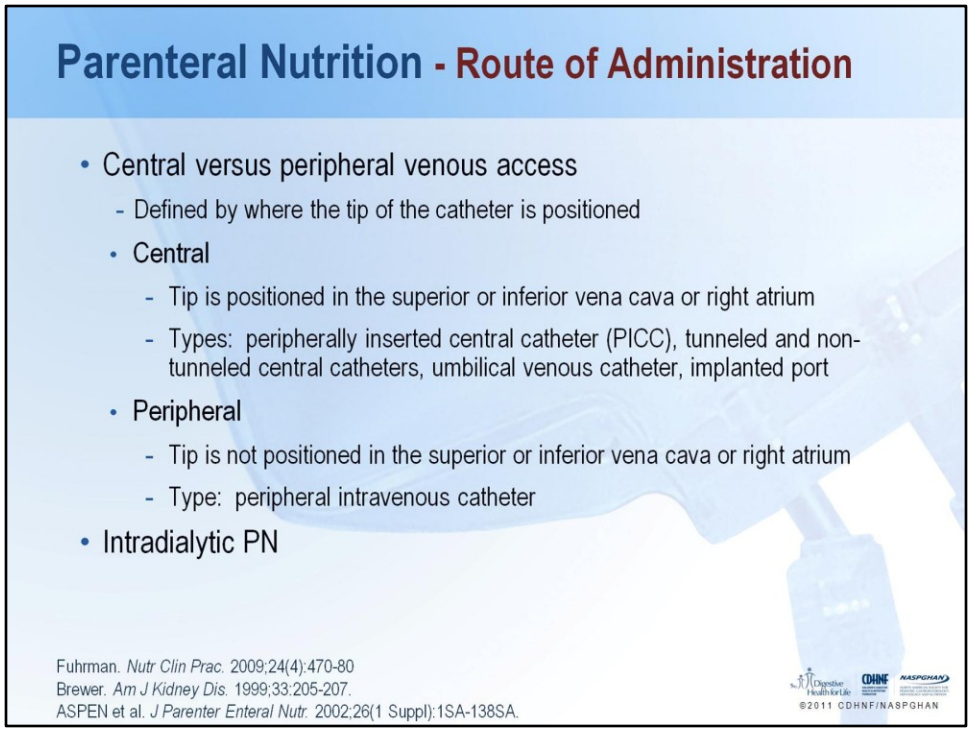
Simpson F., Doig GS. Parenteral vs. enteral nutrition in the critically ill patient: a meta-analysis of trials using the intention to treat principle. Intensive Care Med. 2005;31(1):12-23.

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.

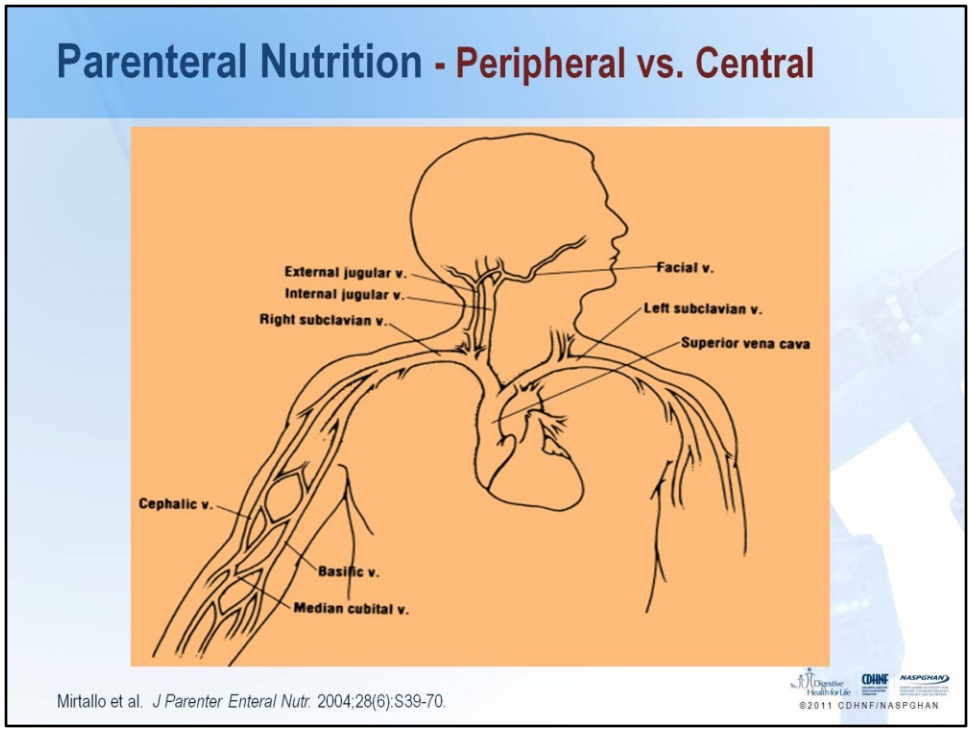
Parenteral Nutrition – Indications

- 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)



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. Intrdialytic parenteral nutrition and intraperitoneal nutrition. Nutr Clin Pract. 2009; 24 (4):470-480
Brewer ED. Pediatric experience with intredialytic 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.



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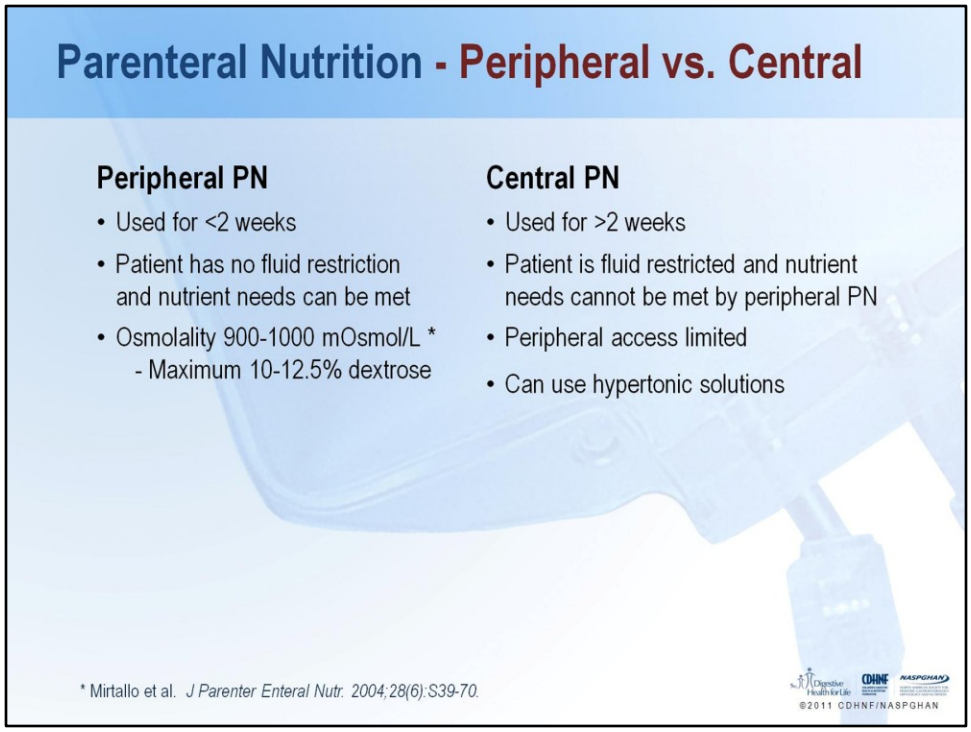
ASPEN Board of Directors and the Clinical Guidelines Task Force. Guidelines for the use of parenteral and enteral nutrition in adult and pediatric patients. J Parenter Enteral Nutr. 2002 Jan-Feb;26(1 Suppl):1SA-138SA. No abstract available. Erratum in: J Parenter Enteral Nutr. 2002 Mar-Apr;26(2):144.



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 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

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

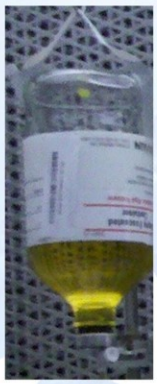
0.22 micron filters	1.2 micron filters
Remove most pathogenic bacteria	Removes only *Candida* and large lipid droplets
Used only with 2-in-1 solutions; Lipid solutions are sheared by the smaller filters	Can be used with 3-in-1 solutions
Never remove a filter!	

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.

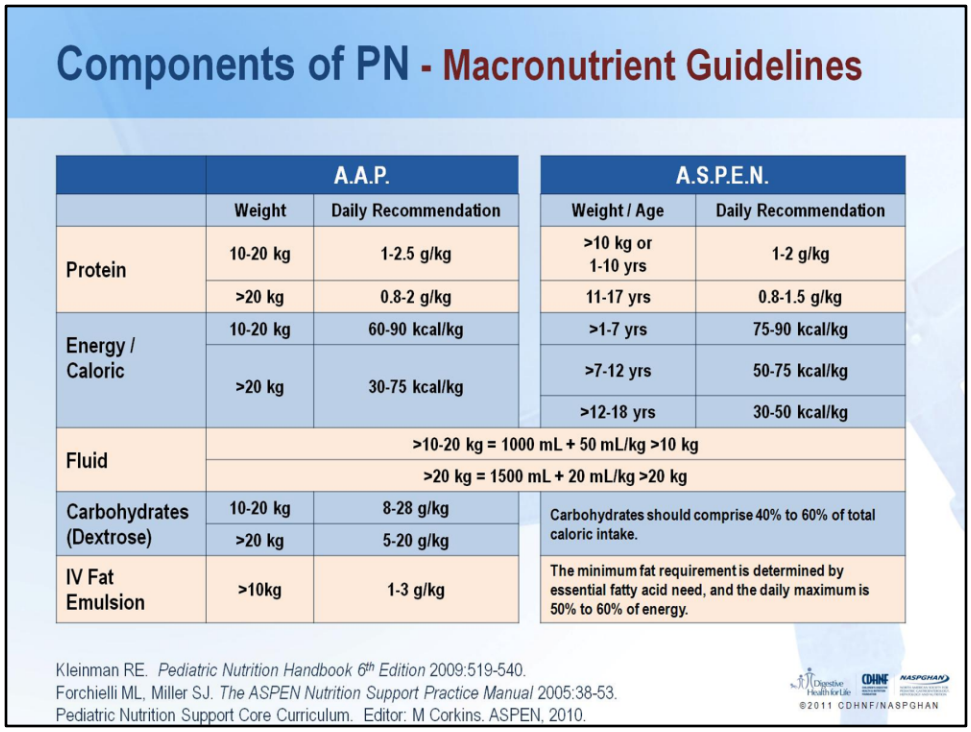
Filters are placed in line between the PN solution and the patient and are very important.

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)



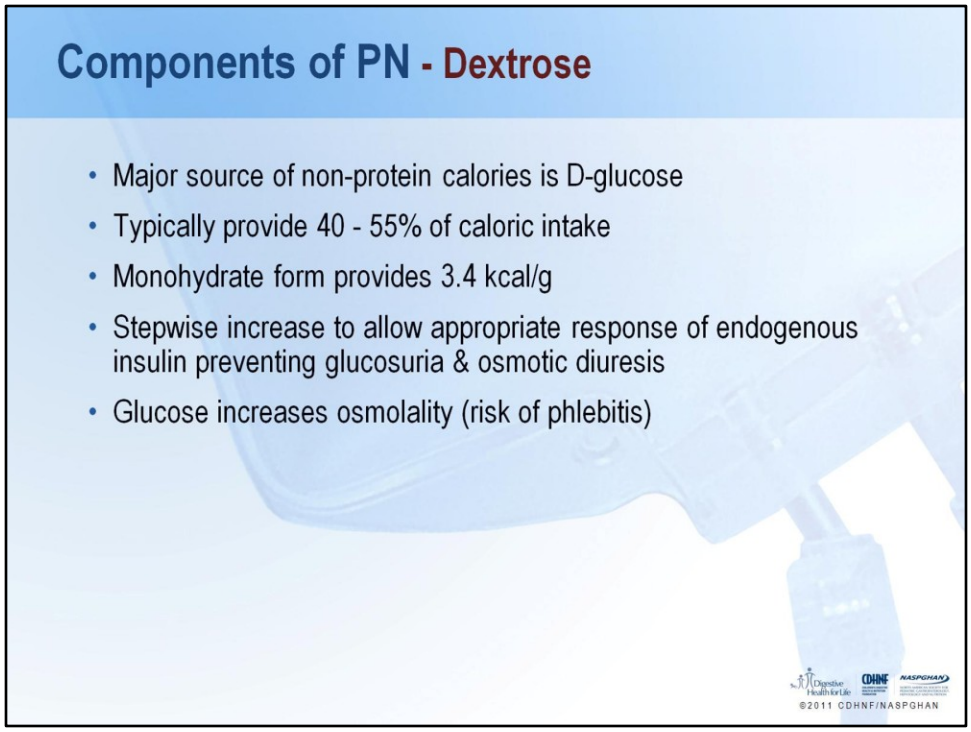
Examples of other additives to PN include vitamin K, cysteine, carnitine, and insulin.



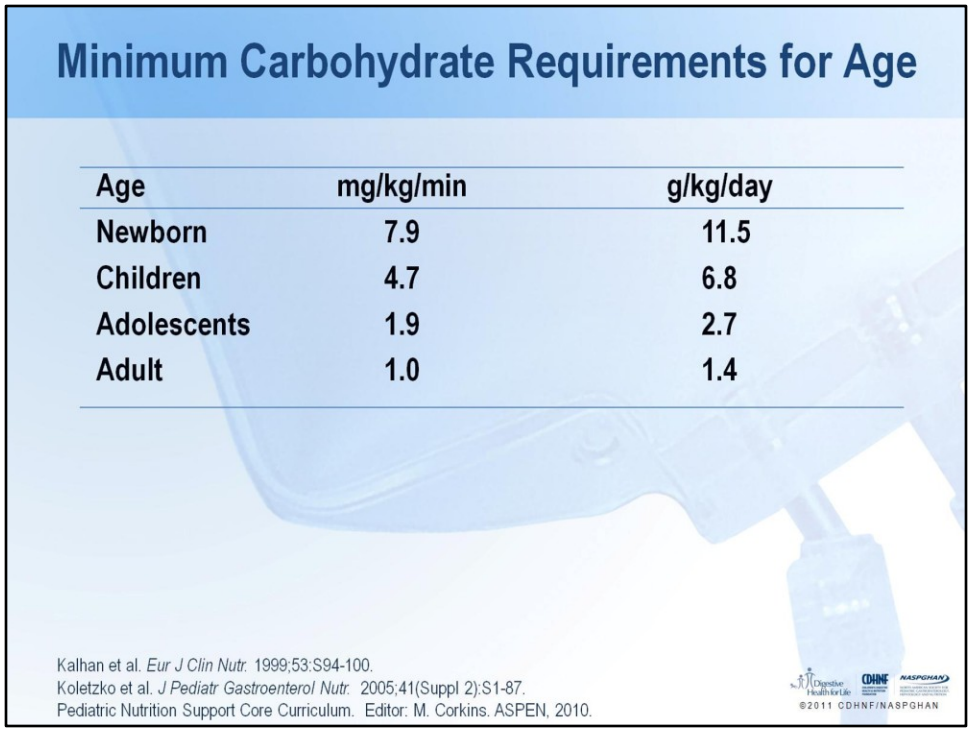
These are suggested macronutrient guidelines from AAP and ASPEN however there are other ways to calculate energy needs using accepted equations.

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.



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.



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.
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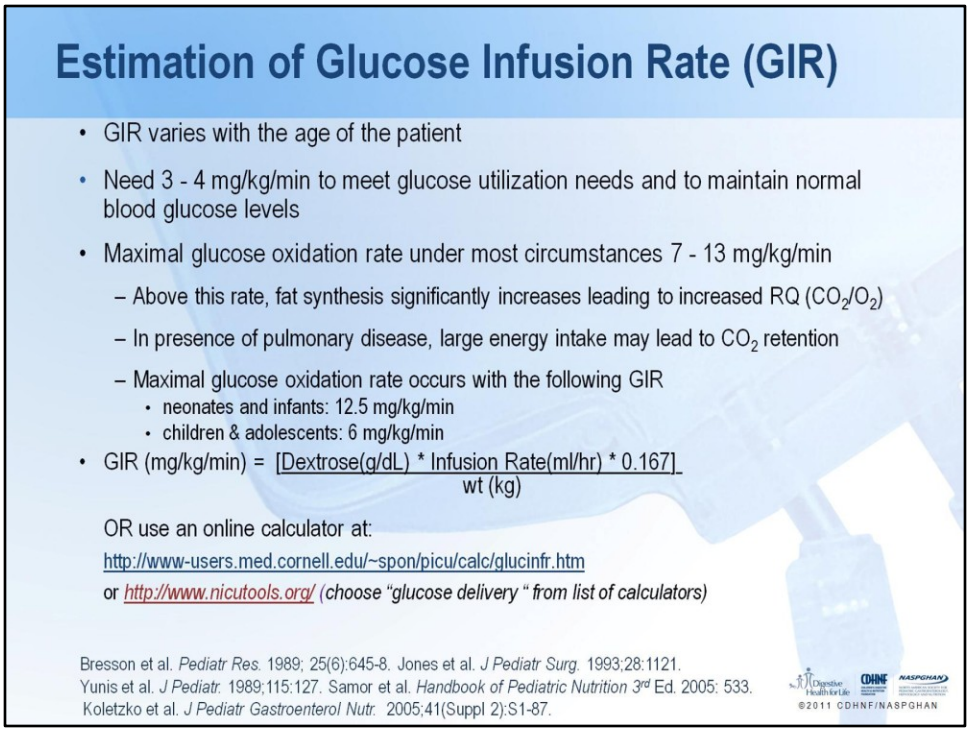


Web based calculators allow calculation of total GIR from multiple infusions with various dextrose concentrations (e.g. dextrose containing rider fluid + PN + dextrose medication carriers).

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.

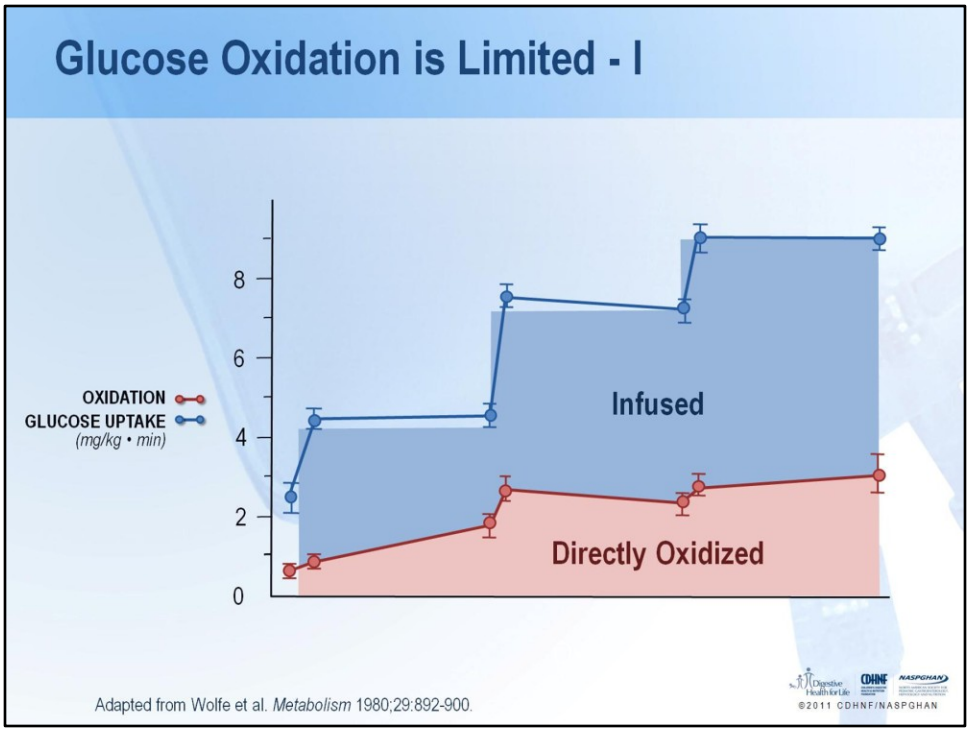
Jones MO, Pierro A, Hammond P, Nunn A, Lloyd DA. Glucose utilization in the surgical newborn infant receiving total parenteral nutrition. J Pediatr Surg. 1993 Sep;28(9):1121-5.

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

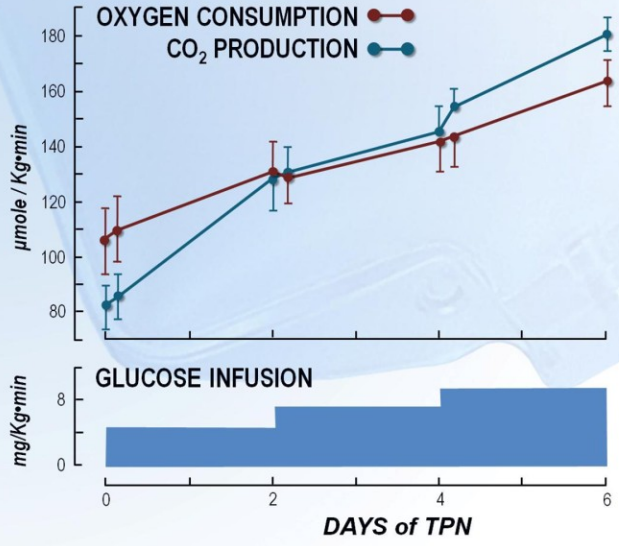
Gastroenterol Nutr. 2005 Nov;41 Suppl 2:S1-87.



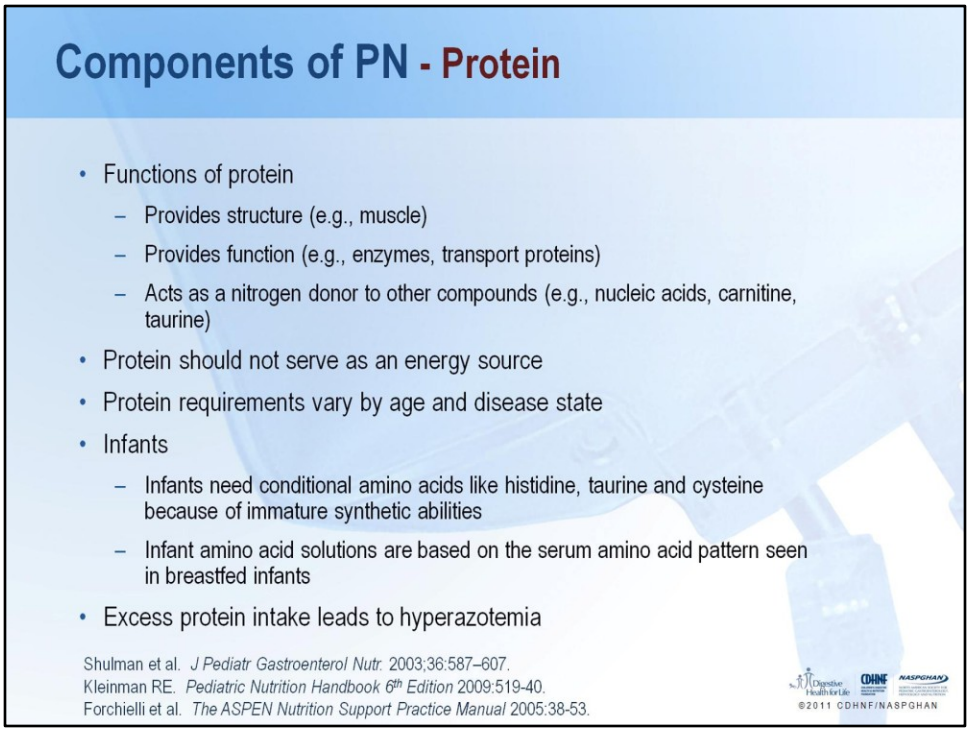
Metabolic study in adults: as the glucose infusion rate is increased, the rate of oxidation begins to plateau. Above this point, glucose is being increasingly converted to fat.

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.

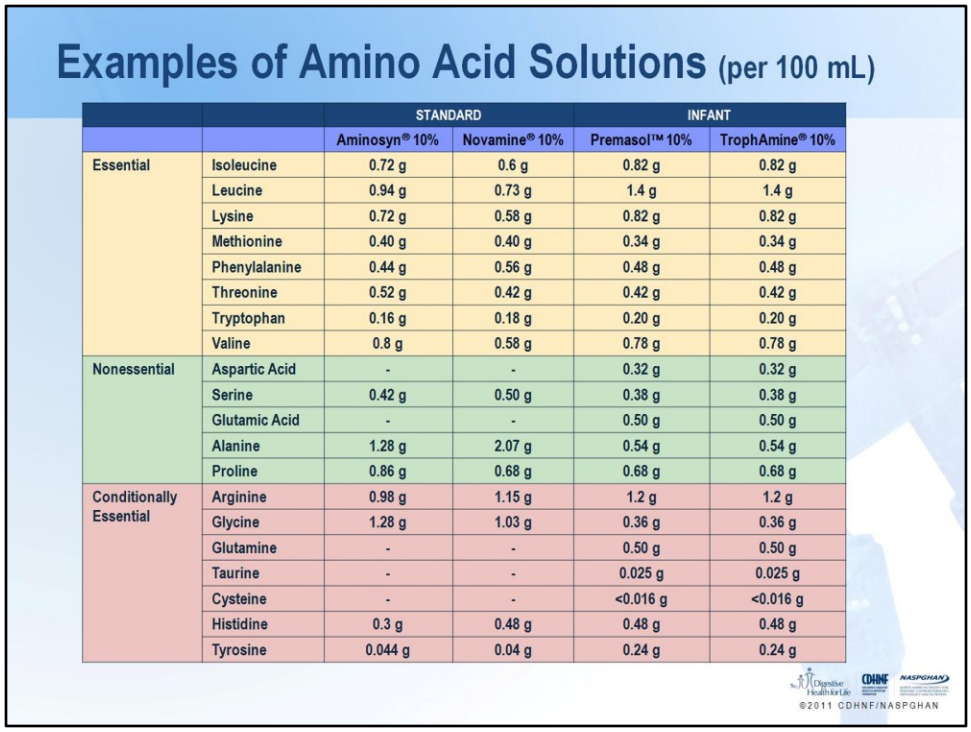
Glucose Oxidation is Limited - II



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

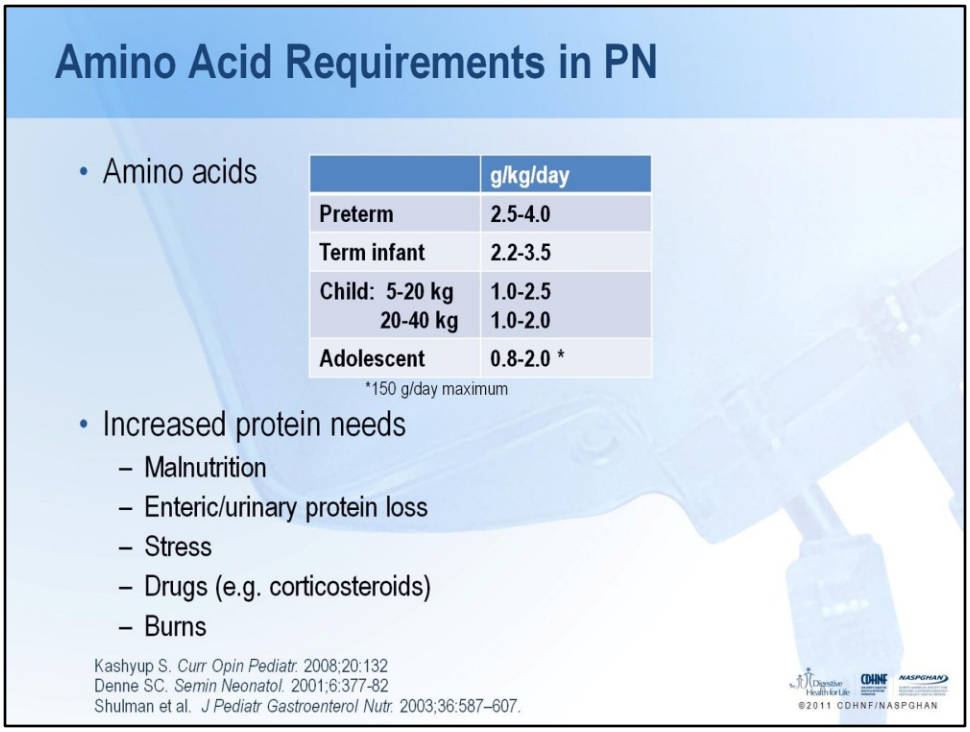


Shulman RJ, Phillips S. Parenteral nutrition in infants and children. J Pediatr Gastroenterol Nutr. 2003 May;36(5):587-607.
Kleinman RE. Pediatric Nutrition Handbook 6th Edition 2009:519-540.
Forchielli ML, Miller SJ. The ASPEN Nutrition Support Practice Manual 2005:38-53.



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.



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.
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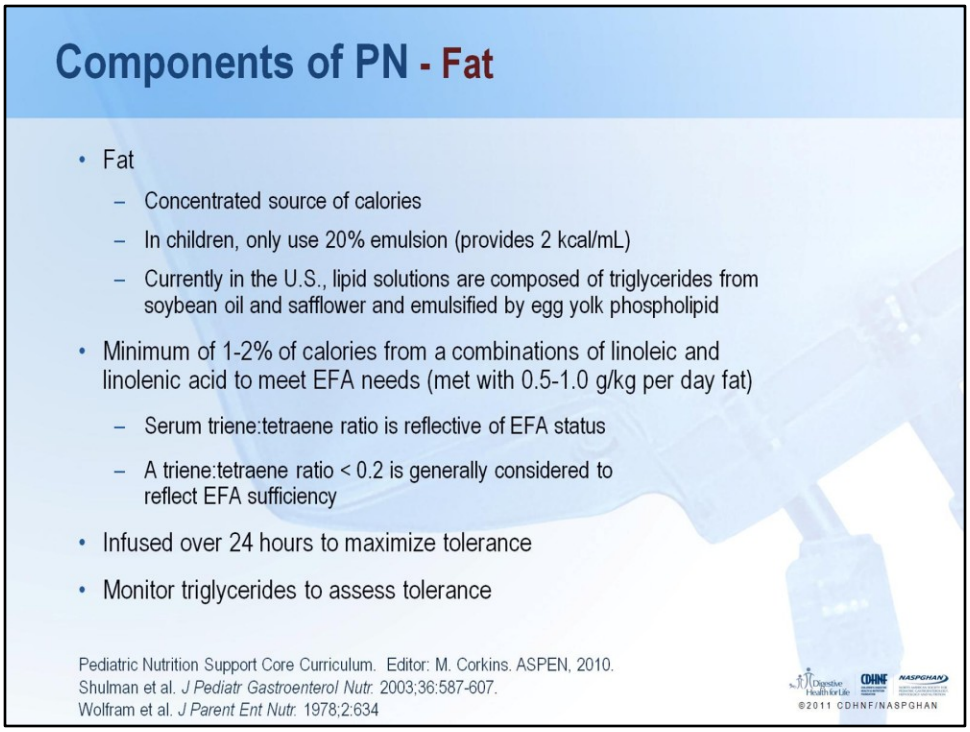

Fat provides calories and meeting EFA needs.

In neonates triglyceride levels upto 200 mg/dL and in older children levels unto 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.

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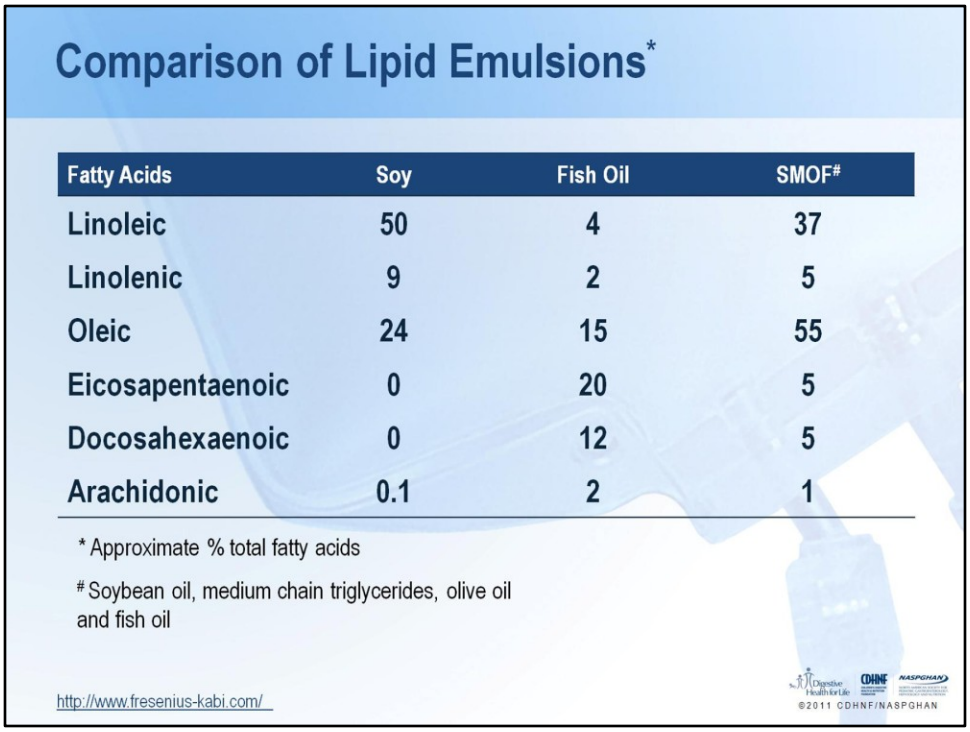
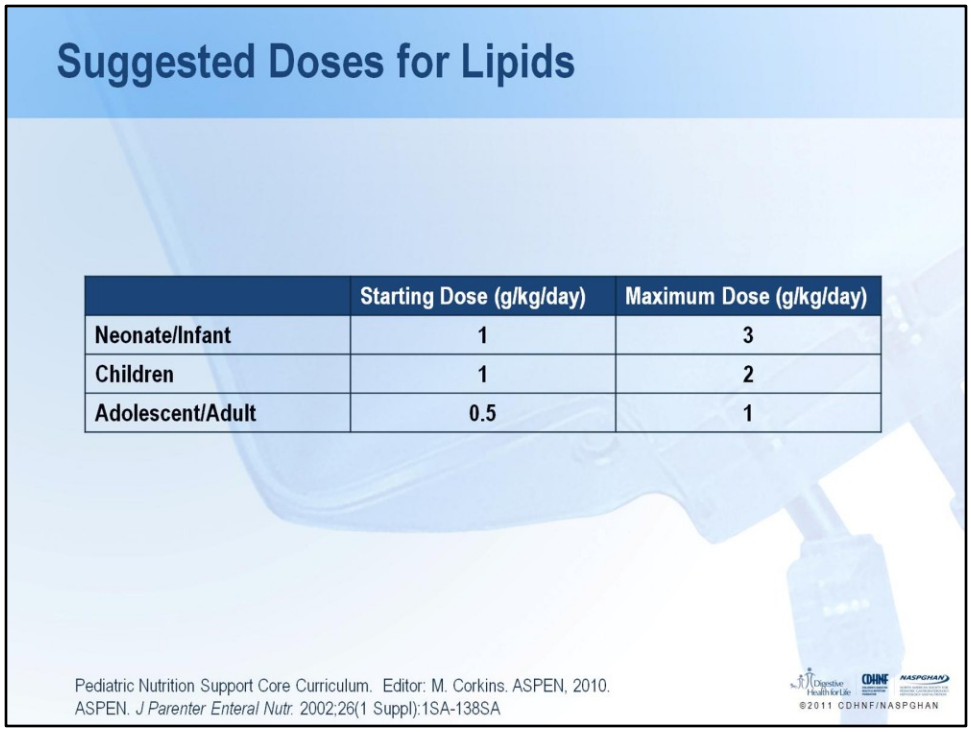
Shulman RJ, Phillips S. Parenteral nutrition in infants and children. J Pediatr

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.



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.



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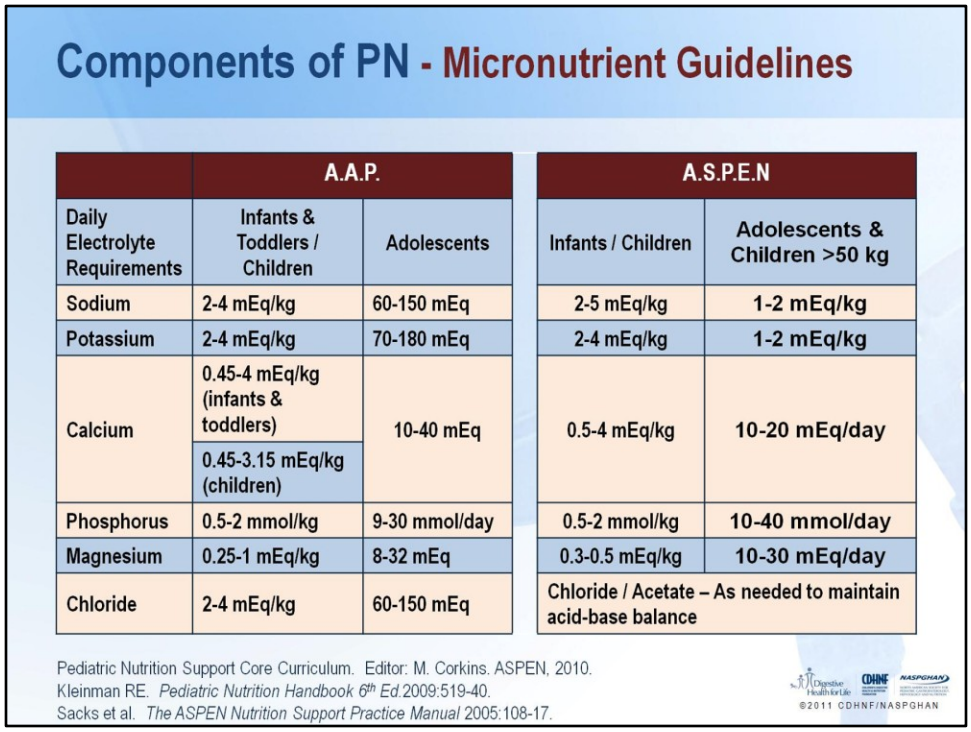
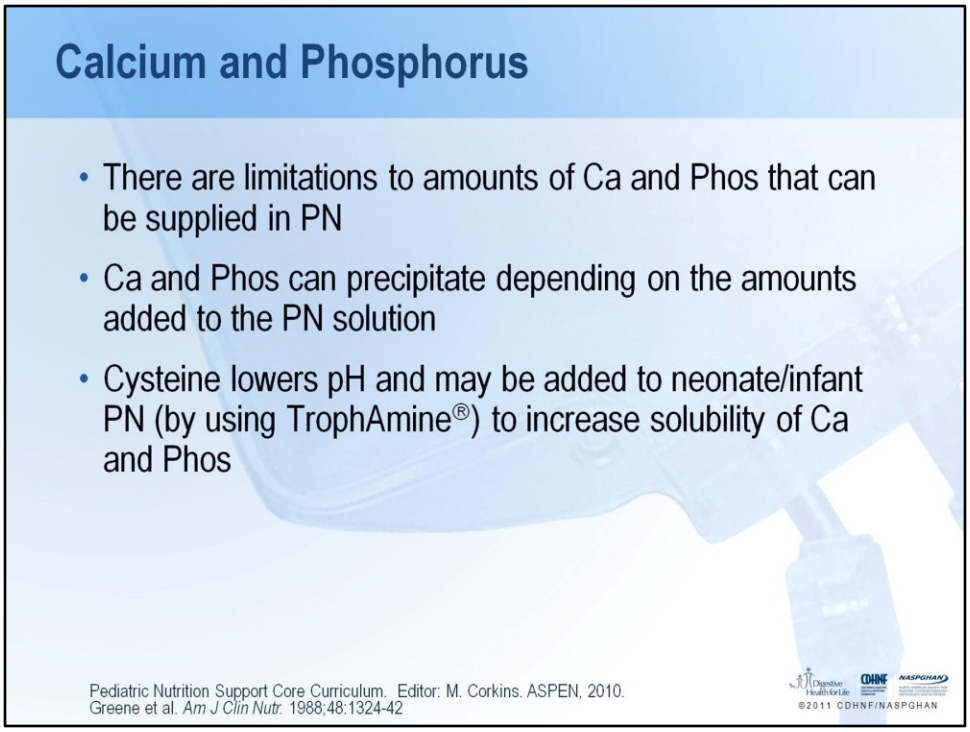


Monitor levels closely and adjust daily in PN if needed. The goal is maintenance of homeostasis; weight based supplementation and altered by disease states.
- Na: Consider acid base balance, and fluids & diuretic therapy prior to adjusting Na in PN
- K: Consider renal function, diuretic therapy, GI losses, 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.

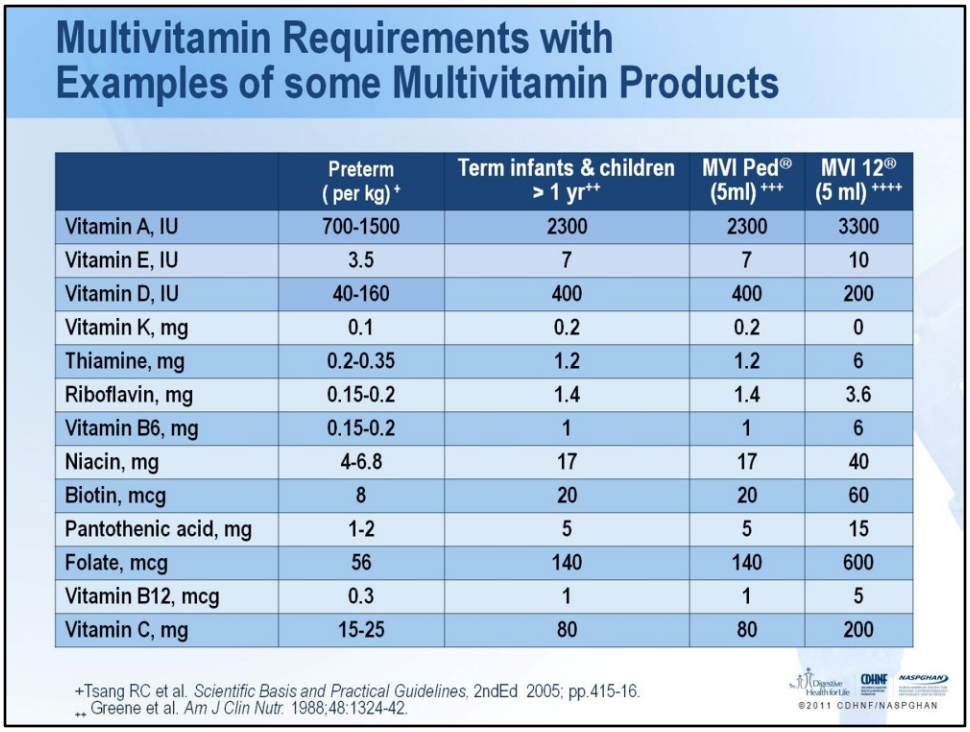
Kleinman RE. *Pediatric Nutrition Handbook 6th Edition.* 2009:519-40.

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



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.



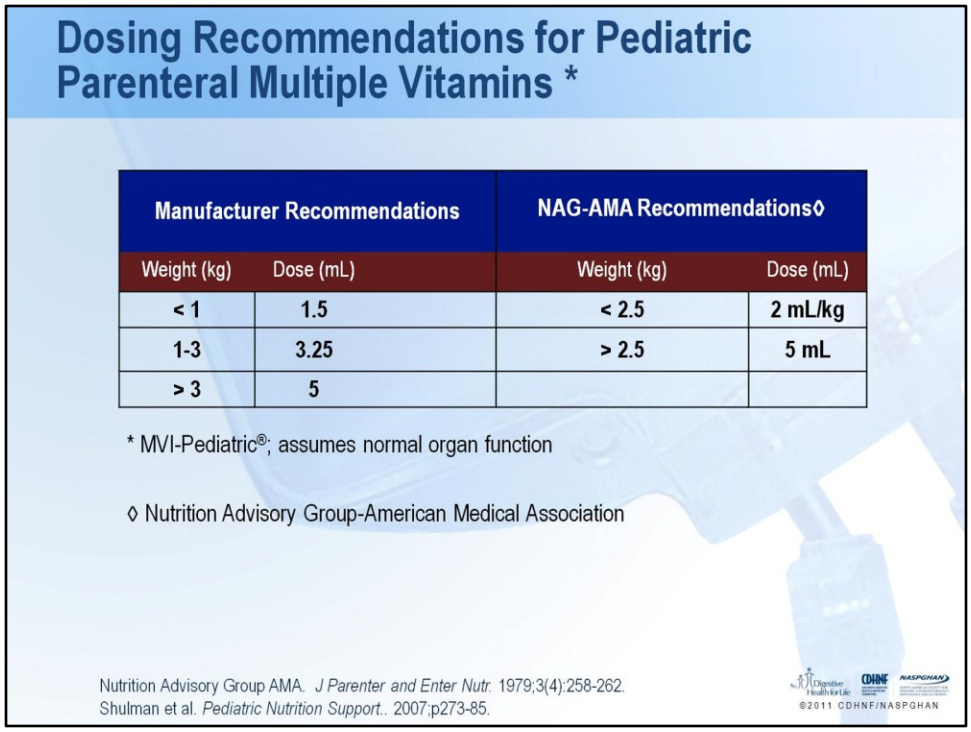
Vitamin A is provided as retinol and vitamin E as tocopherol. Note; there is no vitamin K in MVI 12® and so it will need to be added at a dose of 0.2 mg.
Other vitamins that can be added to PN: Insulin, Levocarnitine, folic acid, hydrochloric acid (only for ECMO patients), cysteine, and Vitamin K.

+ 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.

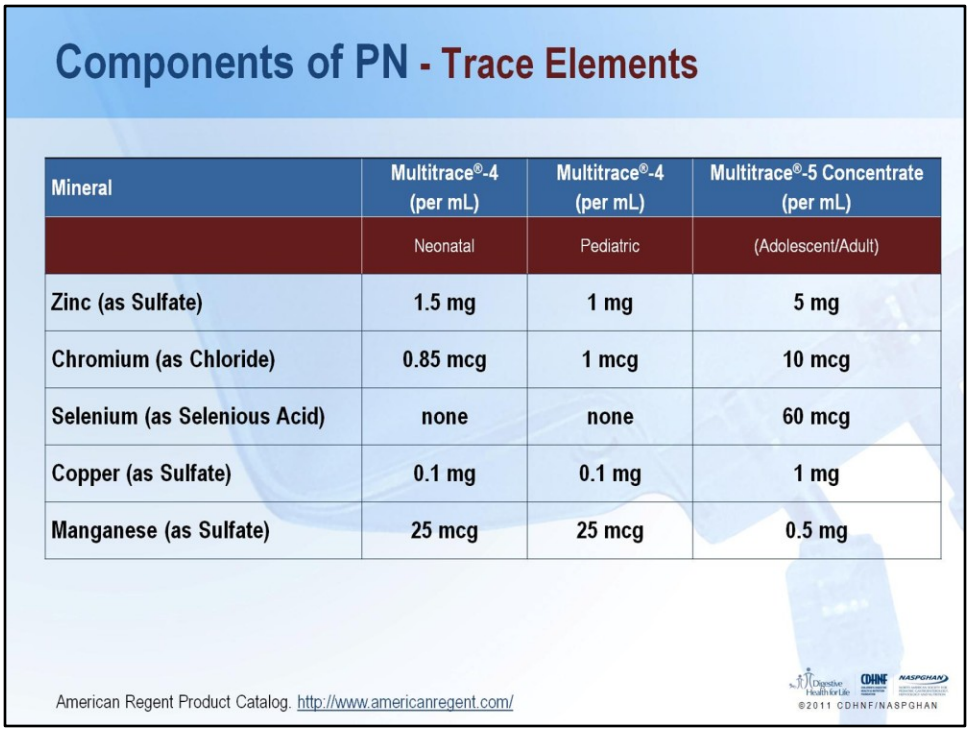
+++ http://www.hospira.com/Files/MVI_pediatric_PI.pdf

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



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.

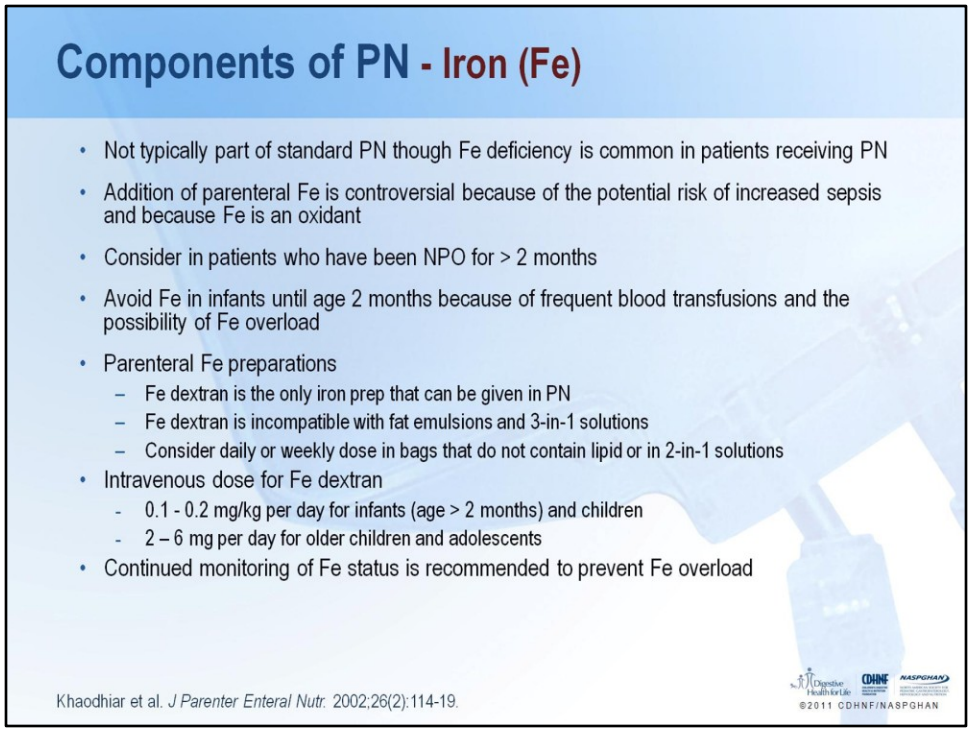
Multivitamin preparations for parenteral use. A Statement by the nutrition advisory group. American Medical Association Department of Foods and Nutrition 1975. J Parenter and Enter Nutr. 1979;3(4):258-262.
Shulman RJ, Philips S. Parenteral nutrition indications, administration and monitoring in Pediatric Nutrition Support. Baker SS, Baker RD, Davis AM. 2007;p273-85.



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
l

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



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.

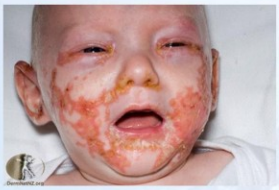
Other causes of anemia in patients on PN are anemia of chronic disease, Zn and Cu deficiency, vitamin E and B12 deficiency, folic acid deficiency, and hemolysis and occult blood loss. In general oral route is preferred over parenteral route for treatment of Fe deficiency anemia.

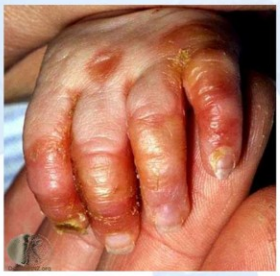
In a retrospective adult study of 55 patients treated with home PN for more than 6 months, 30/55 (55%) had evidence of Fe deficiency anemia (10/30 at time of start of PN and 20/30 between 2-97 months after start of PN (mean age 28 months). Loss from GI tract was most prominent reason.

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.

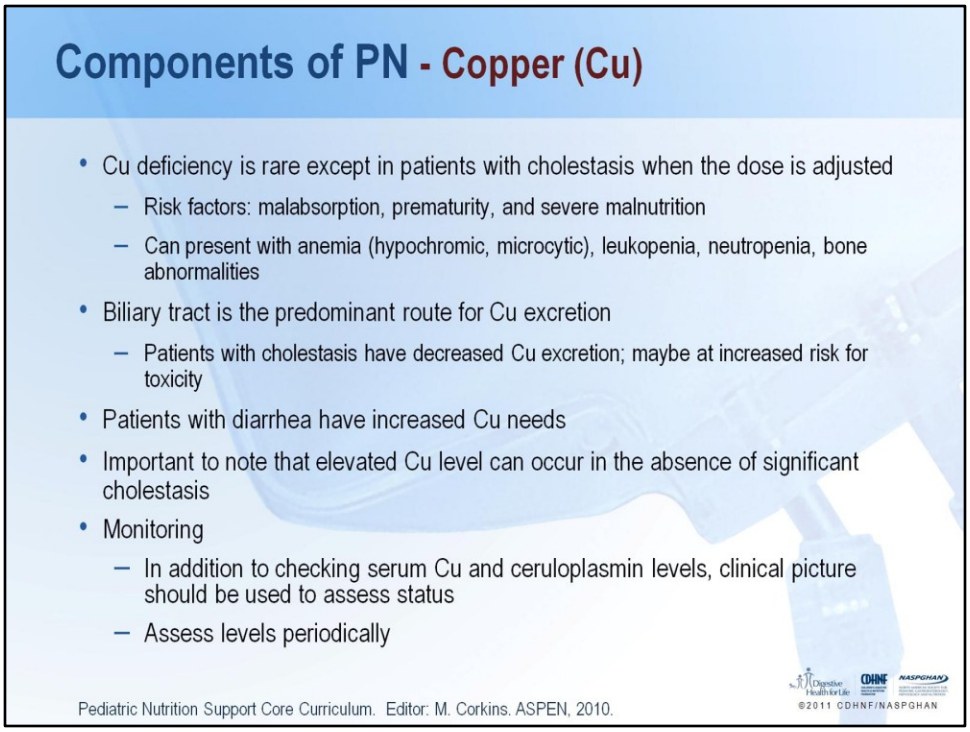
Zn is essential in the structural integrity of proteins, which regulate gene expression, and to nuclear binding proteins that act as transcription factors . It is a component of more than 250 metalloenzymes including alcohol, lactate and pyruvate dehydrogenases, alkaline phosphatase, and DNA and RNA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



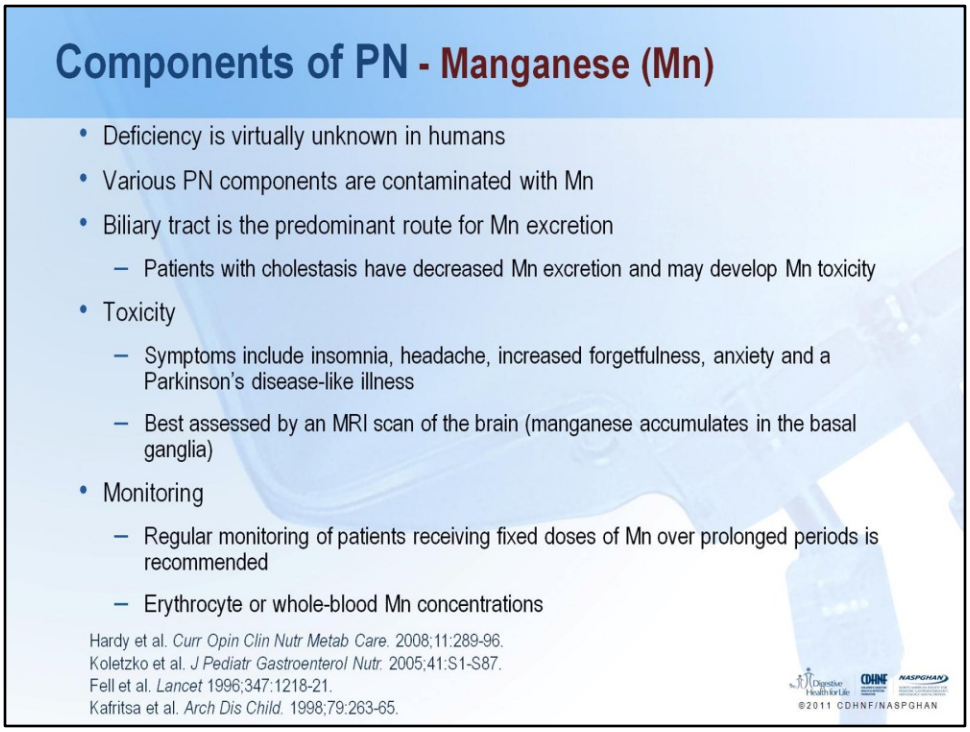
Chronic Cu toxicity is illustrated in Wilson's disease where high levels of Cu occur in the liver, brain, kidney, and other organs. The disease is manifested as cirrhosis of the liver, a variety of neurologic disorders, and renal damage.

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.

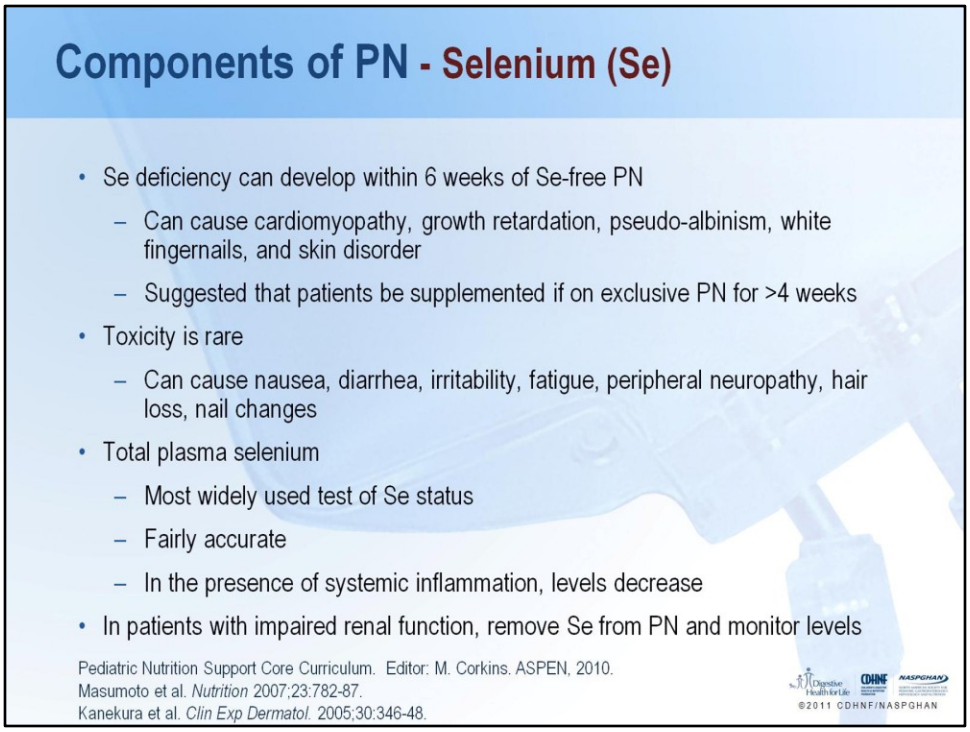
Pediatric Nutrition Support Core Curriculum. Editor: Mark Corkins. American Society for Parenteral and Enteral Nutrition (ASPEN), 2010.
McMillan NB, Mulroy C, McKay MW, McDonald CM, Jackson WD. Correlation of Cholestasis with Serum Copper and Whole Blood Manganese Levels in Pediatric Patients. Nutr Clin 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, Phyliky 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.



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.



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.

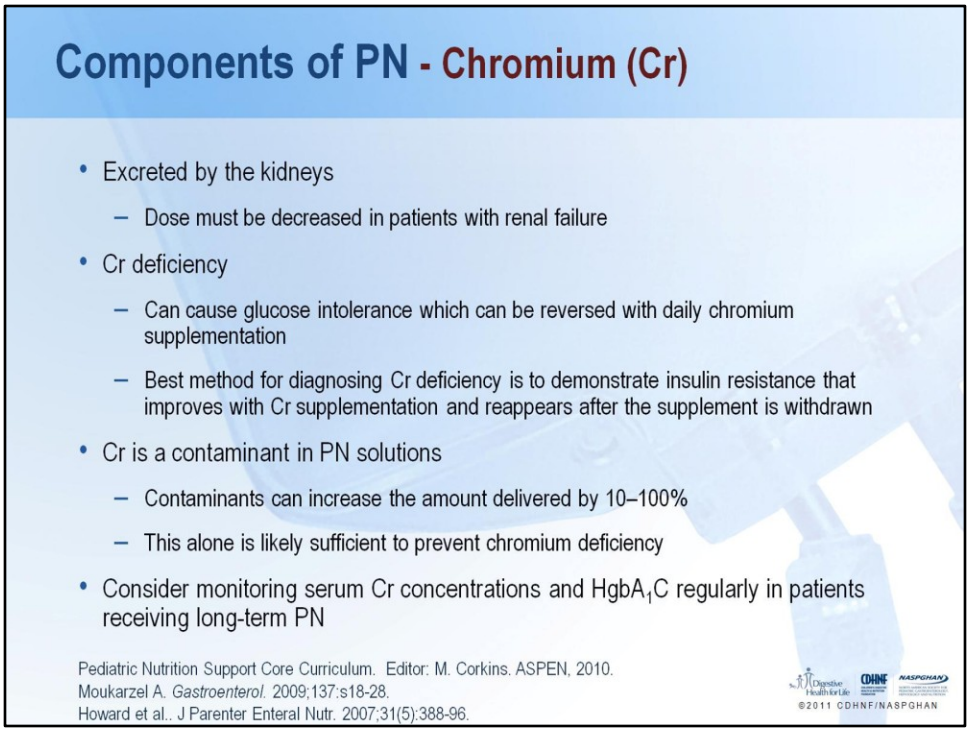
Rotruck JT, Pope AL, Ganther HE et al. Selenium: Biochemical Role as a Component of Glutathione Pexodiase. Science 1973;179:588-90.

Berry MJ, Banu L, Larson PR. Type 1 Iodothyronine Deiodinase is a Selencoysteine-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.



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.

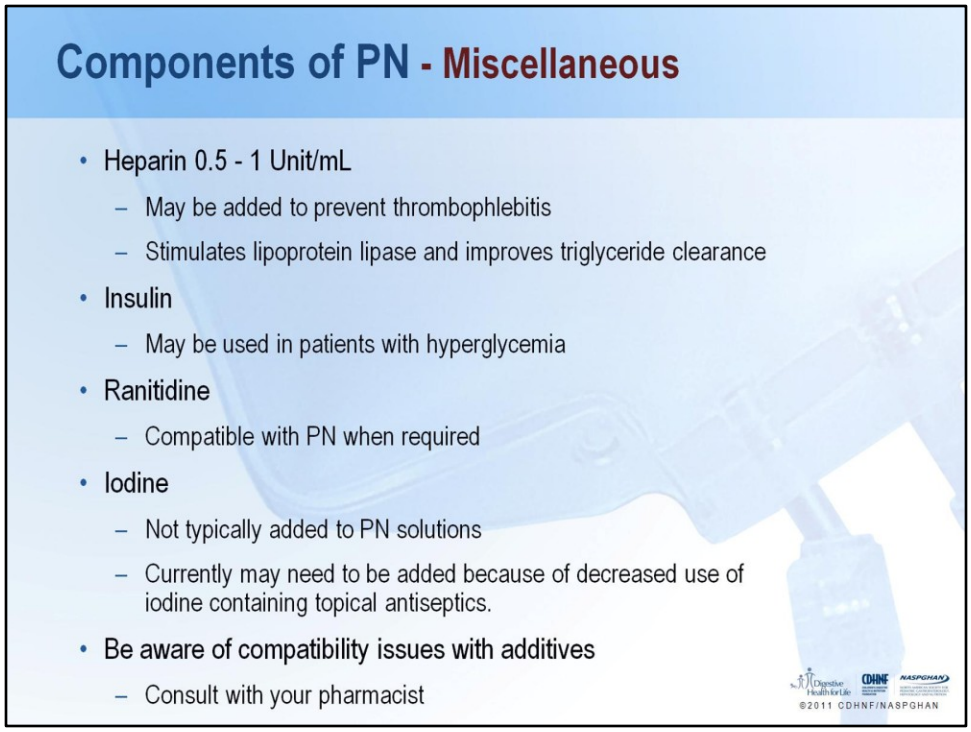
Pediatric Nutrition Support Core Curriculum. Editor: Mark Corkins. American Society for Parenteral and Enteral Nutrition (ASPEN), 2010.

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.

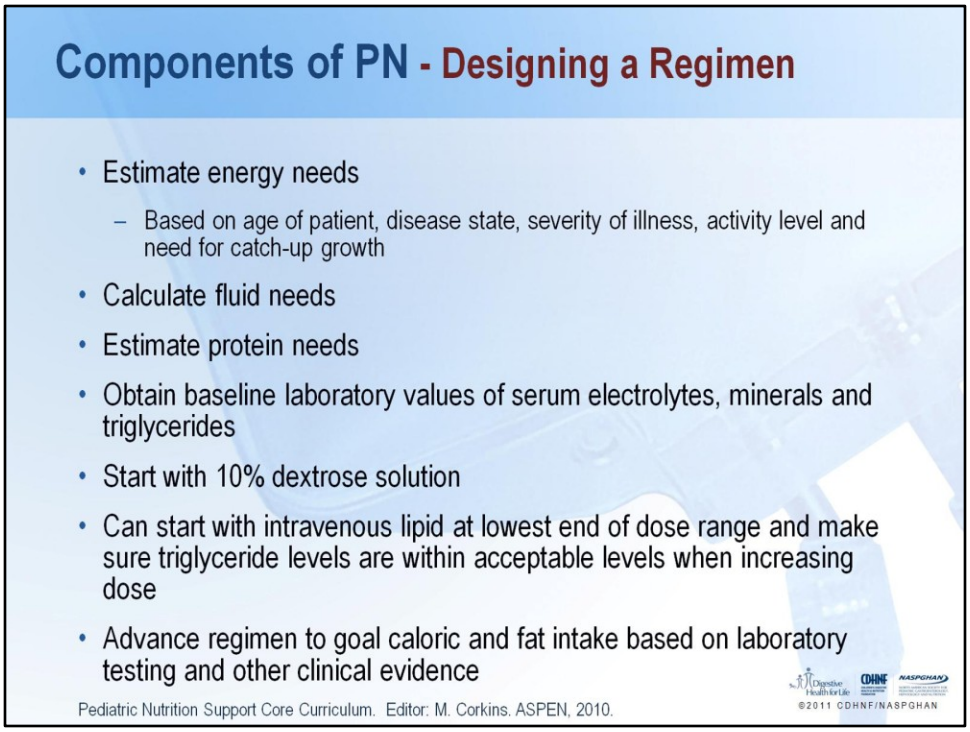
Vincent JB. The Bioinorganic Chemistry of Chromium. Polyhedron 2001;20:1-26.

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



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.

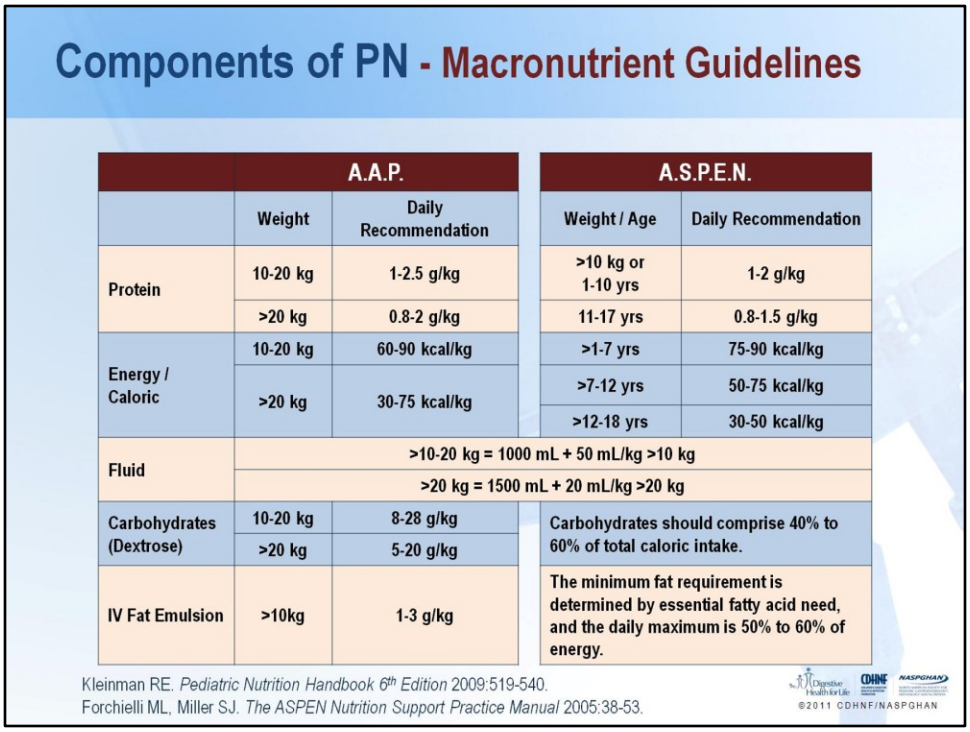


The concentration of the dextrose solutions used at the initiation of PN depends on the patients serum glucose level, glucose content of currently administered fluids, type of catheter through which the PN solution will be administered and desired GIR.

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.

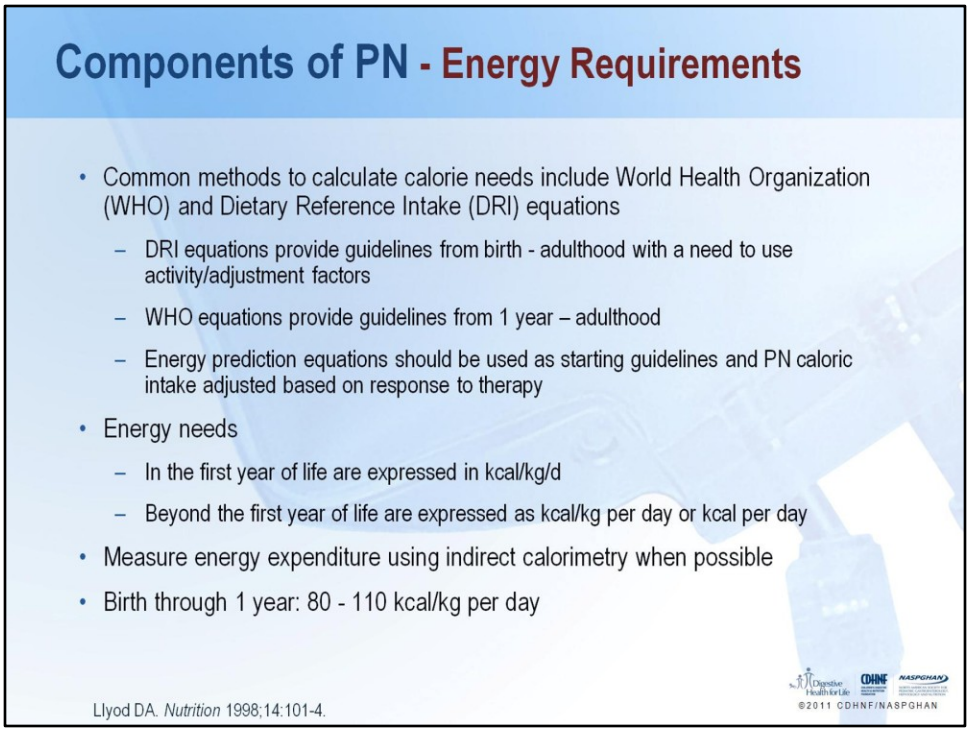
The ideal non-protein calorie to nitrogen ratio or NPC:N ratio reflects the balance in the PN regimen between the non protein calorie (fat and carbohydrate) and protein calories. In stable patients that ratio should be 150-250:1. This ratio may be less in critically ill patients or higher in renal failure 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.



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.

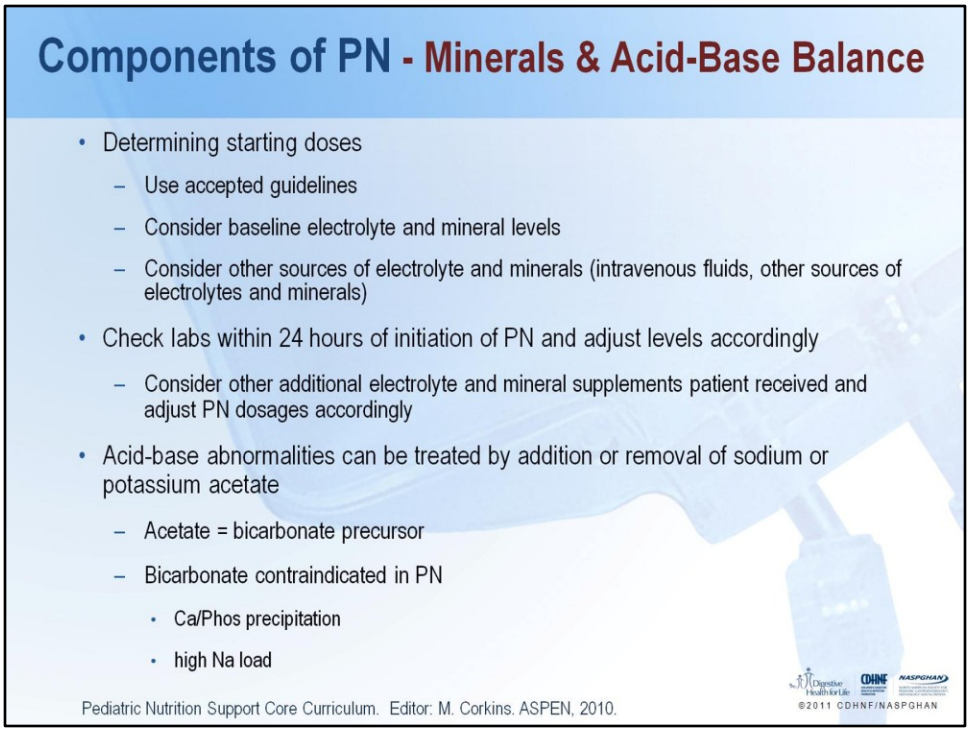


Can use the suggested guidelines from AAP or ASPEN.

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

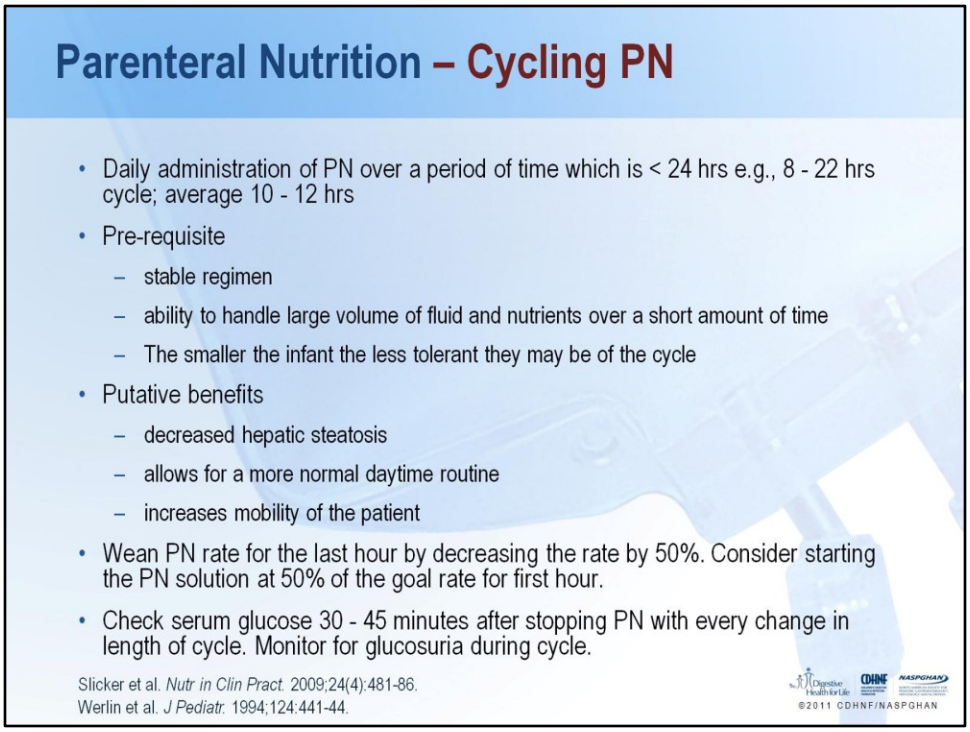
Dietary Reference Intake (DRI): http://fnic.nal.usda.gov/nal_display/index.php?info_center=4&tax_level=2&tax_subject=256&topic_id=1342.

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



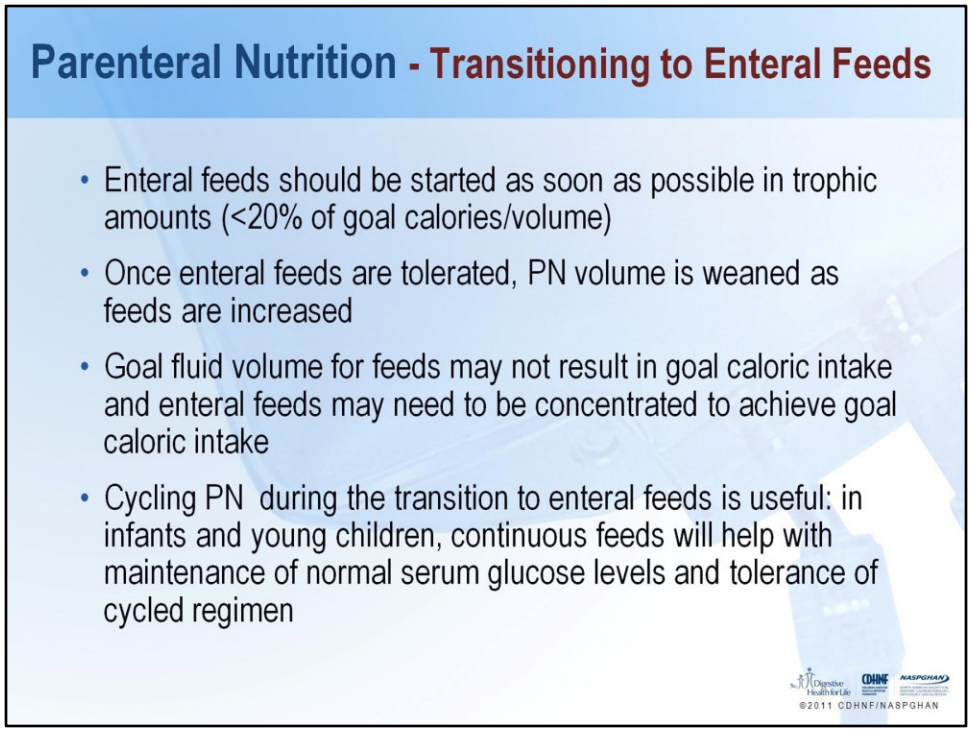
There are maximum amounts of electrolytes that can be added to the PN solutions based on solubility and risk of precipitation.

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

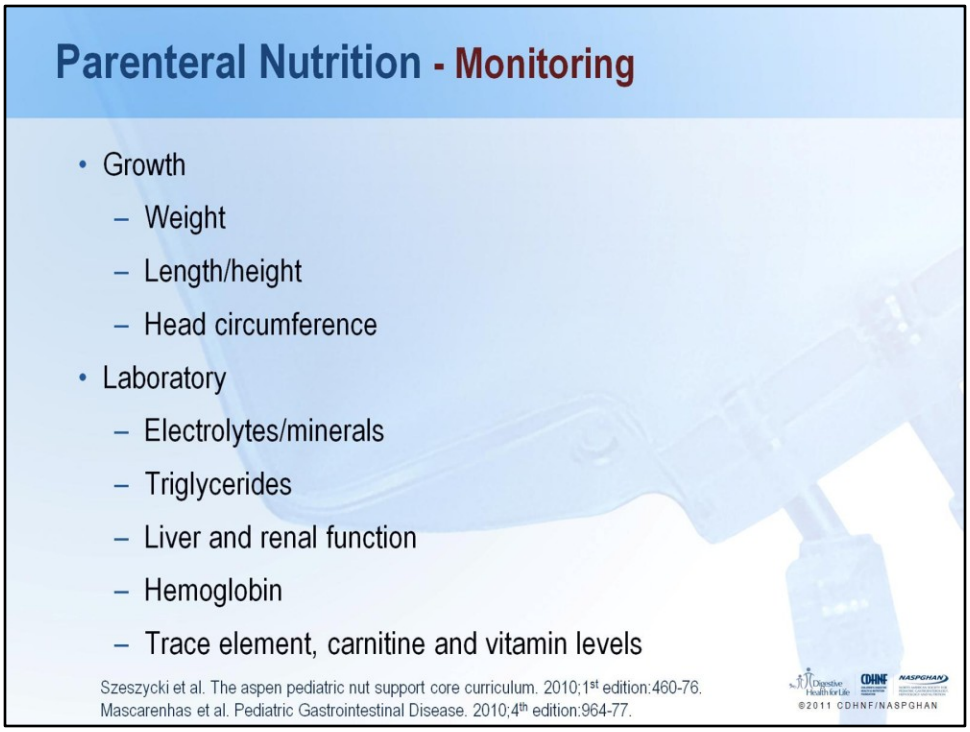


Patients do not need a dextrose rider during hours when they are not receiving PN. The is no true minimum weight to start cycling, but patients should be able to maintain normal glucose values while off PN solution and this is usually around a weight of 5 kg. A potential disadvantage of cycling PN is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

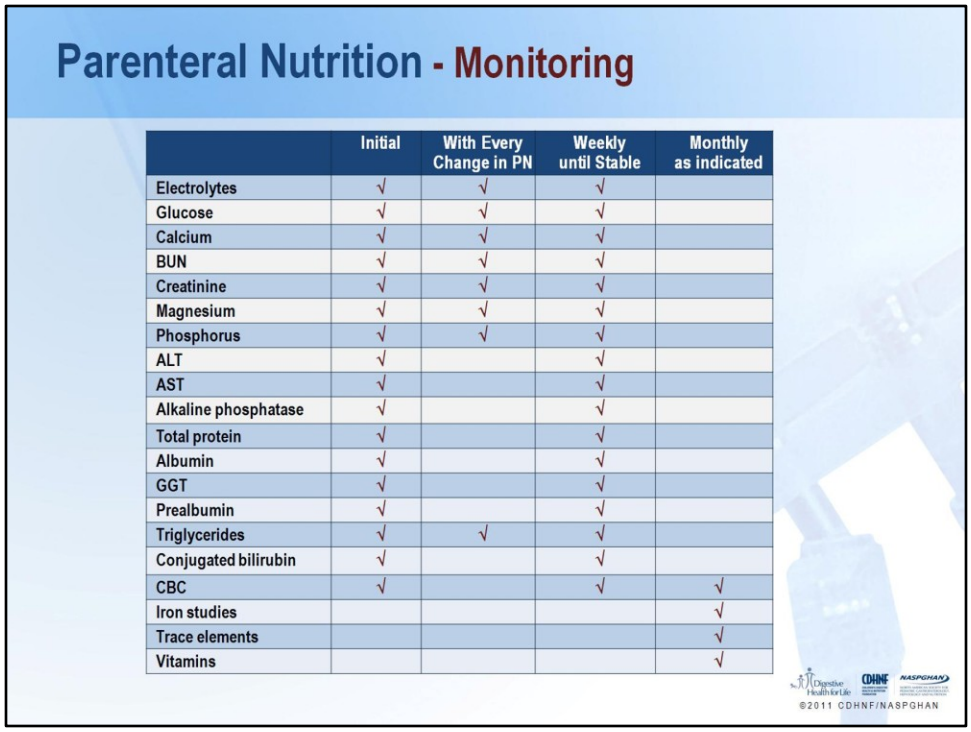


Trophic feeds are considered any volume of feed that is less than 20% of goal.



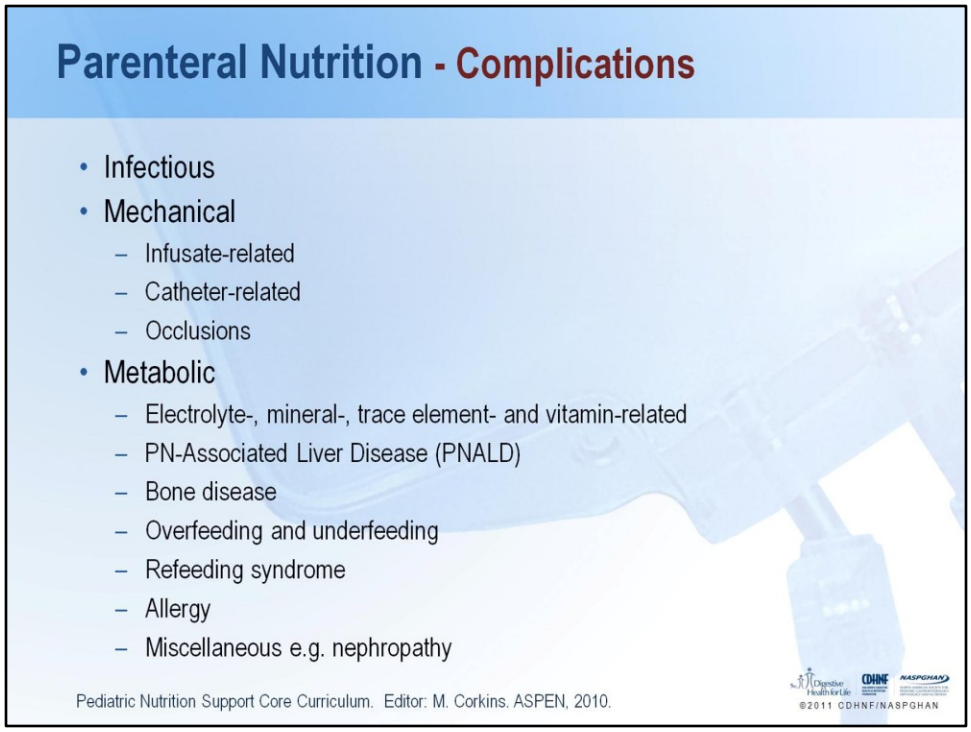
Consider measuring carnitine (ester/free ratio) levels in patients who are NPO for a significant amount of time, as indicated. Some clinicians feel that measuring carnitine levels is not helpful.

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.



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.

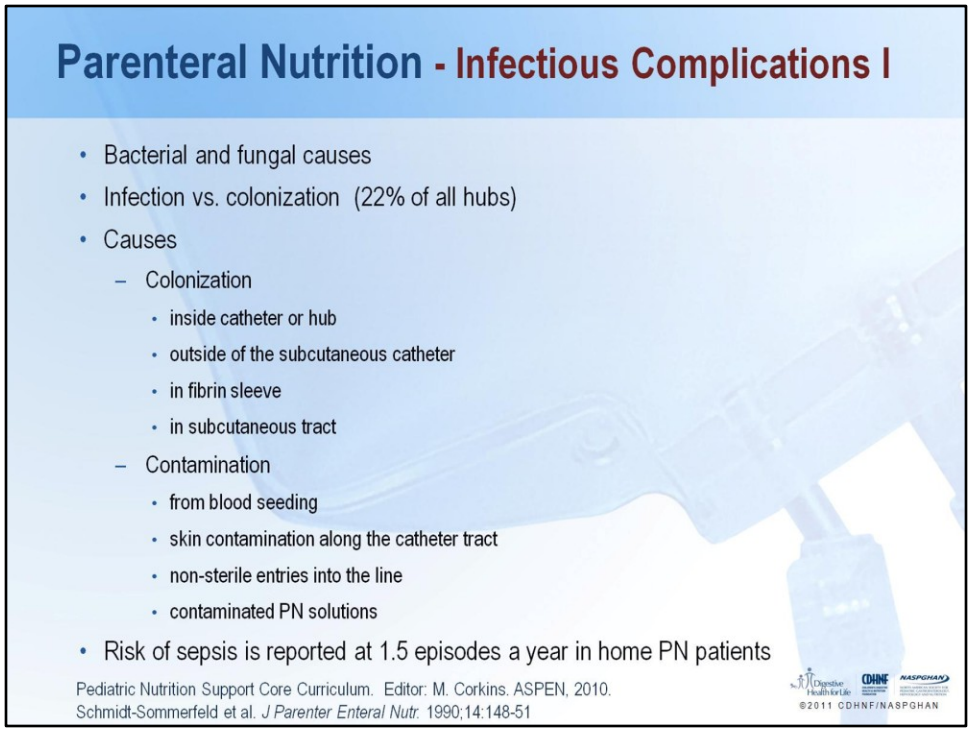
Pediatric Nutrition Support Core Curriculum. Editor: Mark Corkins. American Society for Parenteral and Enteral Nutrition (ASPEN), 2010.



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.

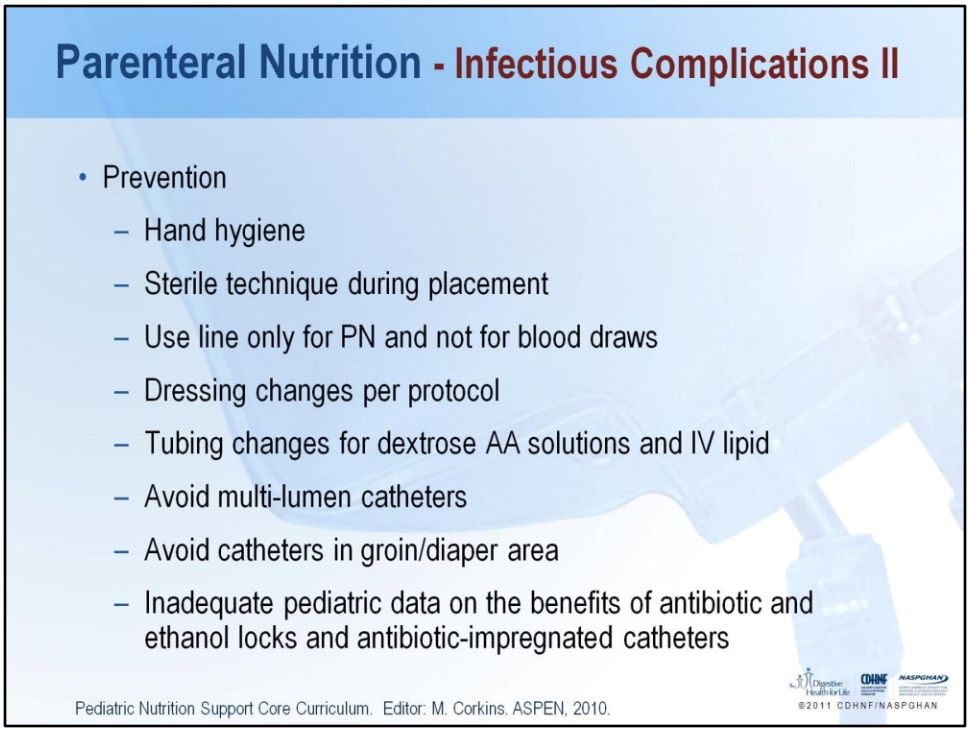
Patients on chronic PN, especially HPN, are at risk for nephropathy. This may be related to subclinical renal damage from components of PN, cumulative drug toxicity from nephrotoxic antibiotics used to treat central line infections.

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.



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 tunnelled 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.



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

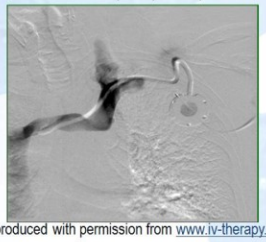
Pediatric Nutrition Support Core Curriculum. Editor: Mark Corkins. American Society for Parenteral and Enteral Nutrition (ASPEN), 2010.

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



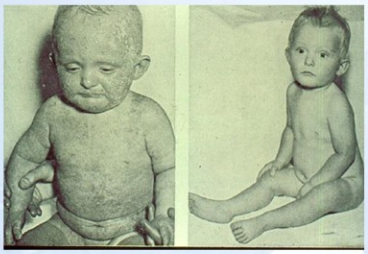
Reproduced with permission from www.iv-therapy.net

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)

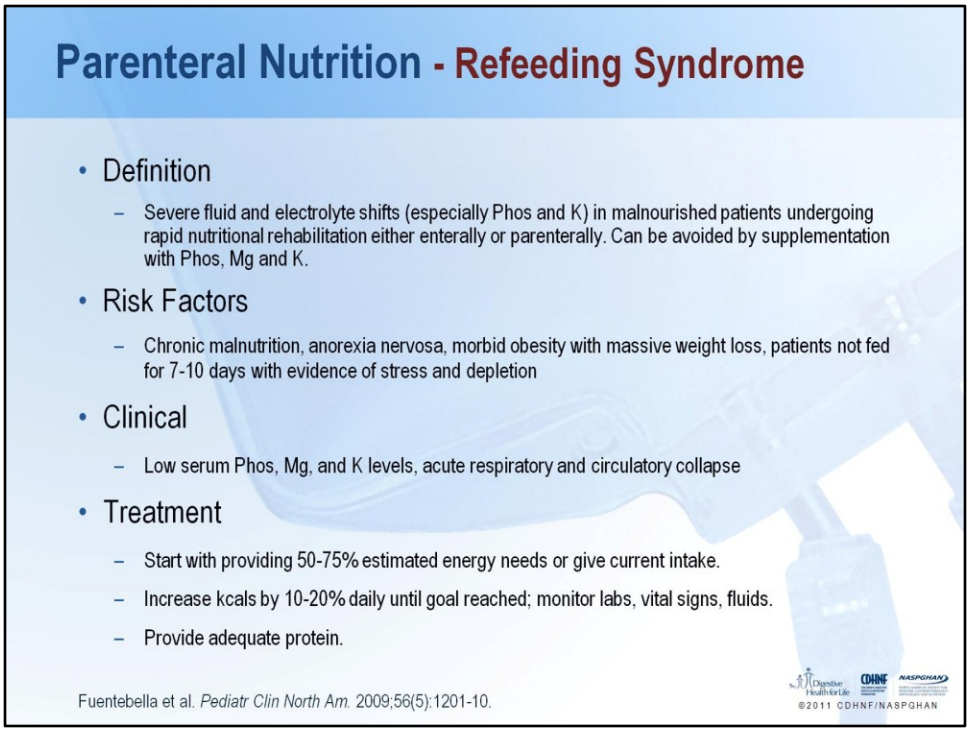
- EFAD can be seen within days of fat-free PN in neonates
- Deficiency is cumulative
- Can cause
  - decreased growth
  - skin and hair changes
  - increased susceptibility to infection,
  - poor wound healing
  - alterations in platelet function
- To avoid EFAD need minimum of
  - 2% to 4% of the total 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



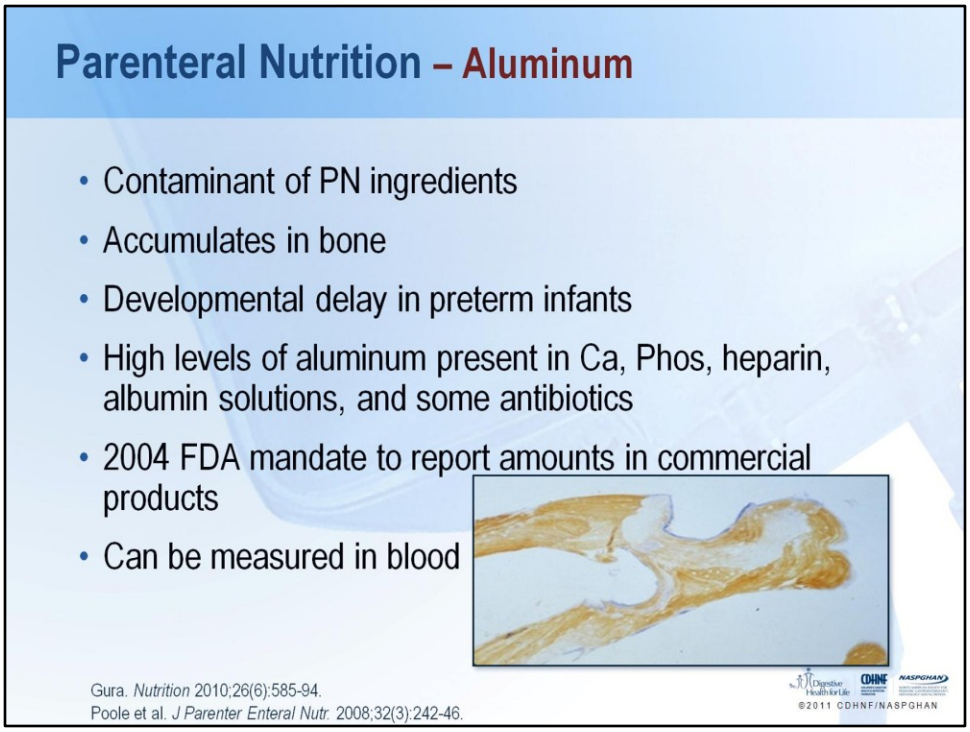
Uauy et al. *Semin Pereinatol.* 1989;13:118-30.

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 Pereinatol* 1989;13:118-30.

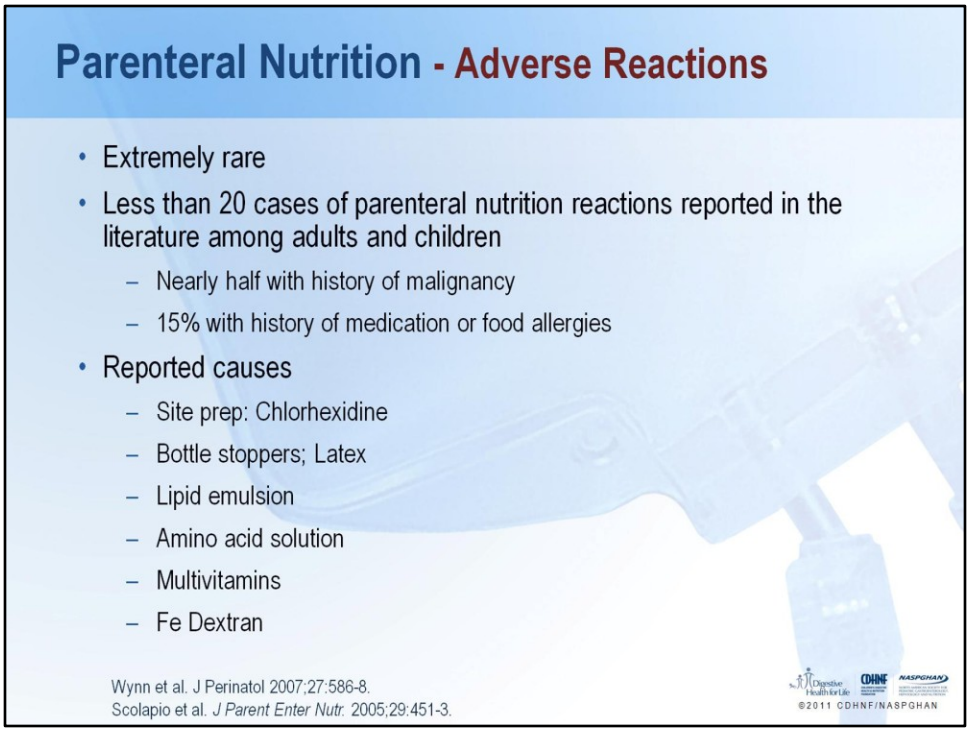


Fuentebella J, Kerner JA. Refeeding syndrome. Pediatr Clin North Am 2009; 56(5):1201-10



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.



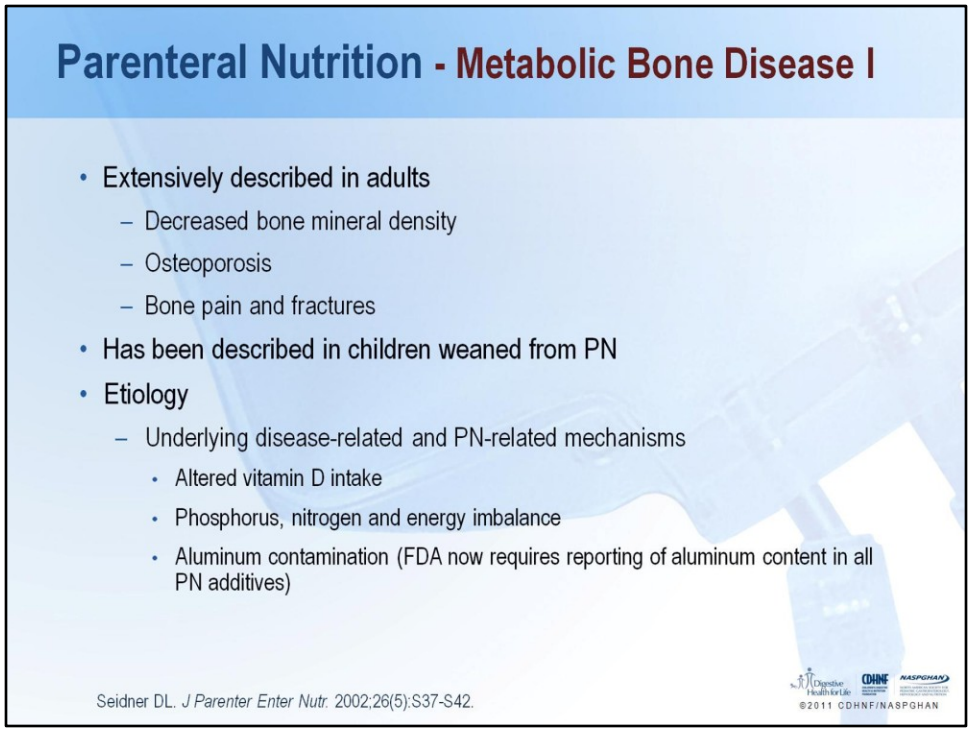
Sulfite are added to crystalline amino acid products to diminish amino acid oxidation. Acute and delayed sensitivity reactions can occur after ingestion of sulfite-containing foods and other products. Bisulfite reacts with disulfide bonds to alter protein structure/configuration thus potentially affecting 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. Polyethyloxylated 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.



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 osteomlacia, reduced bone aposition 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.

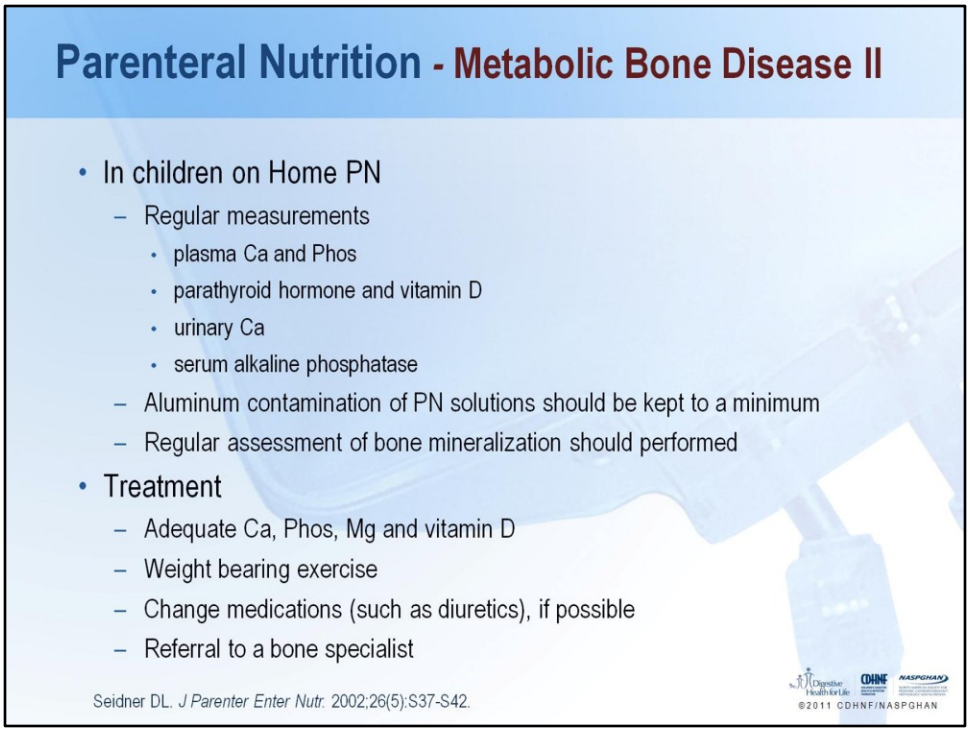
Seidner DL. Parenteral nutrition-associated metabolic bone disease. JPEN 2002; 26(5):S37-S42

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.



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 levelss.

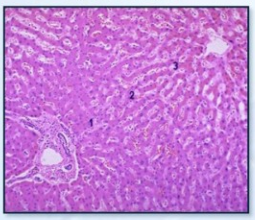
Seidner DL. Parenteral nutrition-associated metabolic bone disease. JPEN 2002; 26(5):S37-S42
Koletzko B, Goulet O, Hunt J, Krohn K, Shamir R; Guidelines on Paediatric Parenteral Nutrition of the European Society of Paediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN) and the European Society 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.

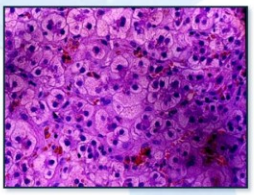
Parenteral Nutrition - Liver Disease I

- 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



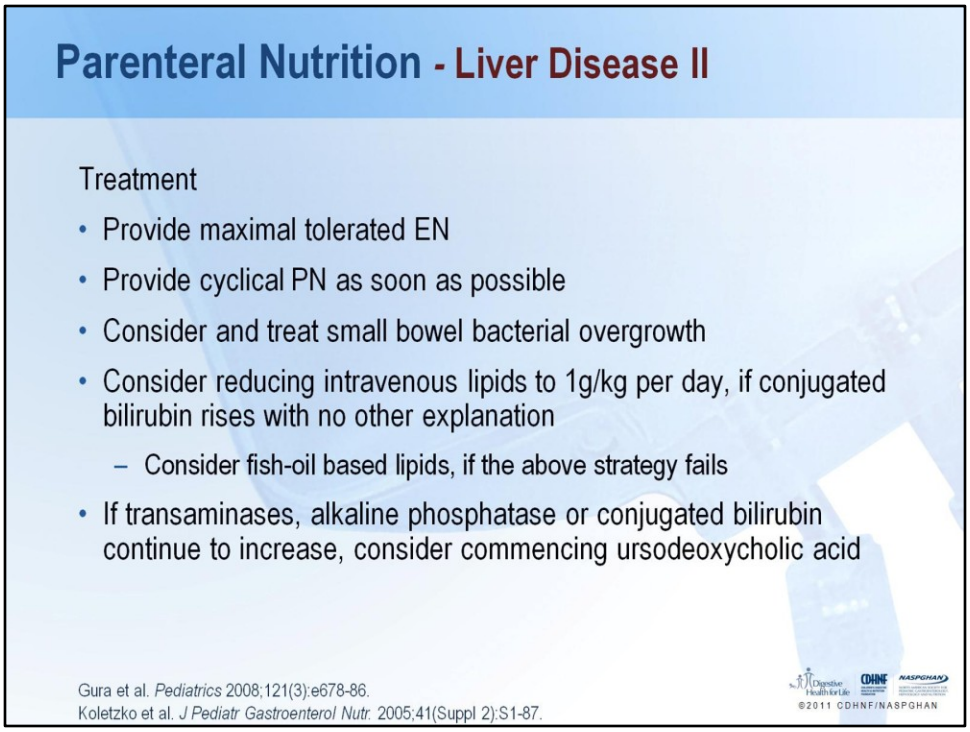
Cholestasis



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

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

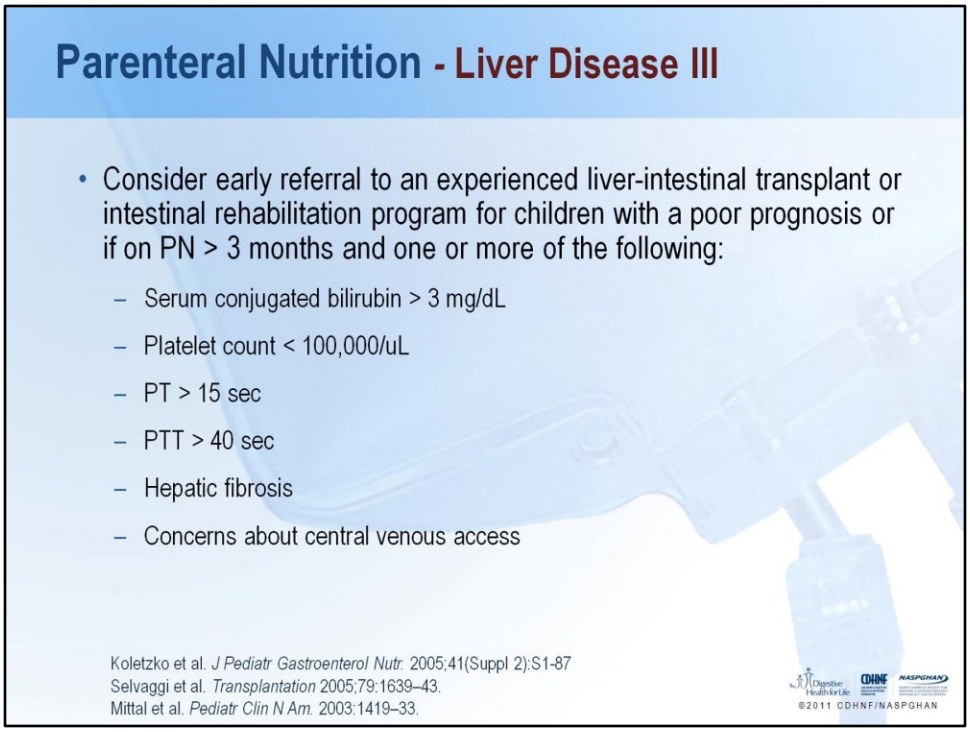
Ovchinsky N. conjugated bile acid as potential early markers of parenteral nutrition associated liver disease. JPEN 2010;34(5):472-473



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.

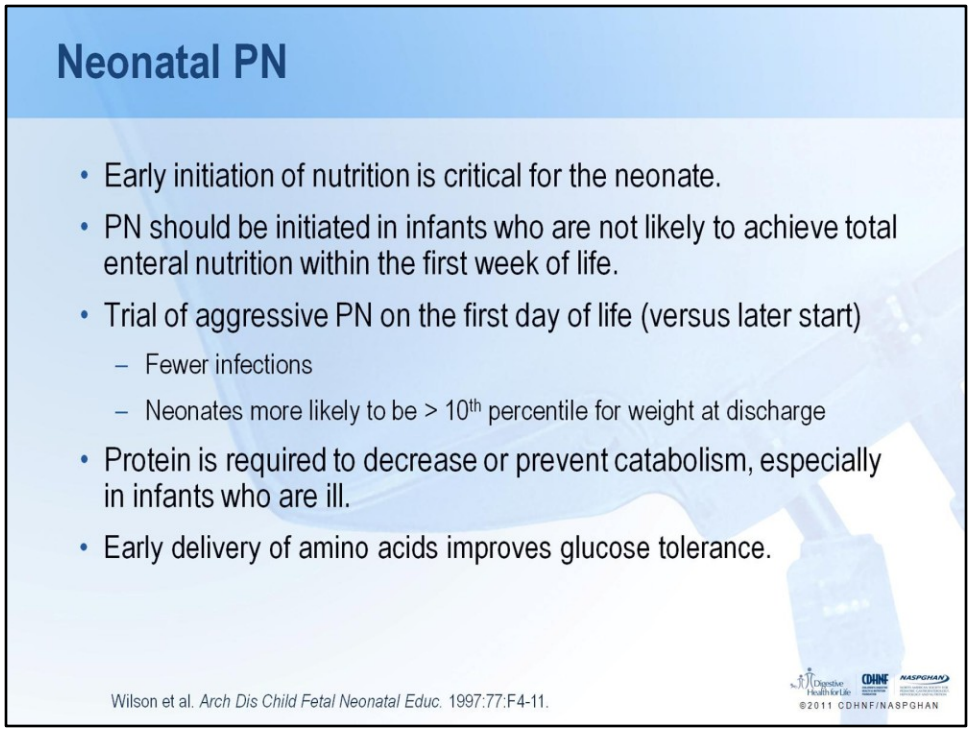


Mittal NK, Tzakis AG, Kato T, et al. Current status of small bowel transplantation in children: update 2003. Pediatr Clin N Am. 50 (2003):1419– 1433.
Selvaggi G, Gyamfi A, Kato T, Gelman B, Aggarwal S,Begliomini B, Bennett J, Nishida S,Tzakis AG. Analysis of Vascular Access in Intestinal Transplant Recipients 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.

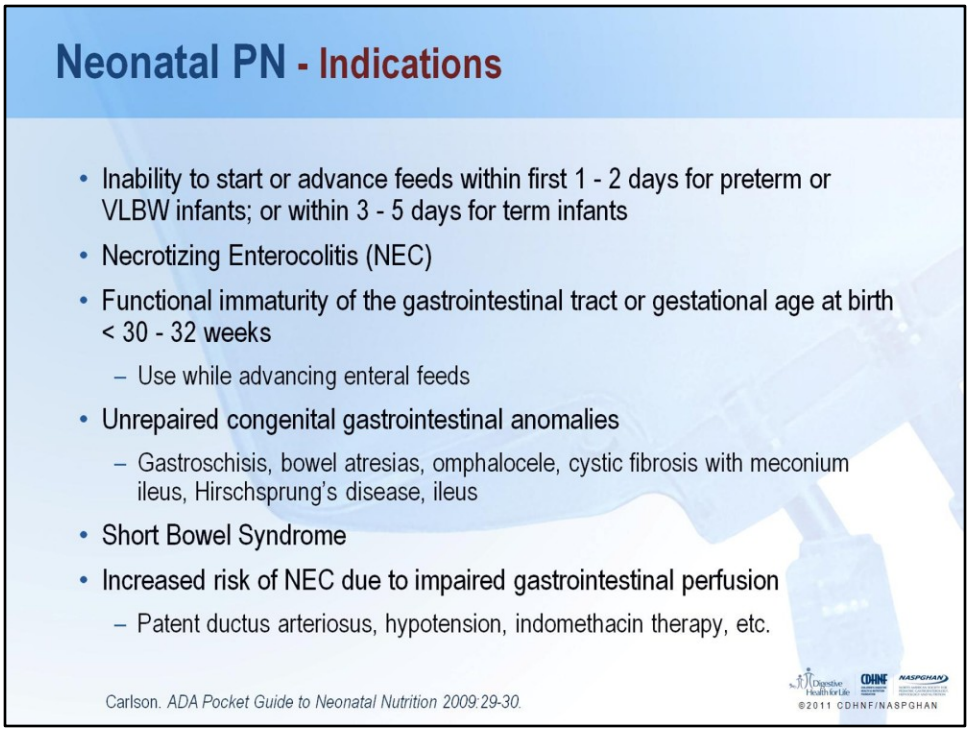
Parenteral Nutrition - Conclusions

- 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

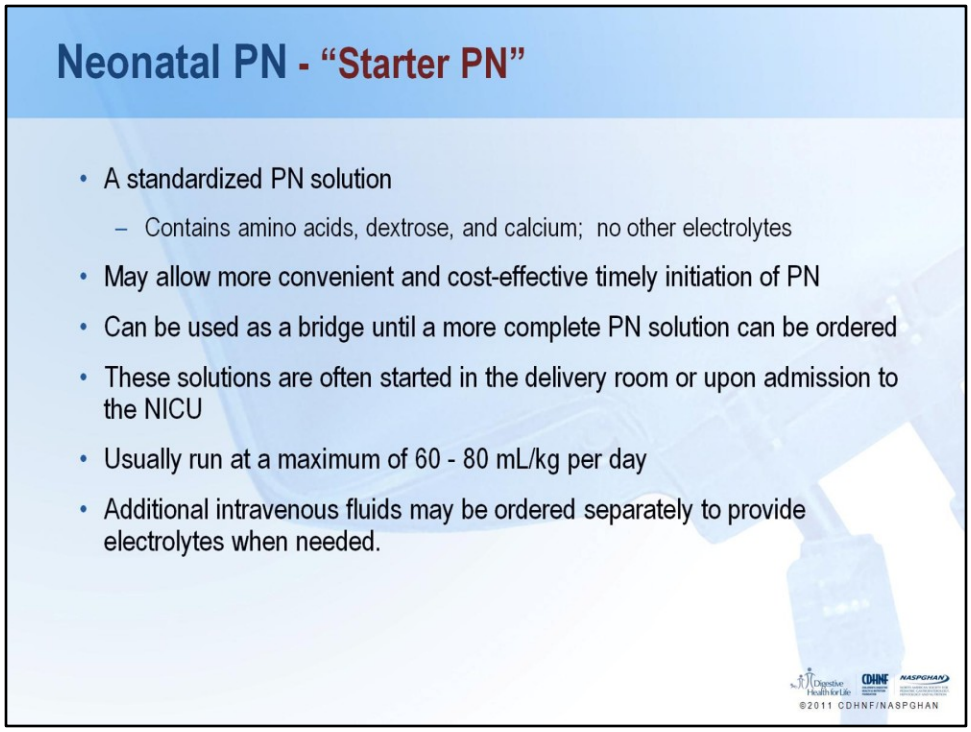
Neonatal Parenteral Nutrition



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.



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



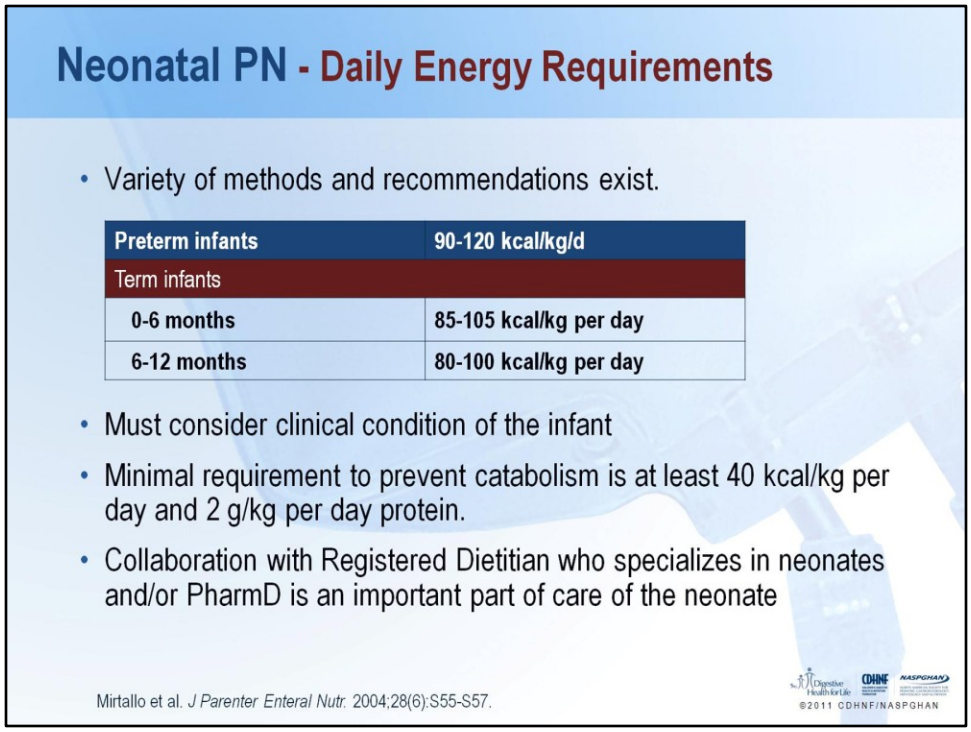
Example Starter PN
•Dextrose 7.5% **OR** 10 %
•Trophamine 4%
•Calcium gluconate 2000 mg/L (9 mEq/L)
•Heparin 0.5 units/mL
•Total volume: 250 mL
•Rate: 60 mL/kg/day

Neonatal PN - Goals

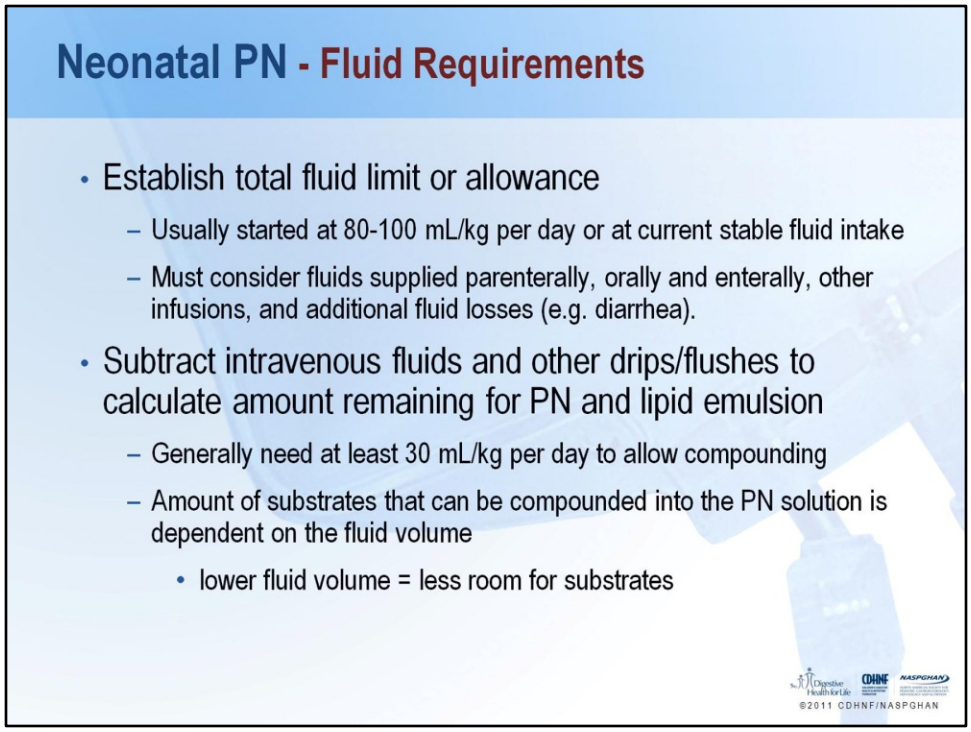
- Primary goals
  - To provide adequate energy and protein to prevent negative energy and nitrogen balance
  - To prevent essential fatty acid deficiency
  - To support normal growth and development
  - To decrease morbidity

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



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.



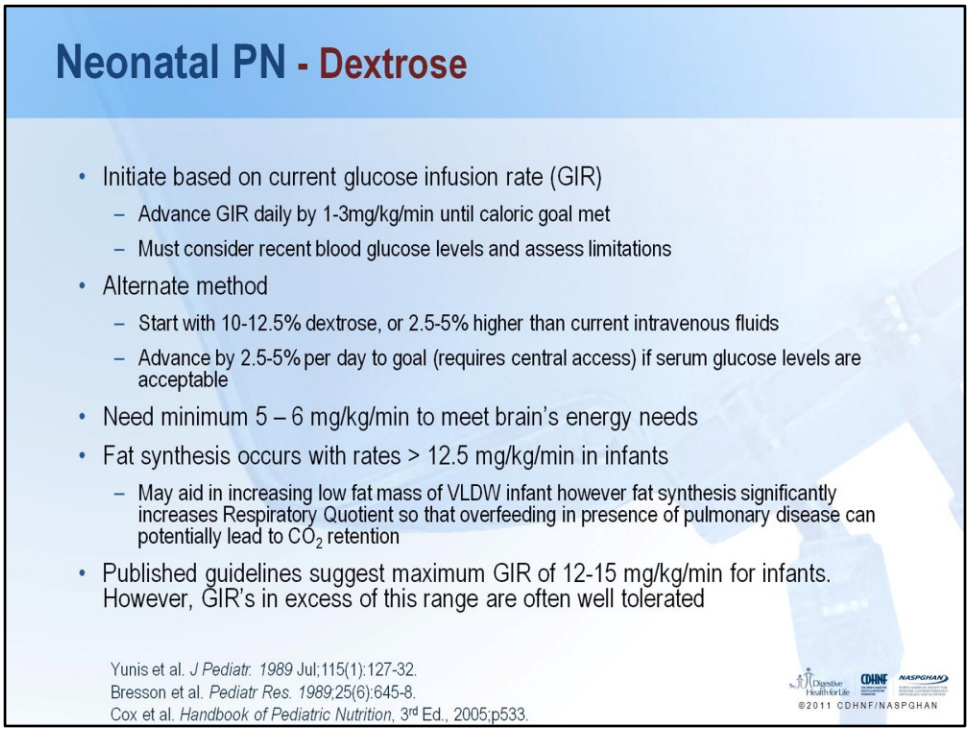
Two options for calculation of PN volume for infants who are also receiving enteral feeds:

(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

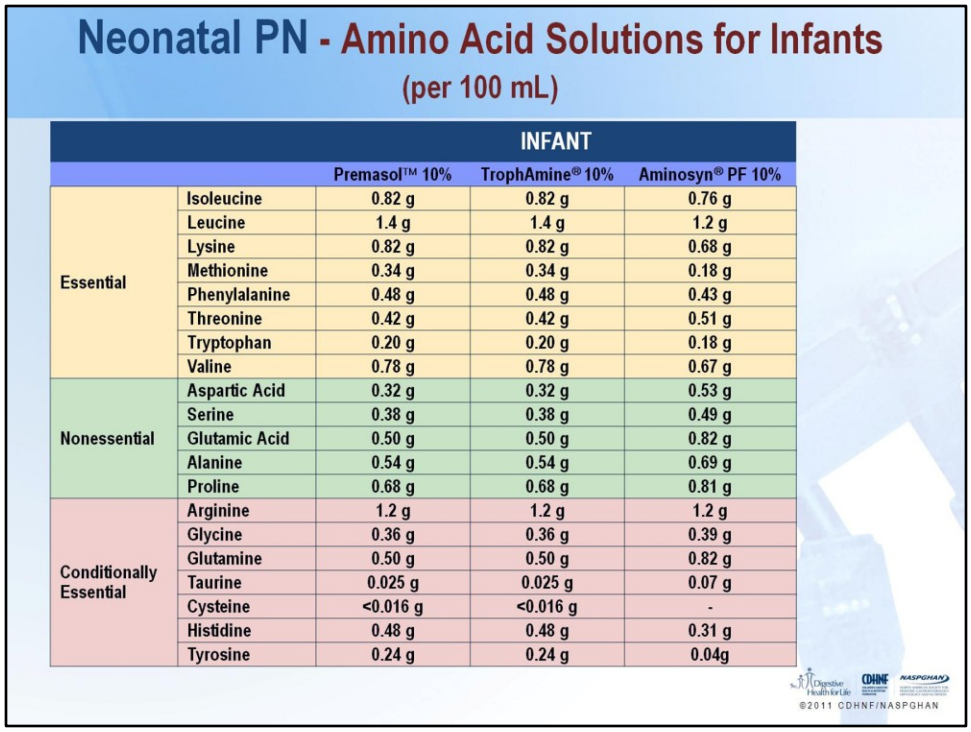
by enteral feedings. The parenteral nutrition composition will vary minimally. The cost of the unused solution is negligible; be aware that the patient will only get a percentage of the micronutrients in the PN bag.

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



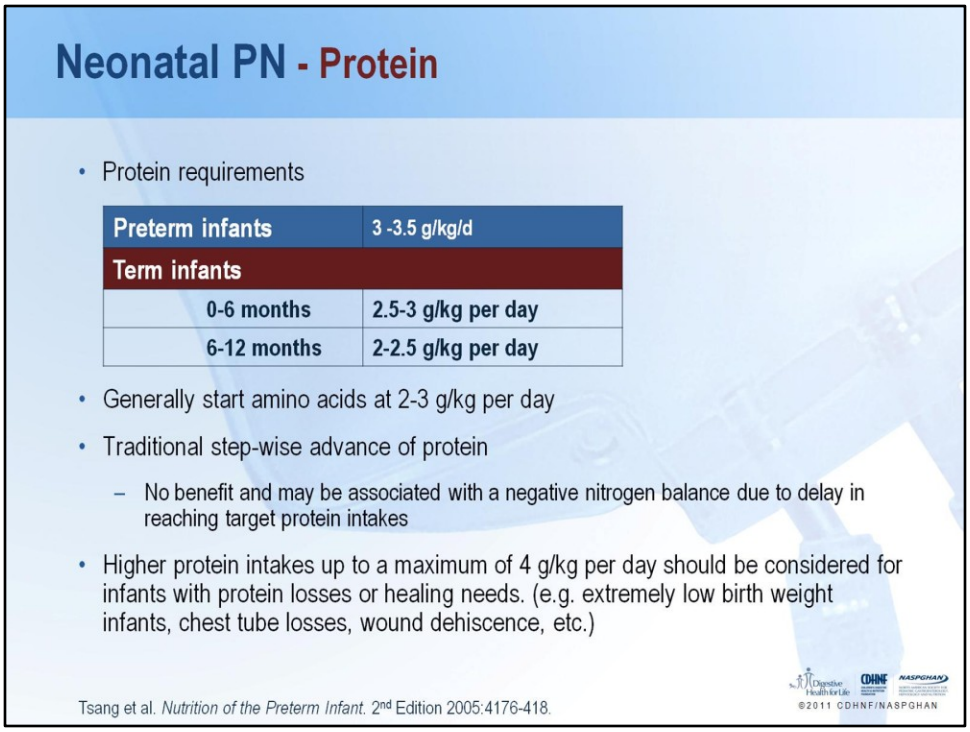
Smaller preterm infants are prone to hyperglycemia and may require a limited GIR or insulin to attain normal glucose levels. The maximum dextrose concentration depends on tolerance and access. A higher GIR is required to compensate for calories when lipids are restricted (e.g. cholestasis prevention, 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.



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.



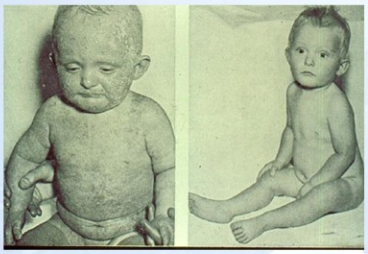
Tsang et al eds. Nutrition of the preterm infant: scientific basis and practical guidelines. *Nutrition of the Preterm Infant*: *Scientific Basis and Practical Guidelines*. Digital Educational Publishing Inc: Cincinnati, OH;2005:4176-418.

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)

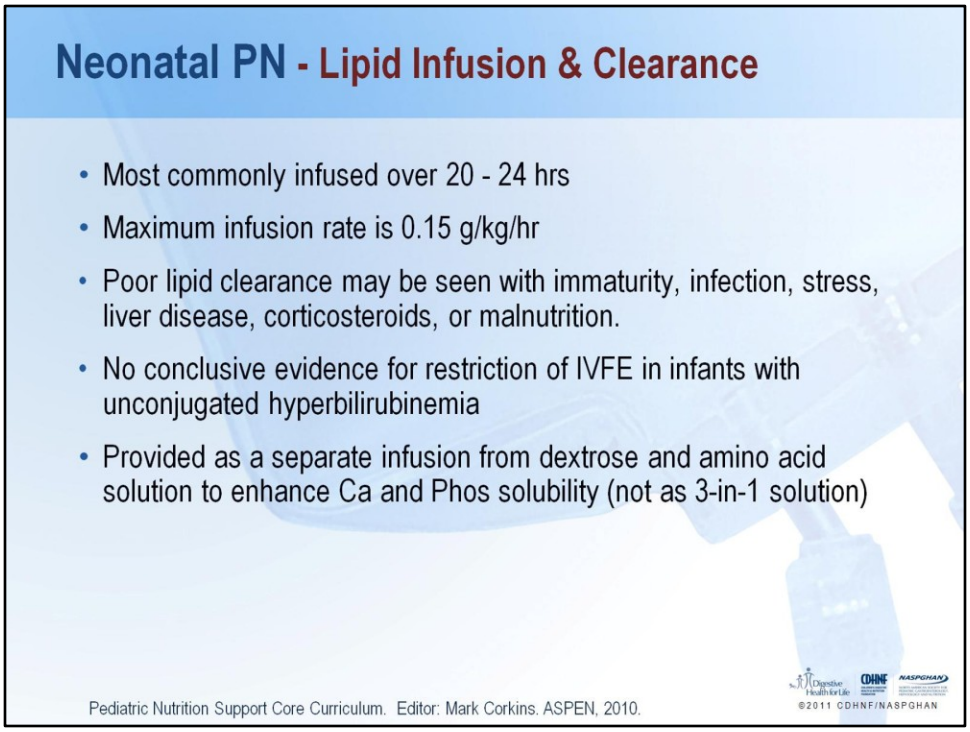
- EFAD can be seen within days of fat-free PN in neonates
- Deficiency is cumulative
- Can cause
  - decreased growth
  - skin and hair changes
  - increased susceptibility to infection,
  - poor wound healing
  - alterations in platelet function
- To avoid EFAD need minimum of
  - 2% to 4% of the total 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 Pereinatol.* 1989;13:118-30.

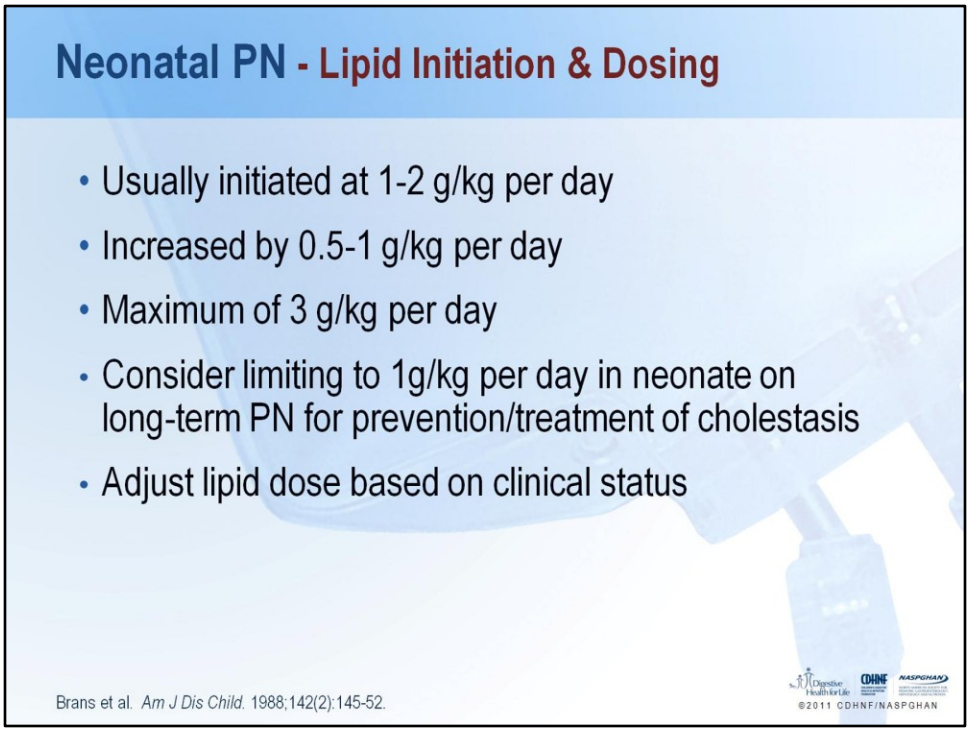
This is a picture of a child with EFAD on the left, and on the right after he was successfully treated.

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



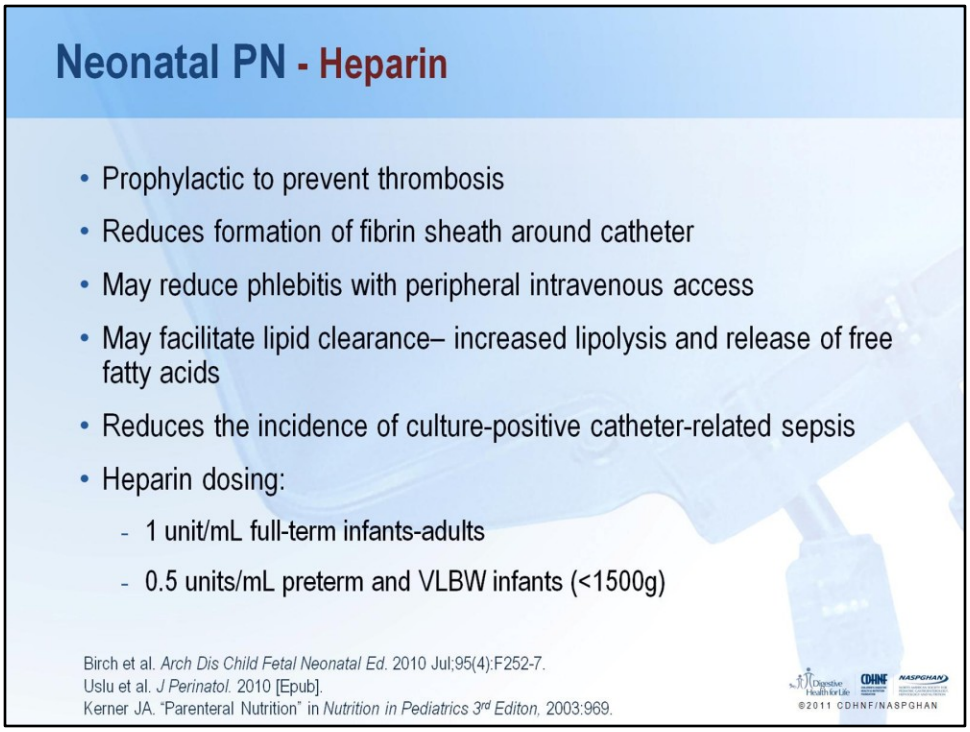
The hang time for lipids is 24 hours for central venous catheters and 12 hours for peripheral catheters.

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



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.

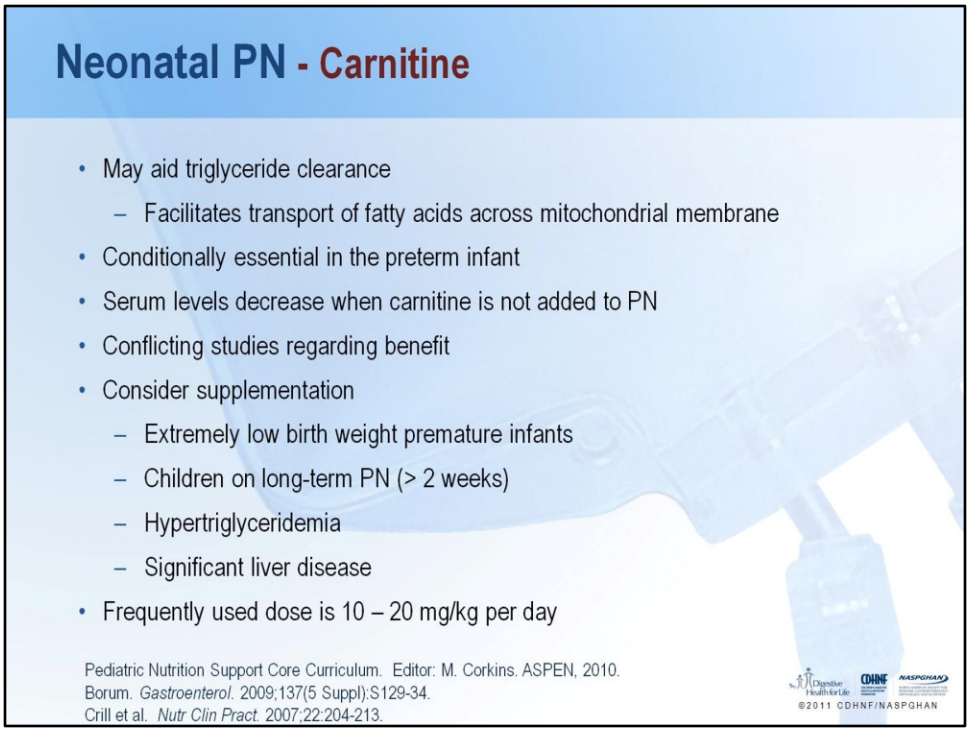


Kerner JA. (2003). Parenteral Nutrition. In Walker, Watkins, & Duggan(Eds.), *Nutrition in Pediatrics , 3rd ed.* (p 969). Hamilton, Ontario: BC Decker, Inc.

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.

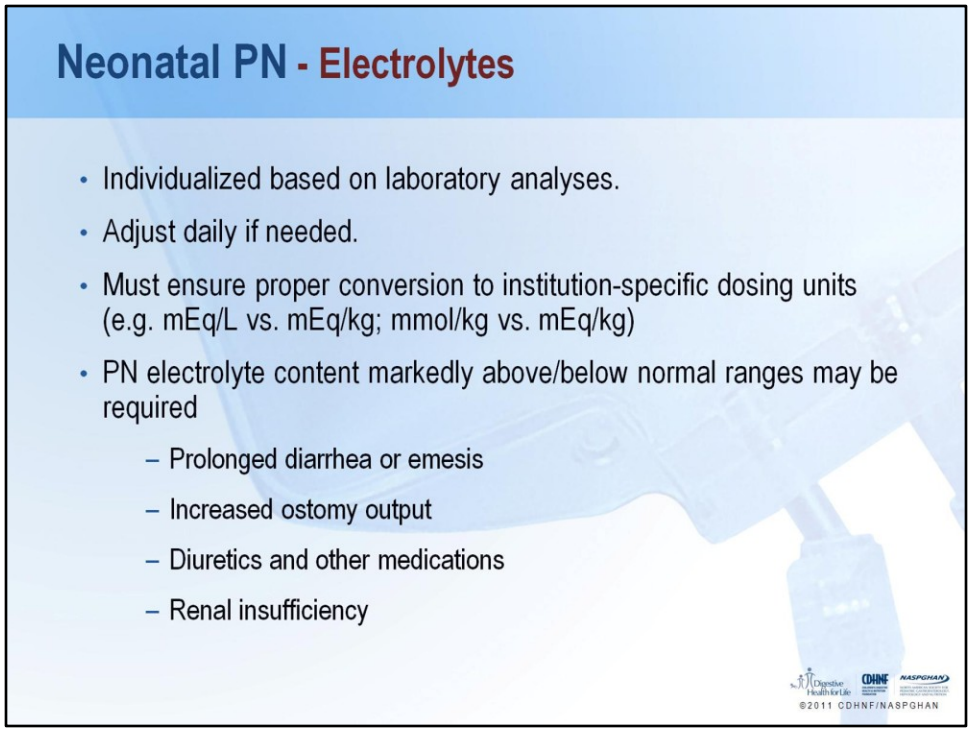
Randolph AG, Cook DJ, Gonzales CA, Andrew M. Benefit of heparin in central venous and pulmonary artery catheters: a meta-analysis of randomized controlled trials.
Chest 1998 Jan;113(1):165-71.

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]

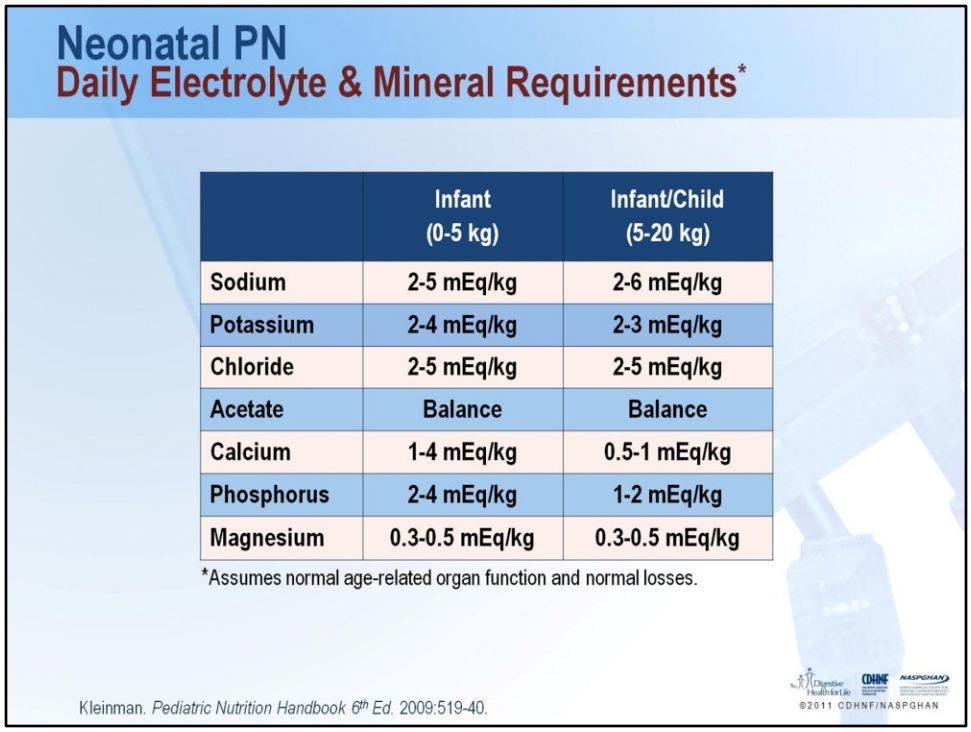


Other published guidelines suggest a frequently used pharmacological intravenous dosage of 10 – 20 mg/kg/day with a maximum dosage of 100 mg/day. However, these dosages are much higher than typical dietary intake and several studies suggest better results with lower doses. Negative effects were exhibited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

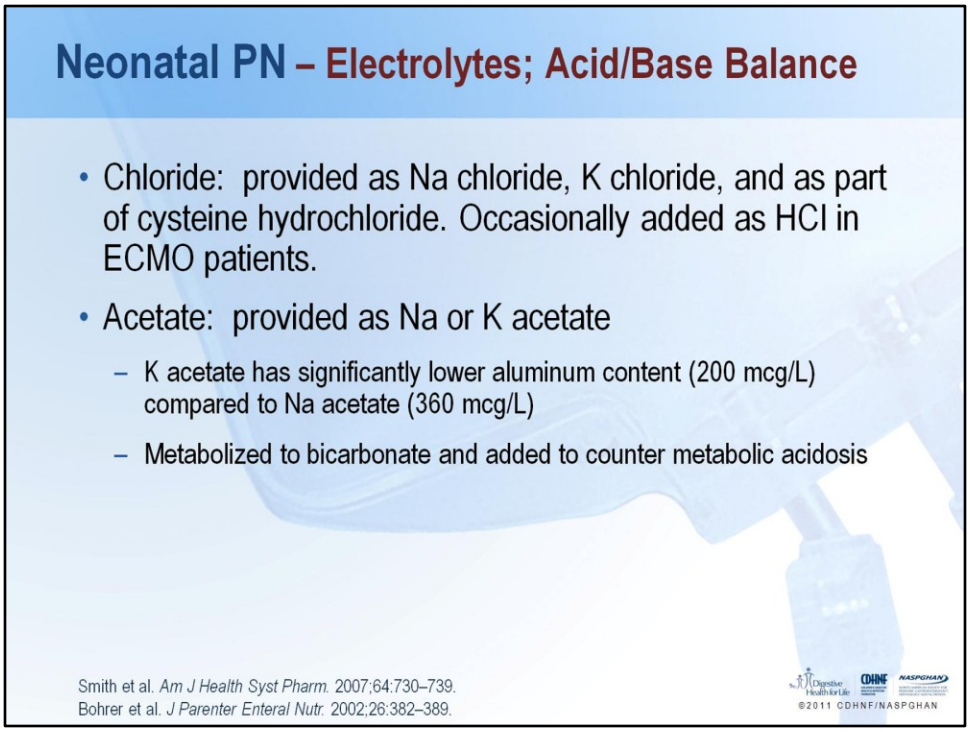


The patient may be getting electrolytes from other sources e.g. umbilical arterial catheter, arterial lines, medications, fluid and electrolyte boluses. Calculation of daily intake should take into consideration these factors and what the patient has received in the last 24 hours.
Consider measuring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



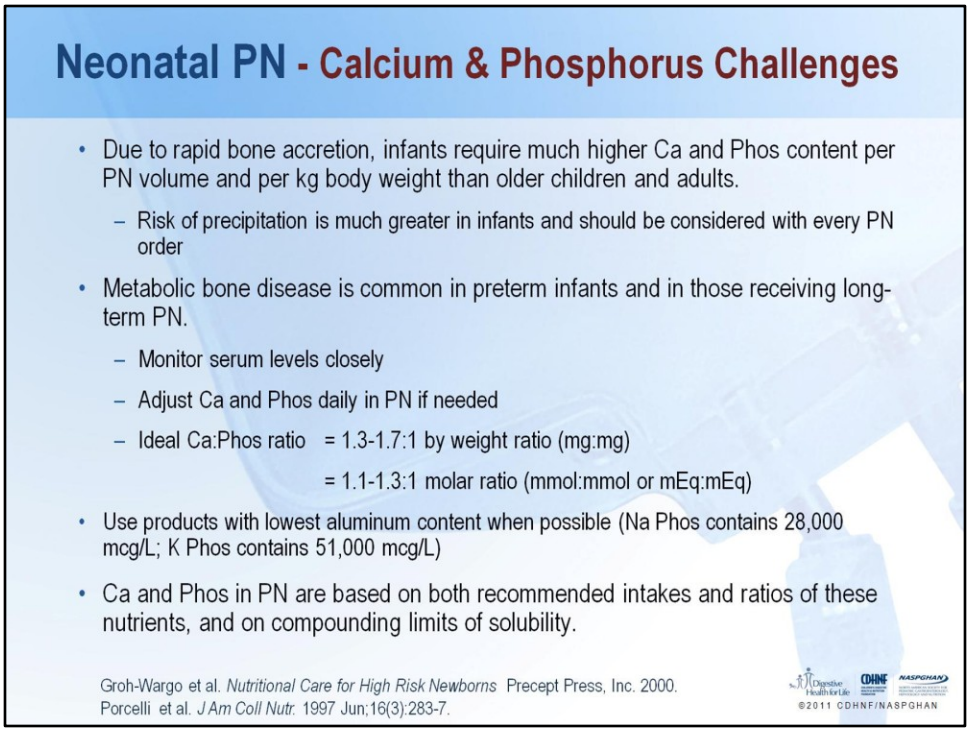
These are suggested daily electrolyte and mineral requirements. Usually start at the lower end of the dose range.
Acetate should be used to correct acidosis and Na or K salt may be used based on serum electrolyte levels.

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.



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.



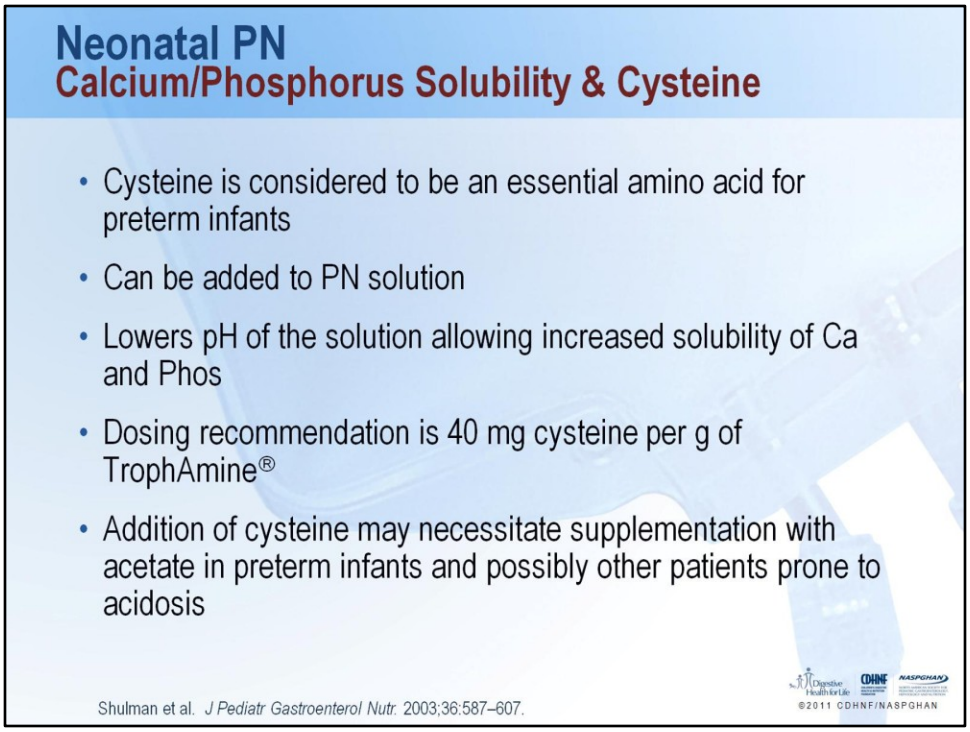
Factors affecting calcium and phosphorus solubility in PN include the following: absolute amounts of calcium and phosphorus, form of calcium salt (calcium gluconate allows improved solubility), order of mixing, pH of the solution (acidic pH allows improved solubility), temperature, amino acid content 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.

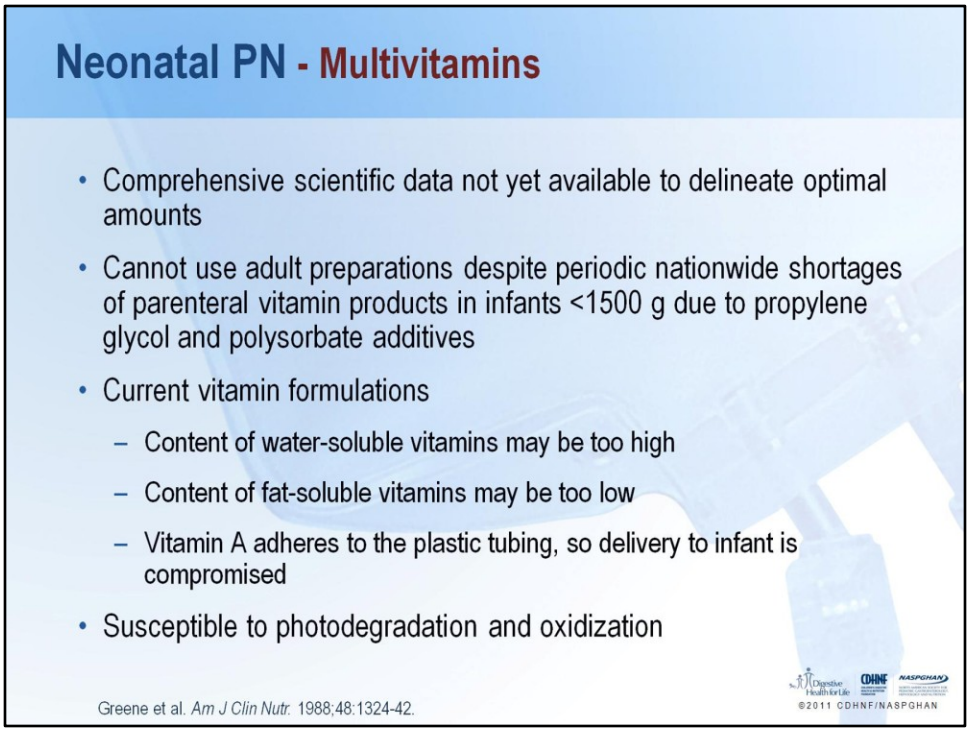
Groh-Wargo, S, Thompson, M, Cox J, (Eds). Nutritional care for high-risk newborns. Chicago, IL: Precept Press, Inc., 2000.

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.

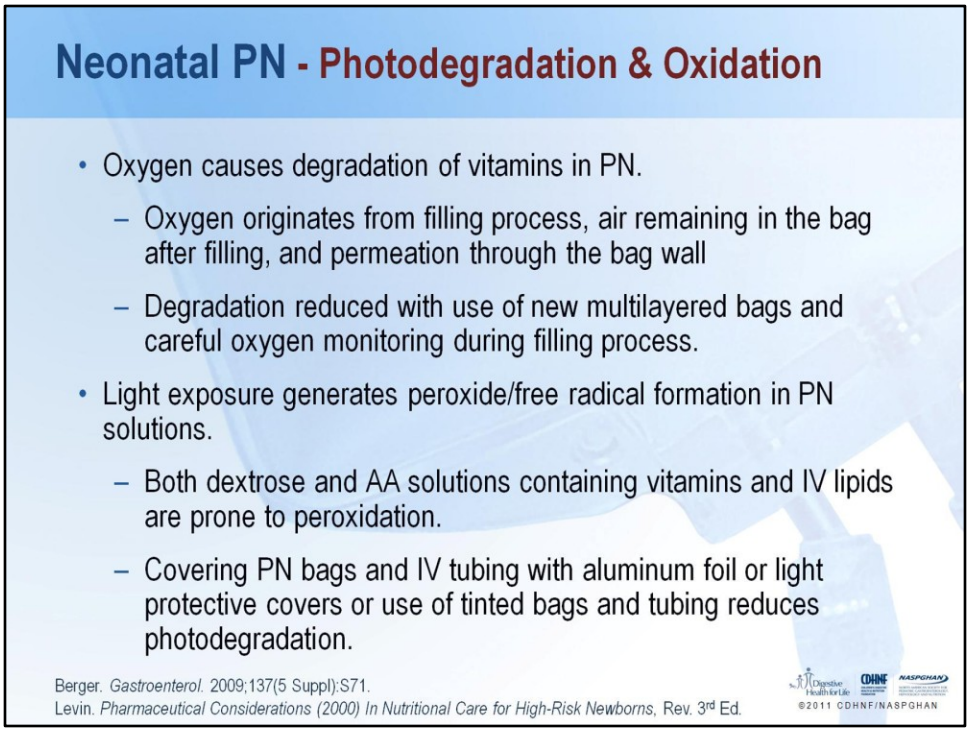


Shulman RJ, Phillips S. Parenteral nutrition in infants and children. J Pediatr Gastroenterol Nutr. 2003 May;36(5):587-607.



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.



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.

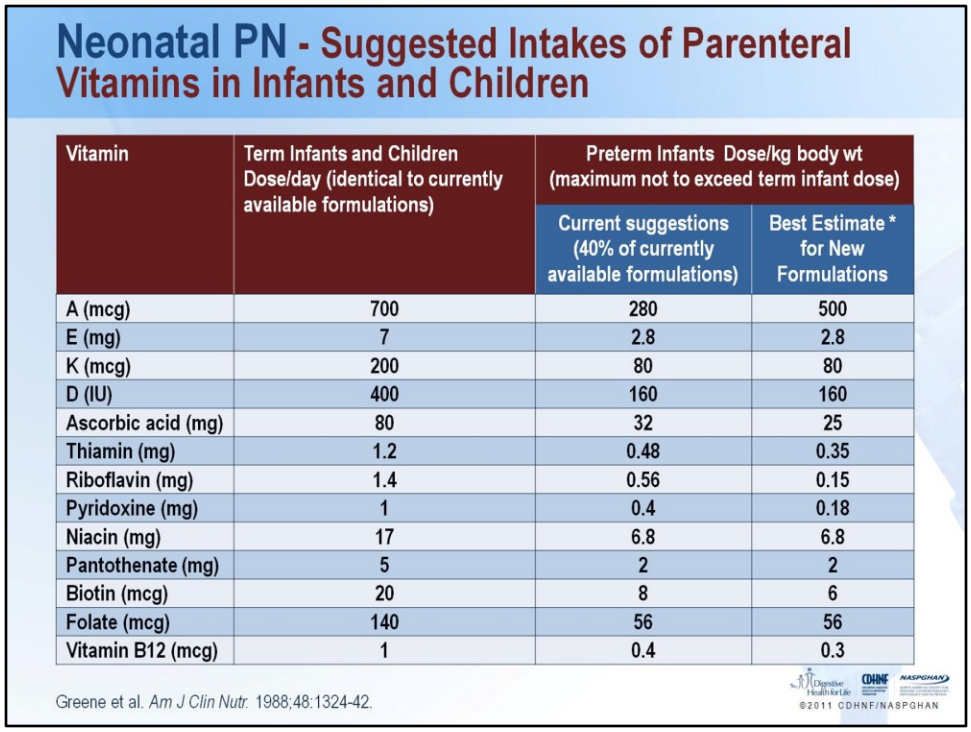
Berger MM. Vitamin C requirements in parenteral nutrition. Gastroenterol. 2009 Nov;137(5 Suppl):S71.
Levin MI and Kyllonen SS. (2000). Parenteral Nutrition: Pharmaceutical Considerations. In S Groh-Wargo, M Thompson, J Cox(Eds.), Nutritional Care for High-Risk Newborns, Rev. 3rd ed. (p. 187). Chicago, 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 mg 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 mg 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_pediatric_PI.pdf
http://www.infuvite.com.PDF/infuvite_PackageInsert.pdf



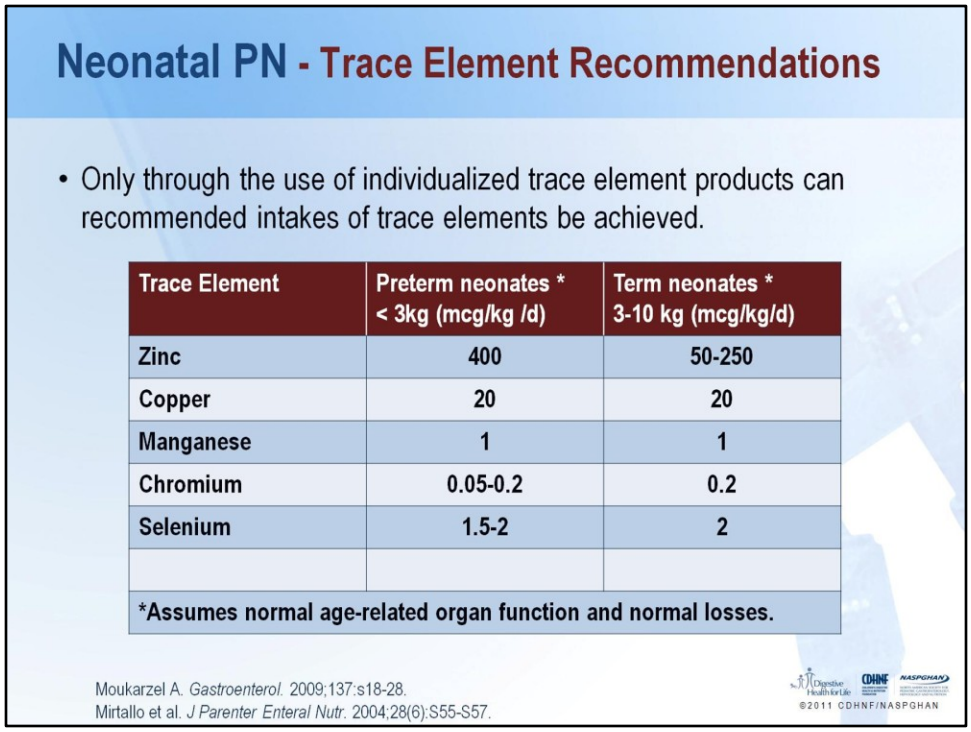
Neonatal PN - Suggested Intakes of Parenteral Vitamins in Infants and Children

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.

*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.



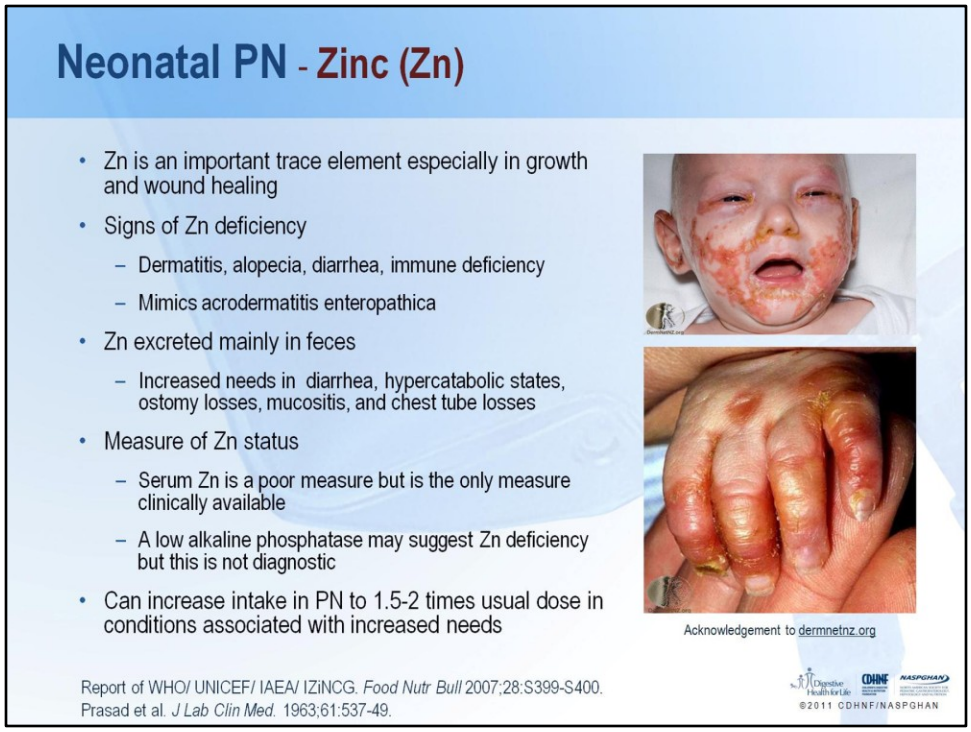
There are more than 60 minerals which are integrated into various body processes: chromium, copper, iodine, manganese, molybdenum, selenium, zinc etc. Zinc is often required in larger amounts than suggested. Iron may not be routinely included to PN solutions. Optimal requirements for trace elements for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

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.

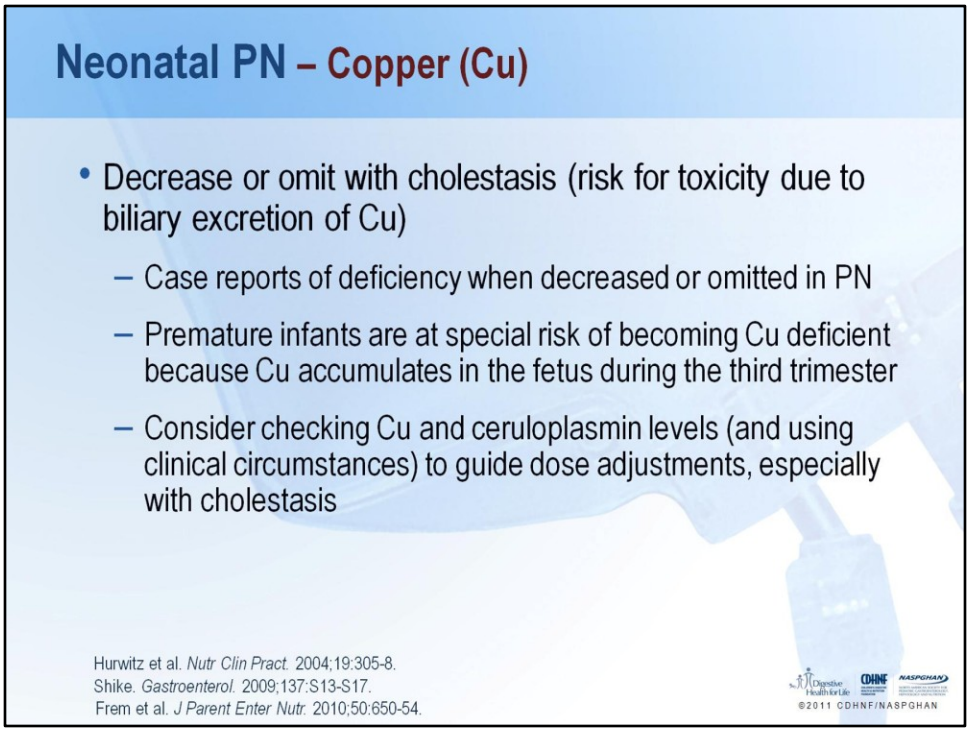


Zinc is essential to the structural integrity of proteins, which regulate gene expression, and to nuclear binding proteins that act as transcription factors . It is a component of more than 250 metalloenzymes including alcohol, lactate and pyruvate dehydrogenases, alkaline phosphatase, and DNA and RNA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

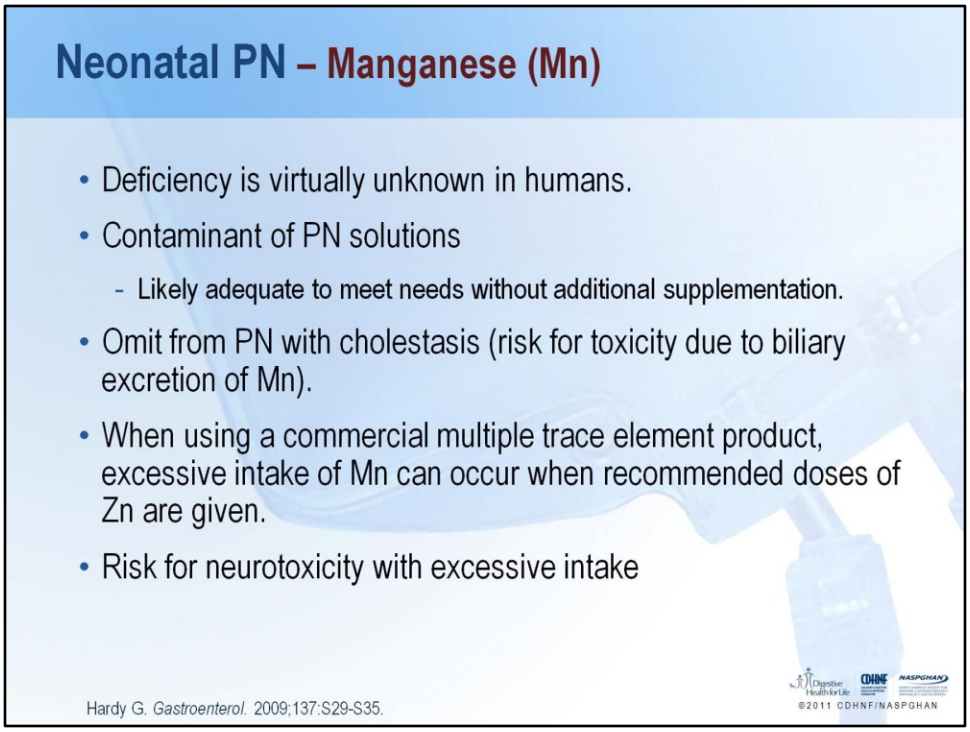
Executive summary. Recommendations for indicators of population zinc status. Report of WHO/ UNICEF/ IAEA/ IZiNCG Interagency meeting on zinc status indicators. Food Nutr Bull, 2007;28:S399-S400.

Standing Committee on the Scientific Evaluation of Dietary References 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).

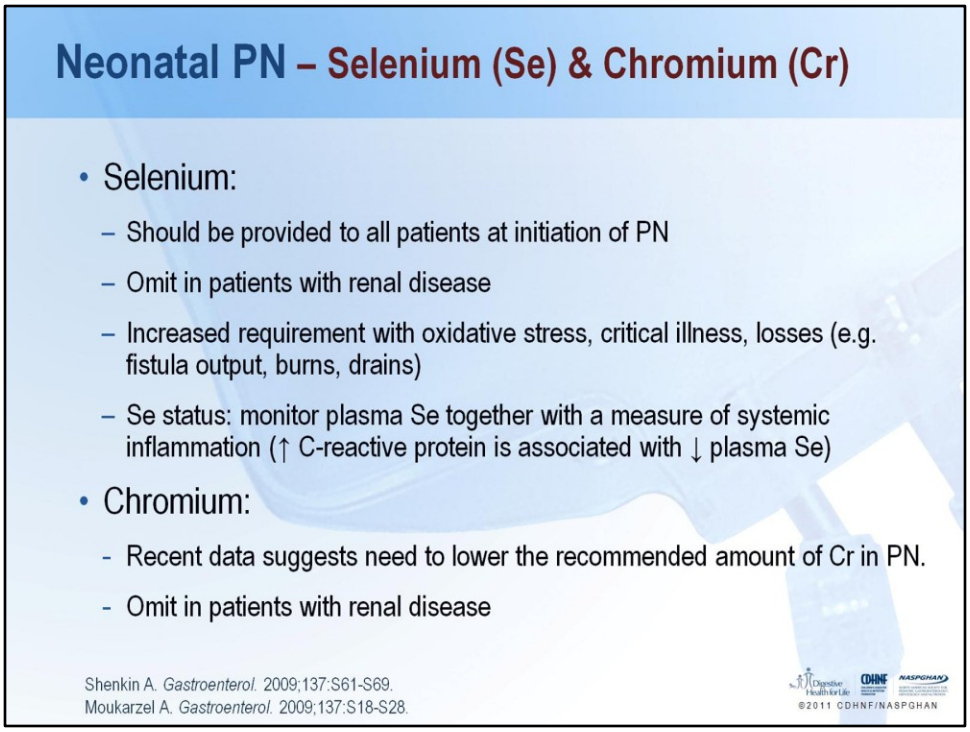
Prasad AS, Miale A Jr, Farid Z, et al. Zinc metabolism in patients with the syndrome of iron deficiency anemia, hepatosplenomegaly, dwarfism, and hypogonadism. J Lab Clin Med. 1963 Apr;61:537-49.



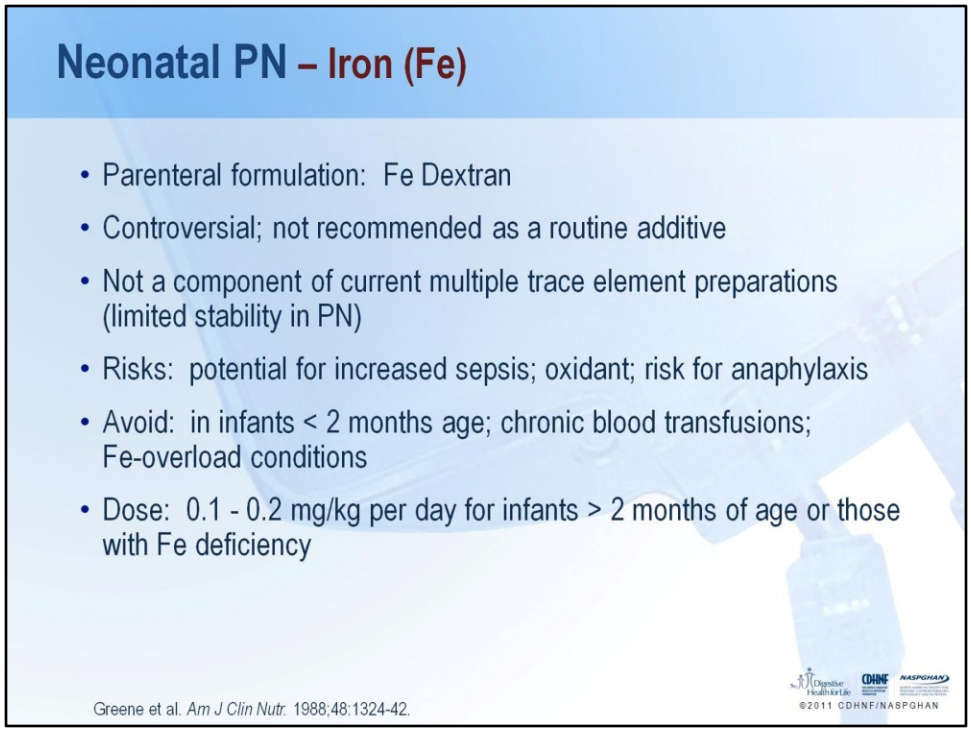
Hurwitz M, Garcia MG, Poole RL, et al. Copper Deficiency. Gastroenterology. 2009 Nov;137(5 Suppl):S13-7.
Shike M. Copper in parenteral nutrition. Nutr Clin Pract. 2004 Jun;19(3):305-8.
Frem J, Sarson Y, Sternberg T, et al. Copper supplementation in parenteral nutrition of cholestatic infants. J Pediatr Gastroenterol Nutr. 2010 Jun;50(6):650-4.



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



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.



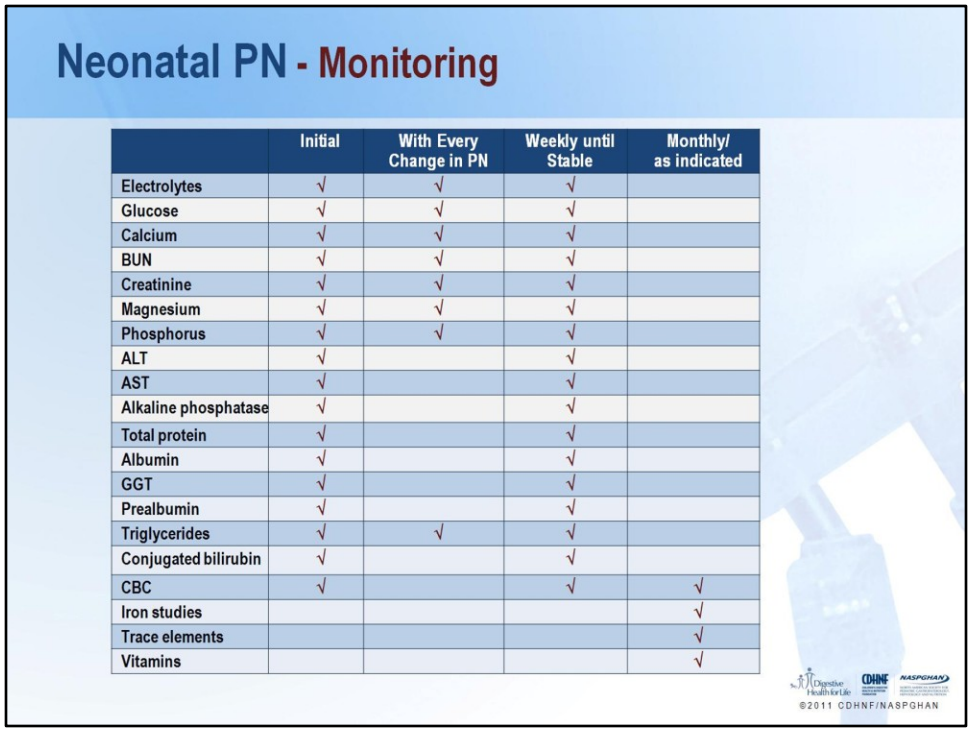
Other parenteral Fe preparations include Fe sucrose and Fe tri-phosphates. Fe Dextran is compatible with non-lipid containing PN. Due to the recent black box warnings, may want to consider administration of Fe Dextran under supervision, at least initially. When Fe Dextran infusions are used to treat 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

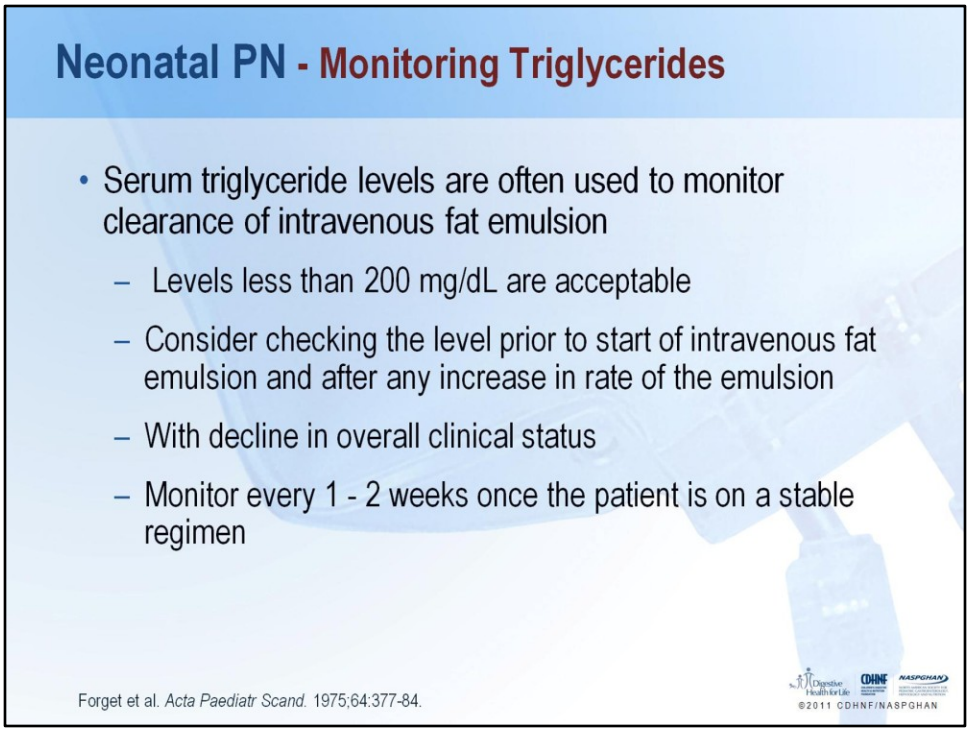
In a retrospective adult study of 55 patients treated with home PN for more than 6 months, 30/55 (55%) had evidence of Fe deficiency anemia (10/30 at time of start of PN and 20/30 between 2-97 months after start of PN (mean age 28 months). Loss from GI tract was most prominent reason.

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.



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.



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

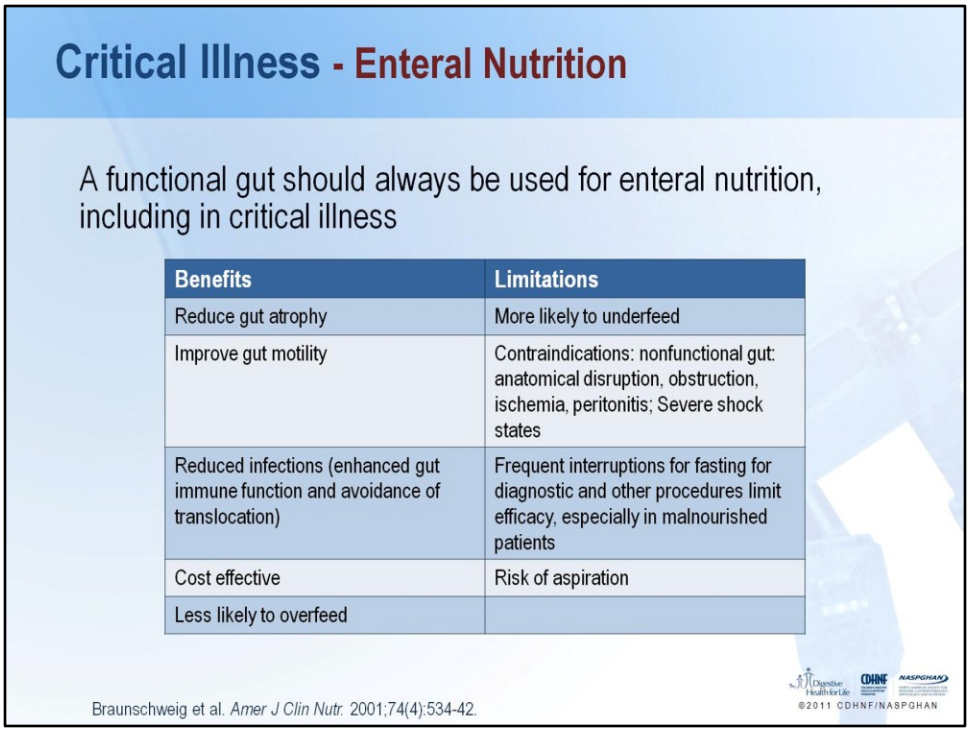
Neonatal PN - Discontinuing Parenteral Nutrition

- 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

Parenteral Nutrition For The Specialized Patient

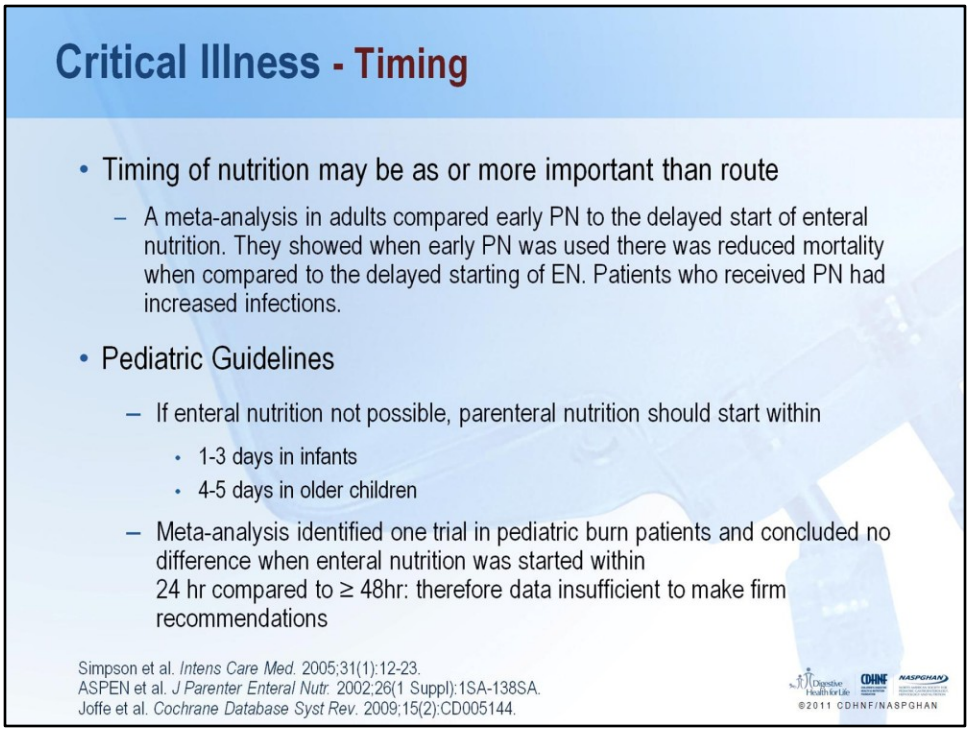
Parenteral Nutrition – Specialized Patient

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



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)

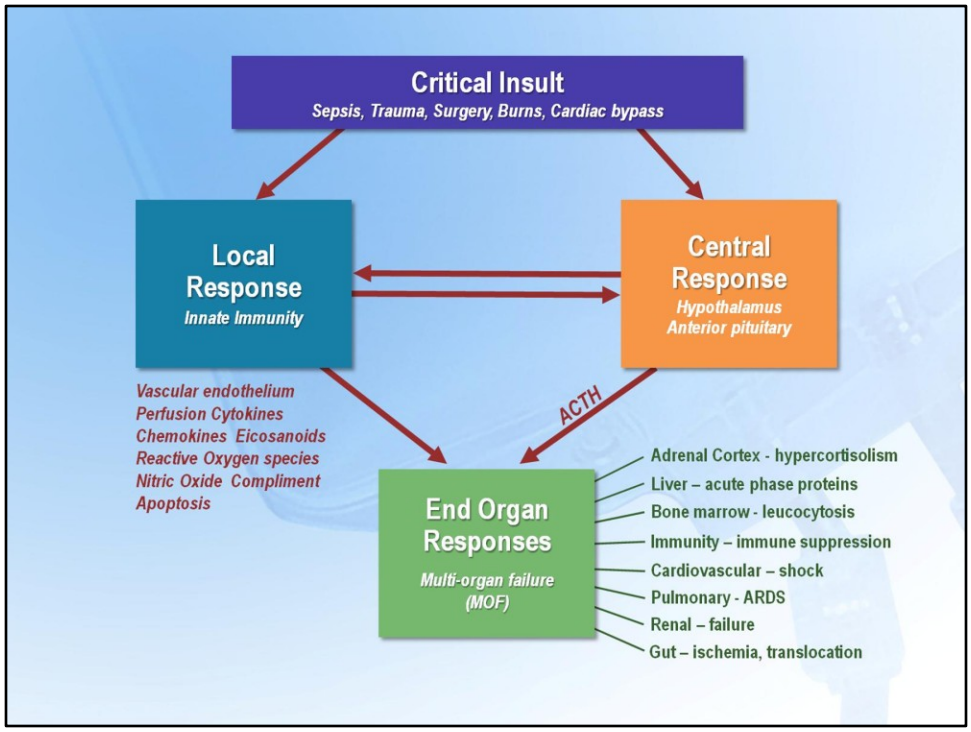
Braunschweig CL, et al. Enteral compared with parenteral nutrition: a meta-analysis. Amer J Clin Nutr. 2001;74(4):534-42.



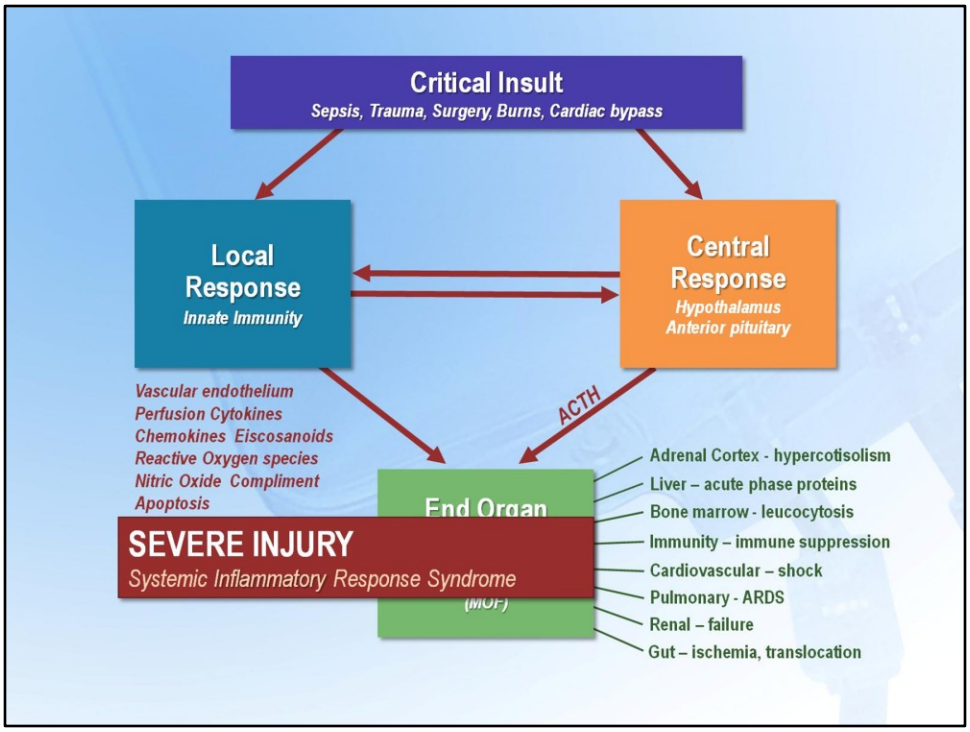
Simpson F, Doig GS. Parenteral vs. enteral nutrition in the critically ill patient: a meta-analysis of trials using the intention to treat principle. Intens Care Med 2005; 31(1):12-23.

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.



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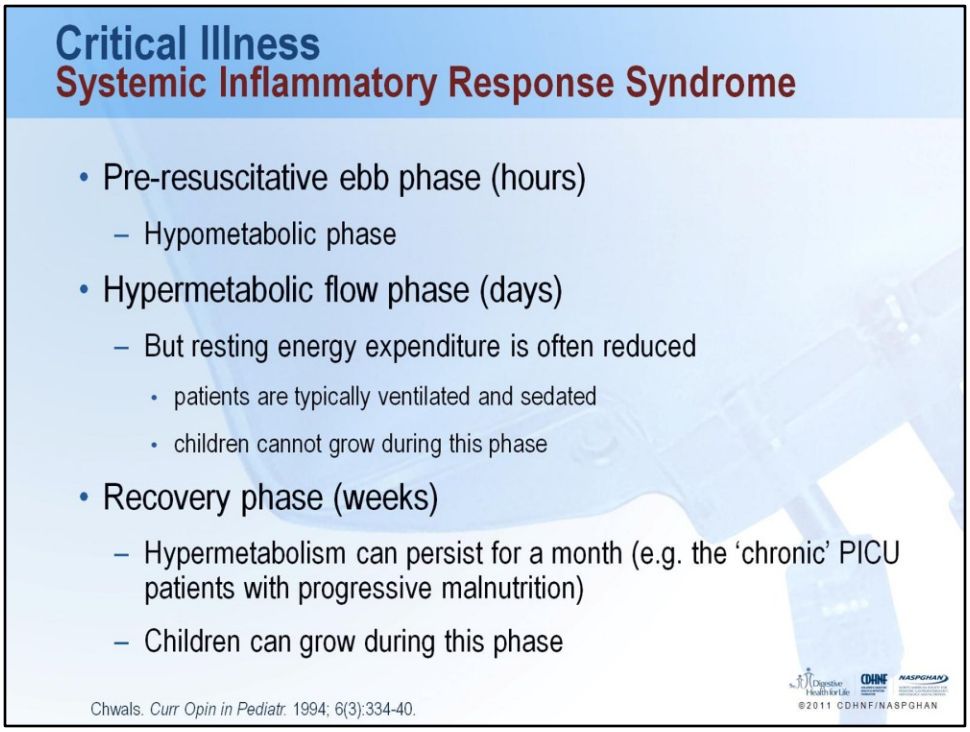


This data is from a review based largely on opinion and clinical experience.

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.

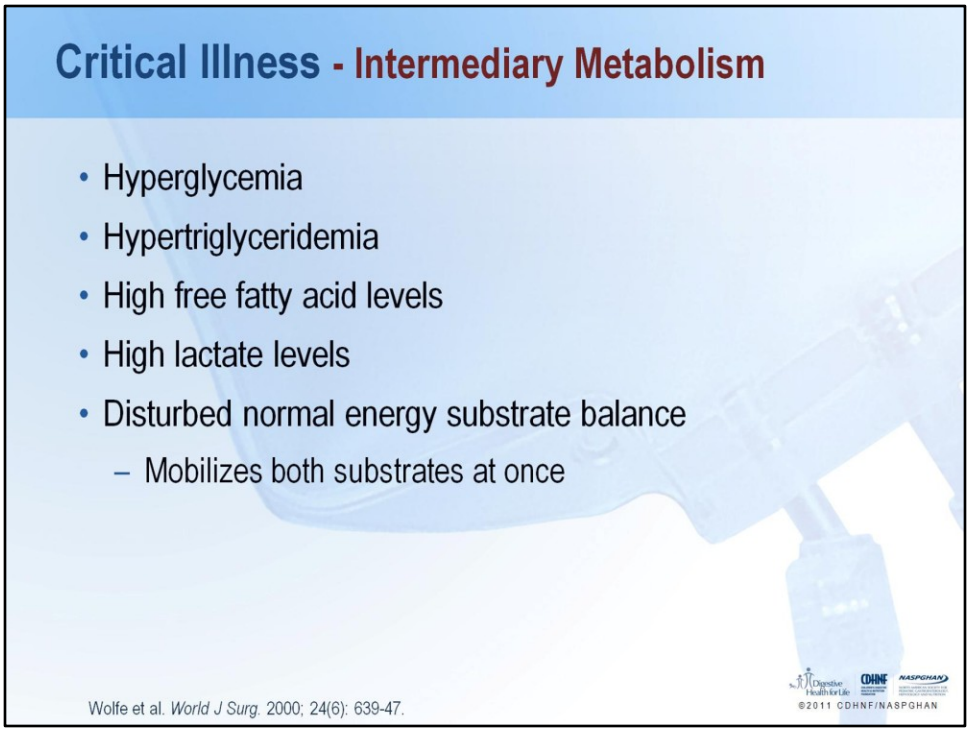
The subsequent hypermetabolic phase last days and is dominated by the production of cytokine, endotoxin and reactive oxygen metabolites which are produced in response to injury, inflammation and often sepsis. Tissue reperfusion occurs at this stage.

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.

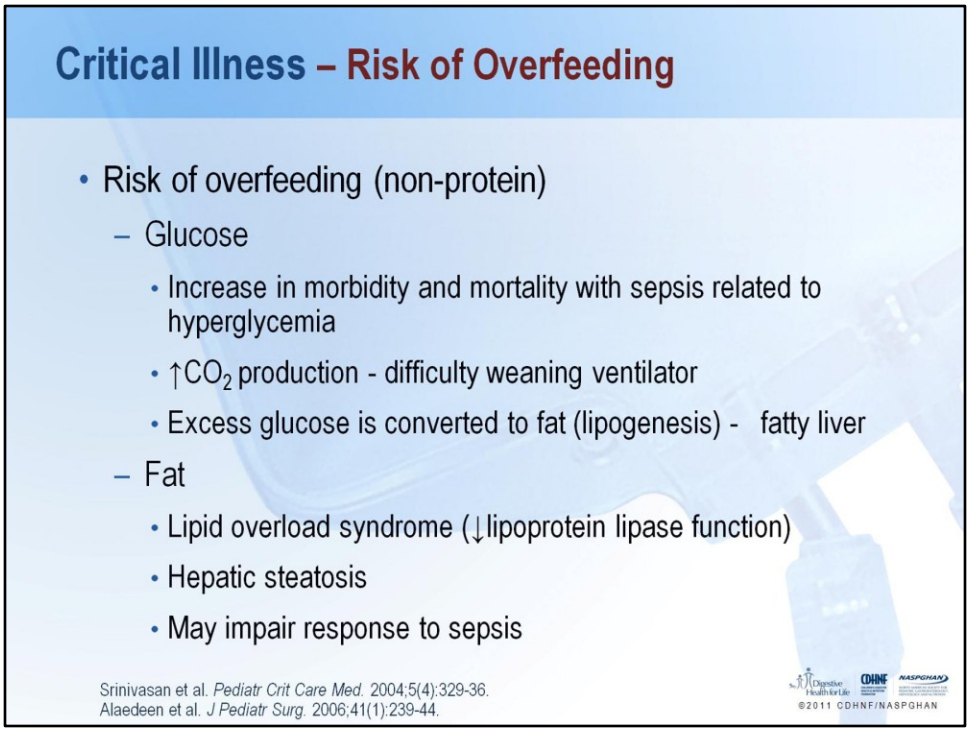
Chwals WJ. The metabolic response to surgery in neonates. Curr Opin Pediatr. 1994;6(3):334-40.



In healthy states our normal response to **fasting** is first to mobilize glycogen stores from the liver. Amino acids are used for gluconeogenisis 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. Trigylcerides 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.



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.

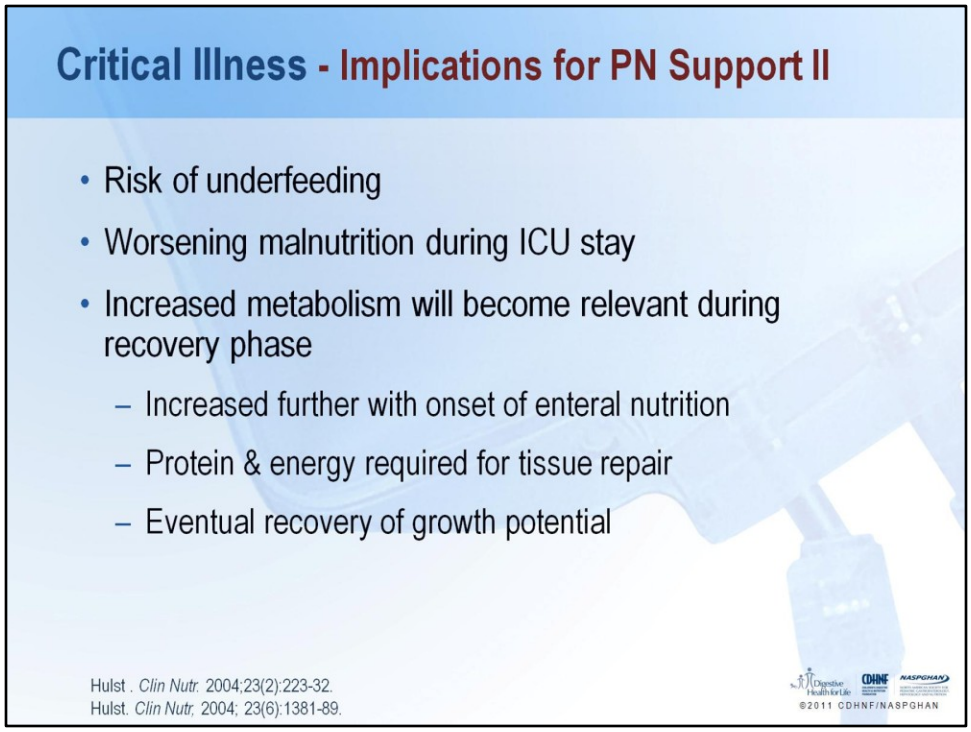
High glucose levels in children with critical illness are associated with more mortality, length of stay and ventilator days, particularly given concomitant sepsis. Poor diabetic control is also associated with poor wound healing and sepsis and supports the role of elevated circulating glucose in critical 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.
Alaedeen 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.

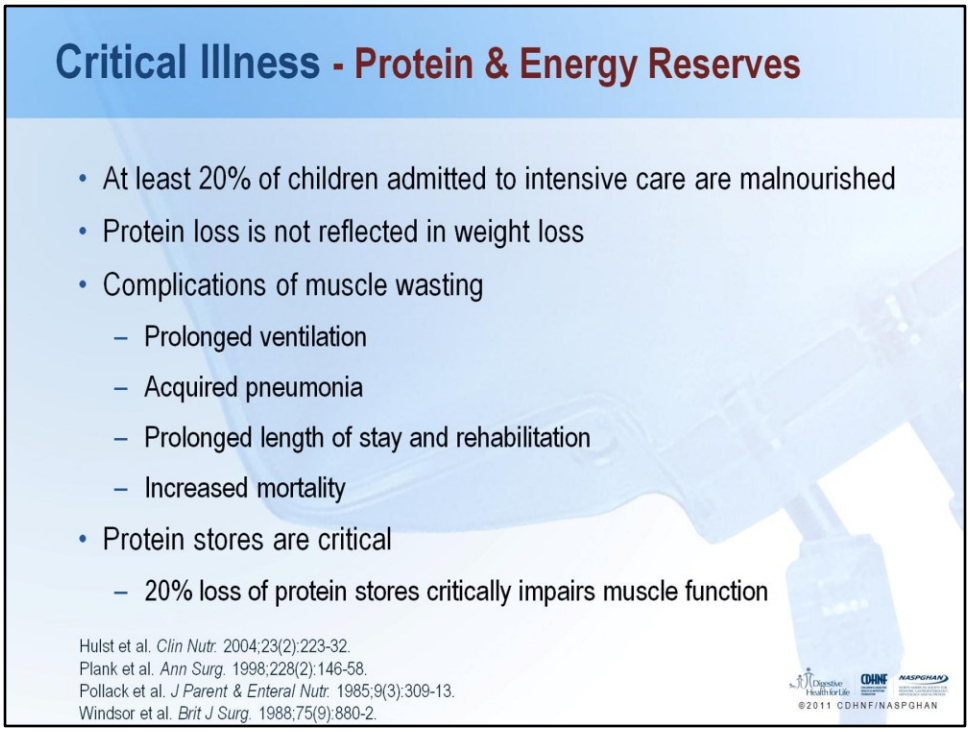


The critical care patient is also at risk of not meeting intended nutrient delivery due to the following reasons:
1) frequent interruptions from fasting for procedures or investigations
2) limitations in fluid delivery and need for fluid restriction
3) delayed introduction of caloric feeding and the difficulties in accurately predicting calorie requirements (predicting energy requirements).

Pediartic 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.

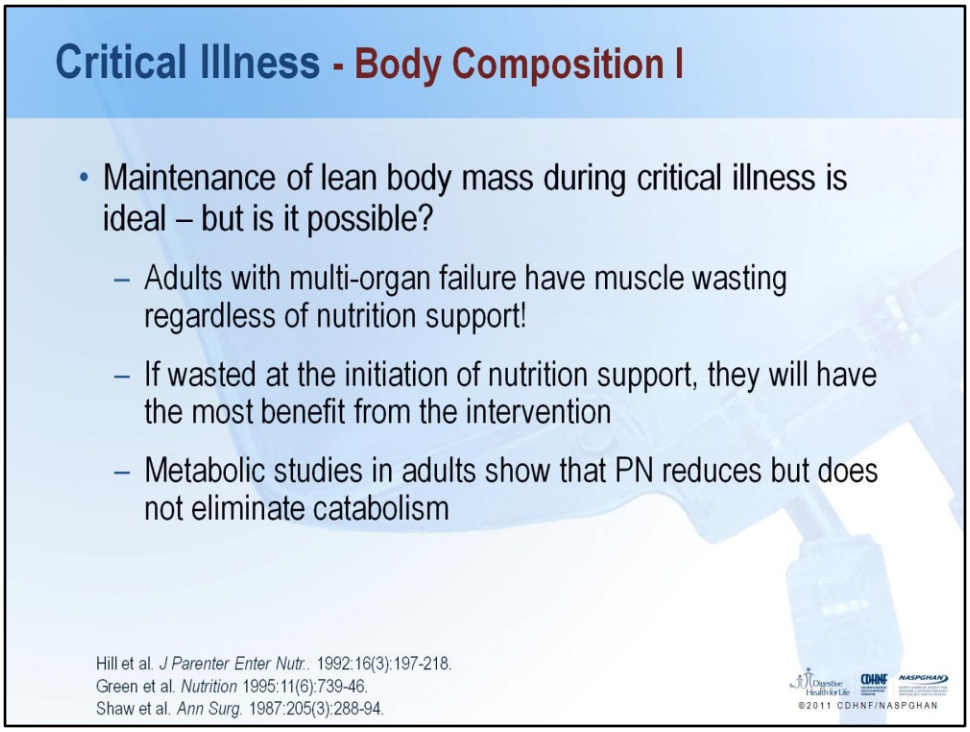
Specifically as patients enter the recovery phase of the systemic inflammatory response and when they begin enteral feeding, they are at risk of not having calorie delivery increased to meet the requirements for tissue repair, re-emerging growth potential and increased thermic effect of food.

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.

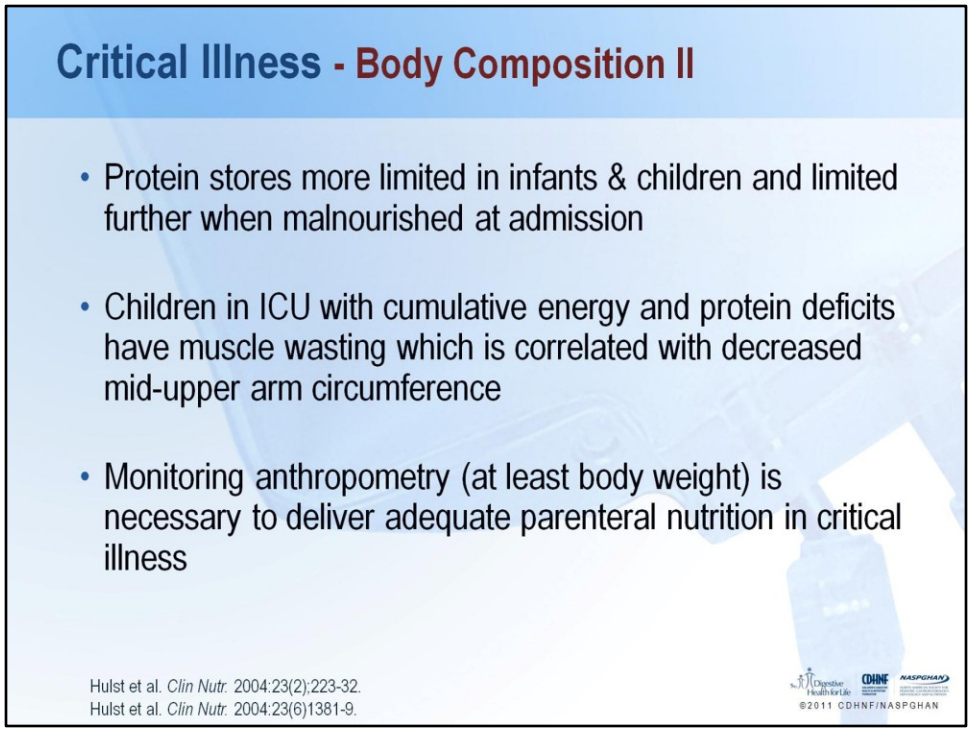


Malnutrition is common in children admitted to PICU (Hulst et al) and worsens over the length of stay.

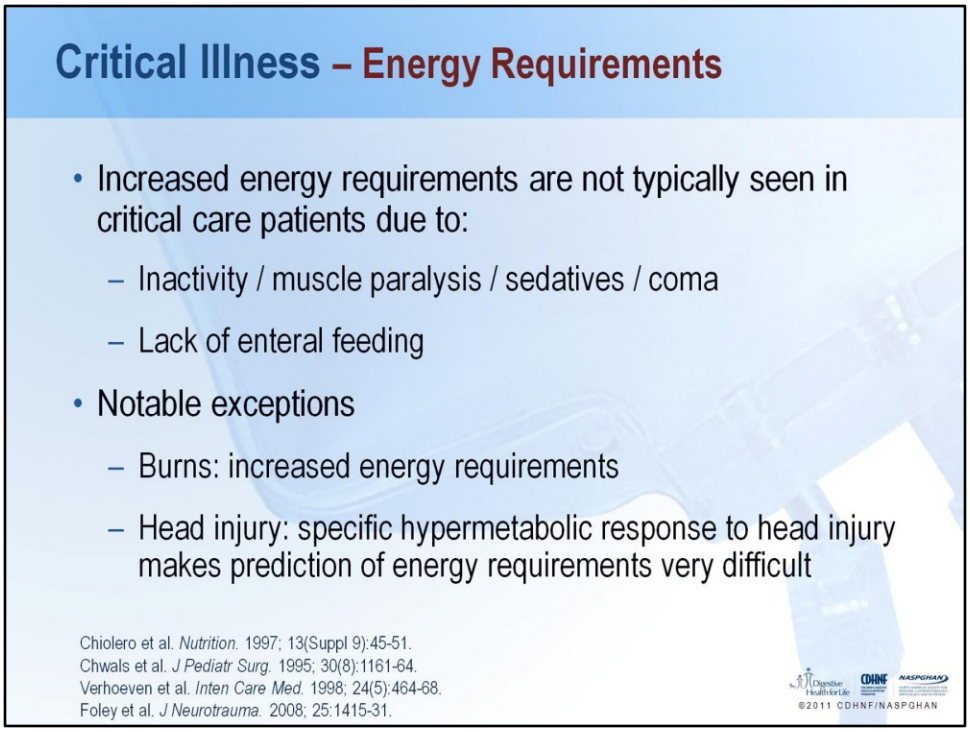
The main prognostic factor is loss of lean mass – associated most importantly with increased mortality (Pollack et al).



Hill GL. Body composition research: implications for the practice of clinical nutrition. J Parenteral 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.



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.



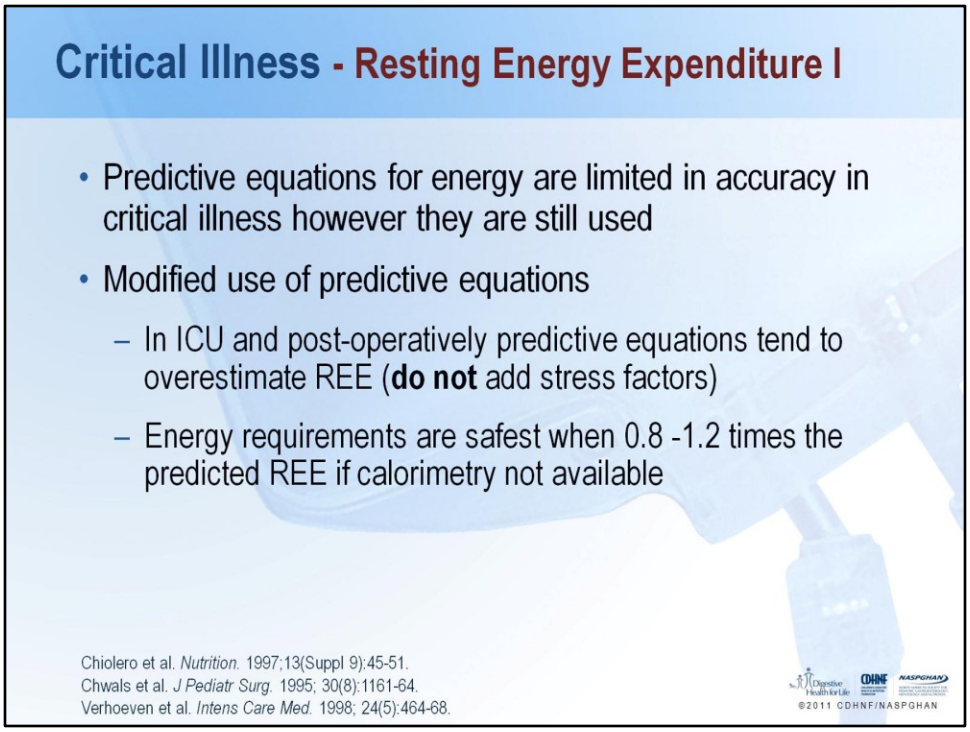
We used to think that hypermetabolic patients required more energy however this is not the case! Factors to explain this are documented on this slide and these inlcude: 1) neuro-protection through cooling, 2) lack of thermic effect of enteral feeding, and 3) use of drugs like sedatives, beta blockers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

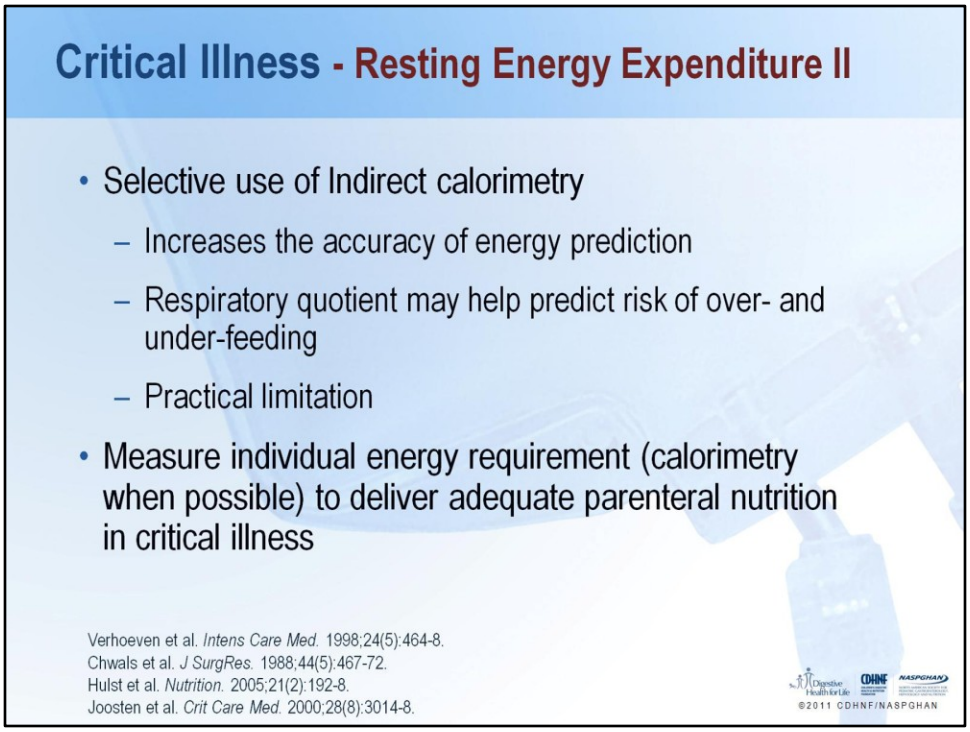
Chioléro R, Revelly JP, Tappy L. Energy metabolism in sepsis and injury. *Nutrition*. 1997 Sep;13(9 Suppl):45S-51S.
Chwals WJ, Letton RW, Jamie A, et al. Stratification of injury severity using energy expenditure response in surgical infants. *J Pediatr Surg.* 1995;30(8):1161-4.
Verhoeven JJ, Hazelzet 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.

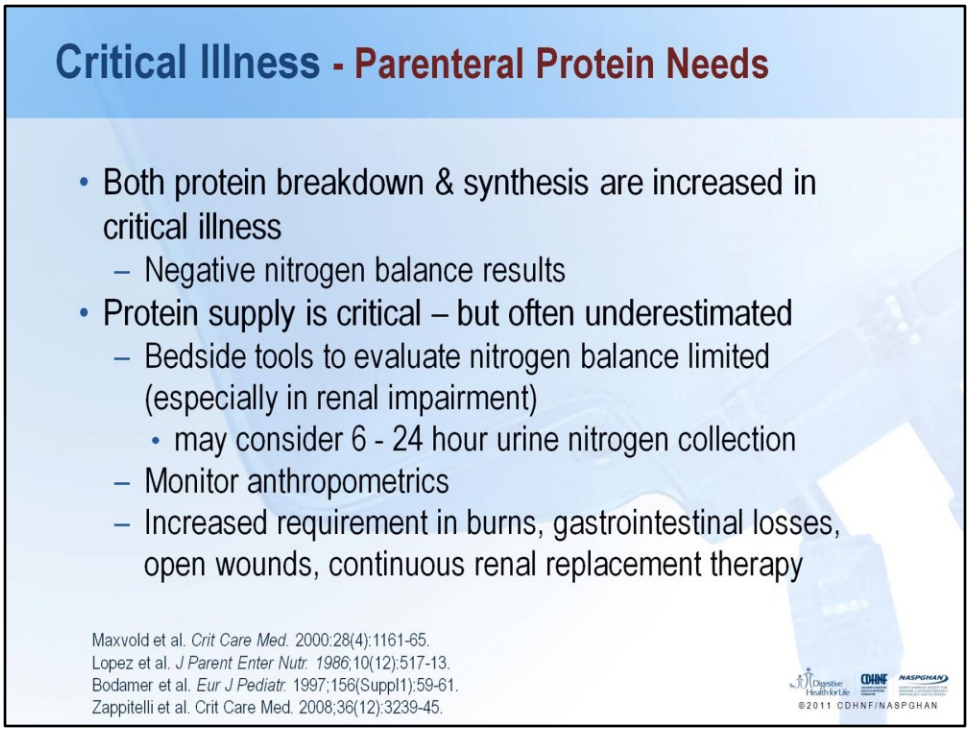


More information can be found on energy expenditure via the following references:

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.

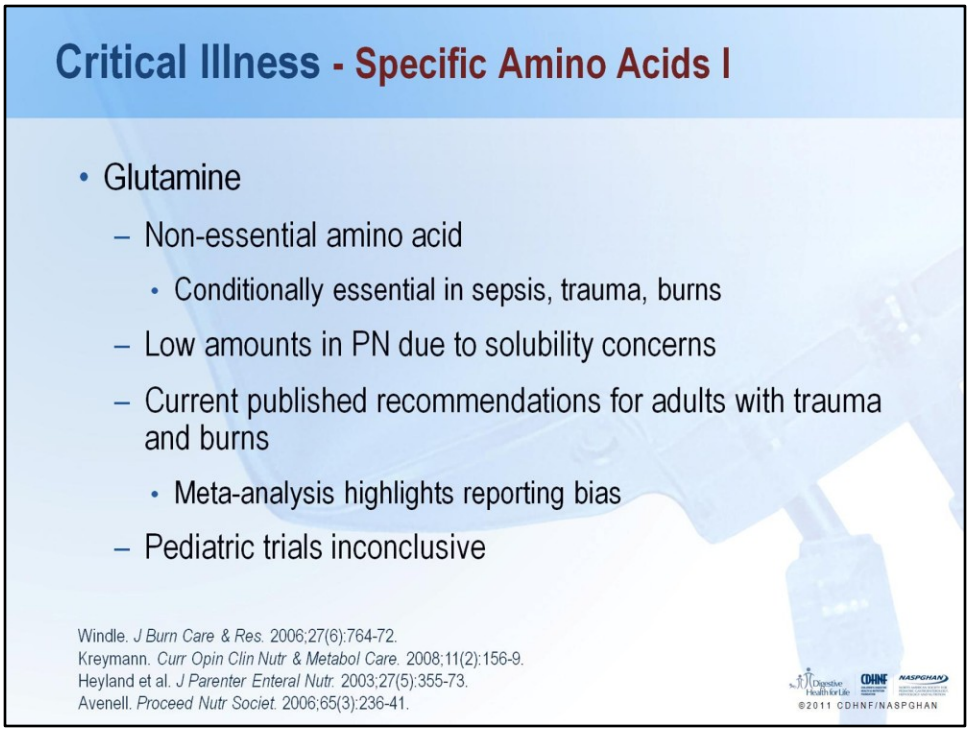


Verhoeven JJ, et al. Comparison of measured and predicted energy expenditure in mechanically ventilated children. Intens Care Med 1998;24(5):464-8.
Chwals WJ, et al. Measured energy expenditure in critically ill infants and young children. Journal of Surgical Research 1988;44(5):467-72.
Hulst JM, et 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.



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.



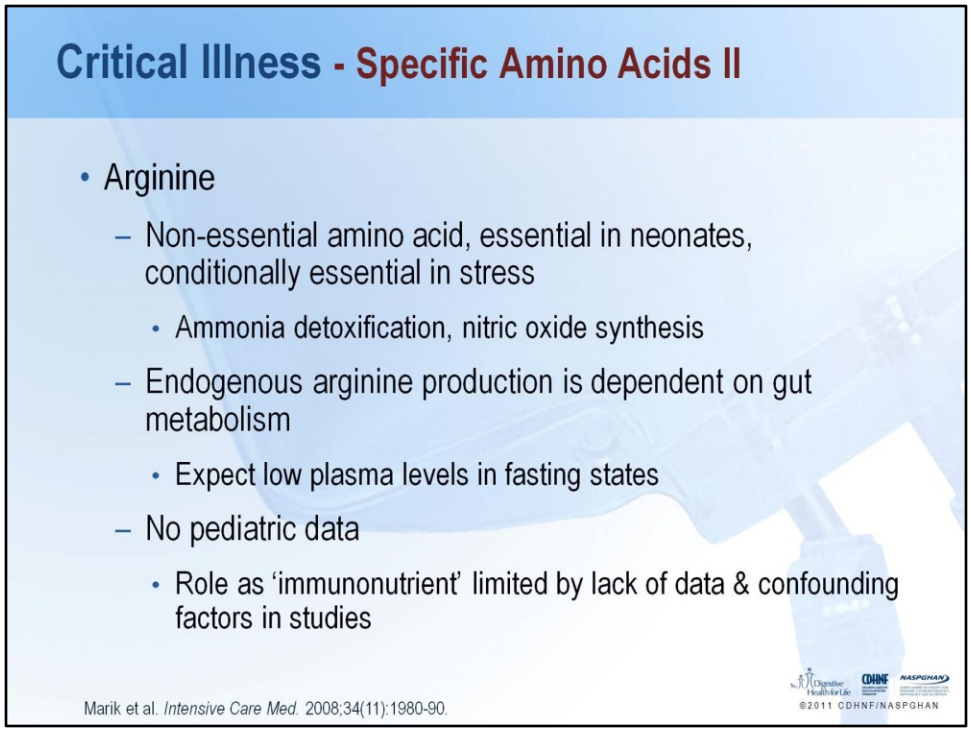
Glutamine is not commercially available in the USA. Some experts consider its use investigational since it is not FDA approved.

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.

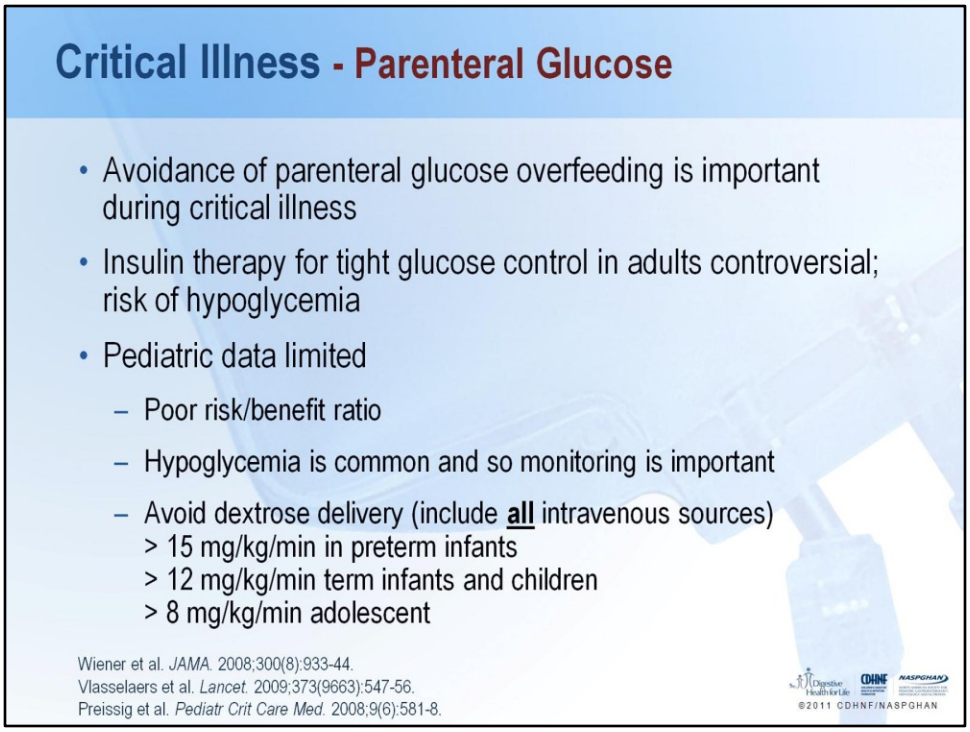
Notable Pediatric trials:

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.

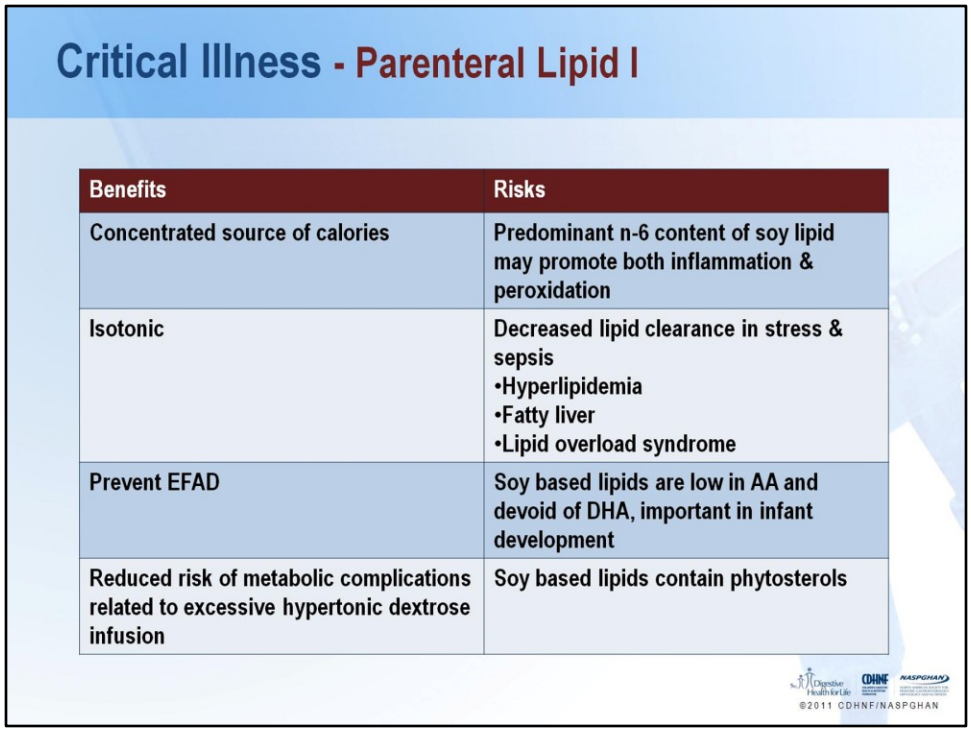
Grover Z, Tubman R, and McGuire W. Glutamine supplementation for young infants with severe gastrointestinal disease. Cochrane Database Syst Rev. 2007 Jan 24;(1):CD005947.



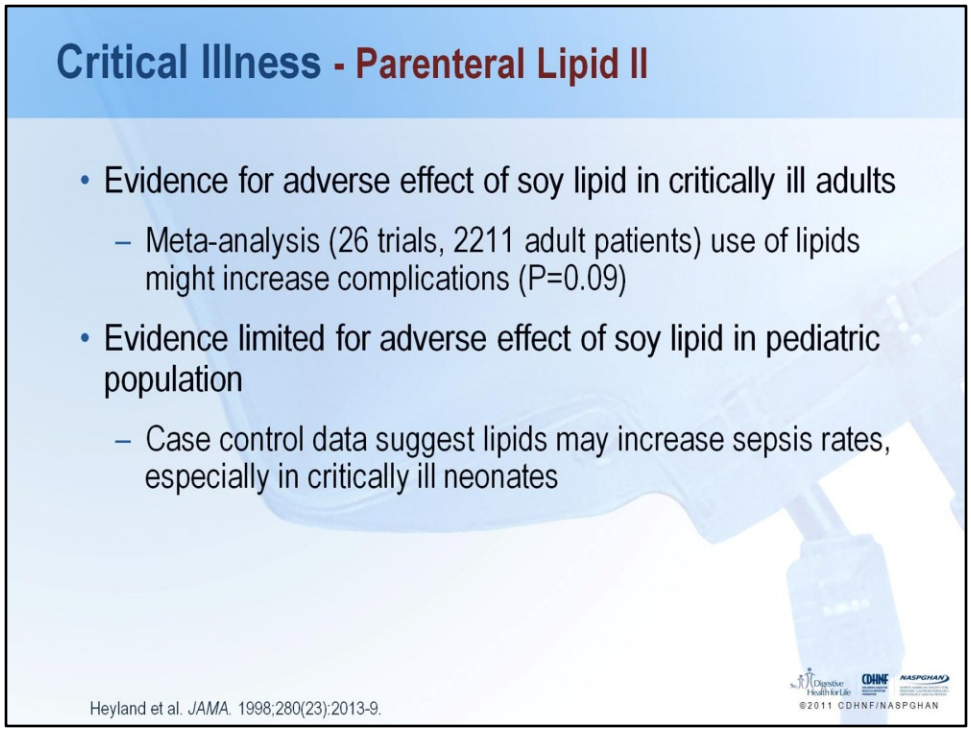
Marik PE and Zaloga GP. Immunonutrition in critically ill patients: a systematic review and analysis of the literature. Intensive Care Med. 2008;34(11):1980-90.



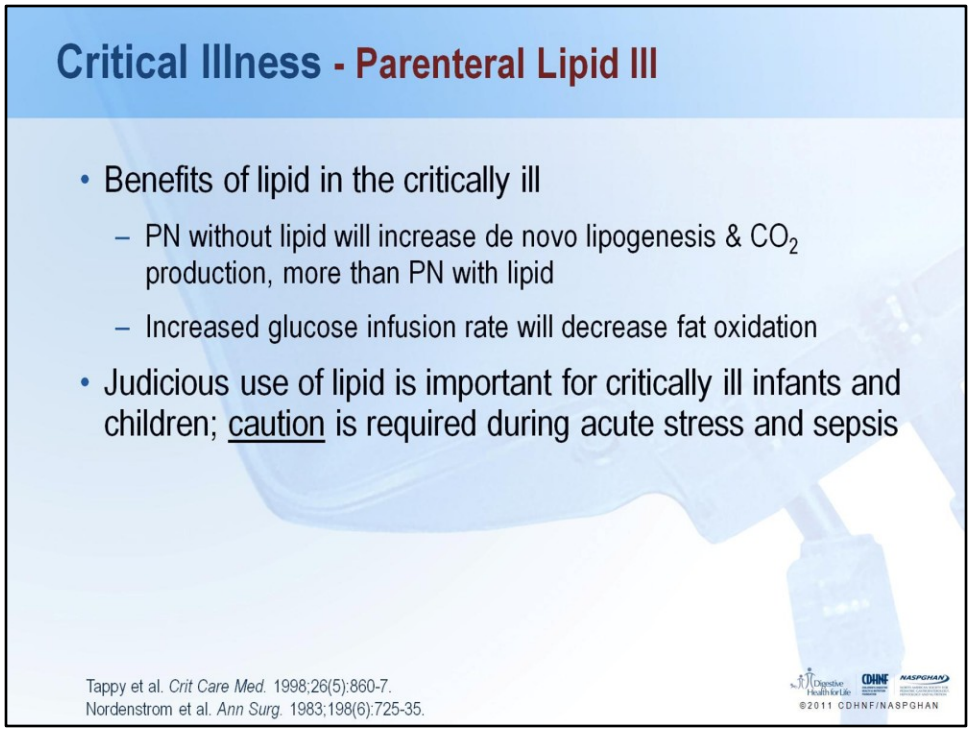
Wiener RS, Wiener DC, and Larson RJ. Benefits and risks of tight glucose control in critically ill adults: a meta-analysis.[Erratum appears in JAMA. 2009 Mar 4;301(9):936]. JAMA 2008;300(8):933-44.
Vlasselaers D et al. Intensive insulin therapy for patients in paediatric intensive care: a prospective, 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.



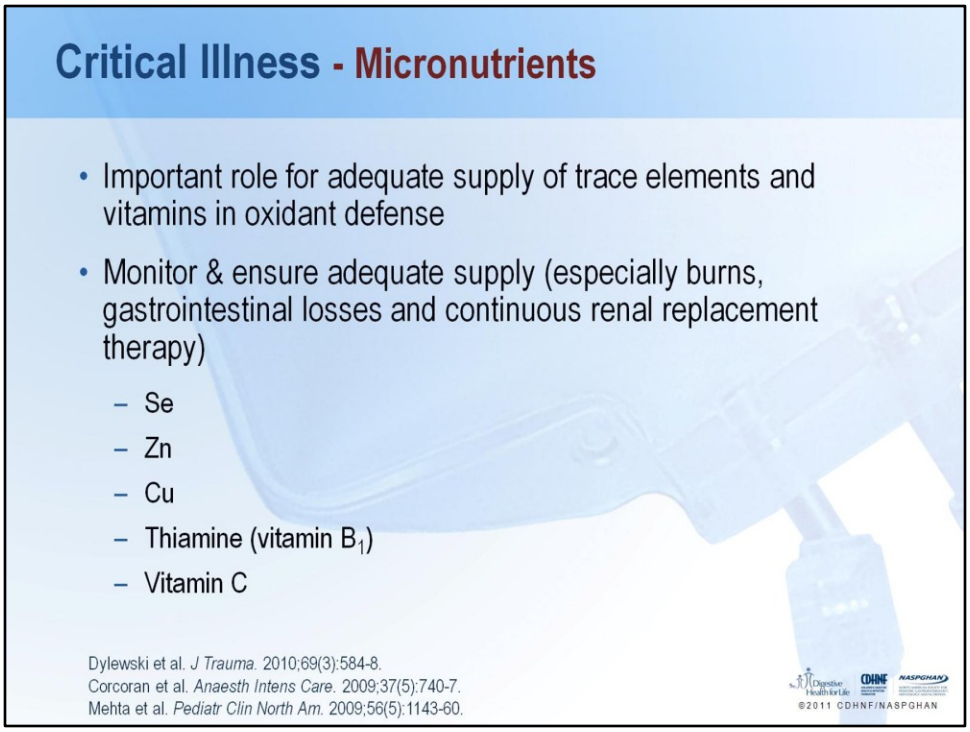
It has been suggested that phytosterols content of IV lipid may be related to PNALD.



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



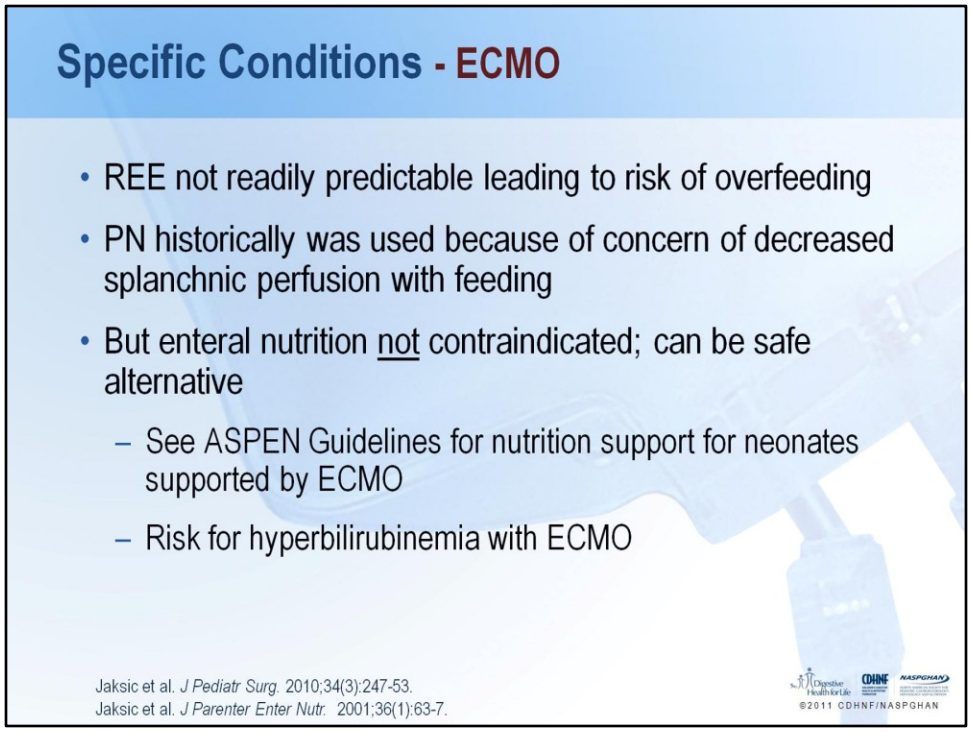
Tappy L et al. Effects of isoenergetic glucose-based or lipid-based parenteral nutrition on glucose metabolism, de novo lipogenesis, and respiratory gas exchanges in critically ill patients. Crit Care Med. 1998;26(5):860-7.
Nordenstrom J et al. Free fatty acid mobilization and oxidation during total parenteral nutrition in trauma and infection. Ann Surg. 1983;198(6):725-35.



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.

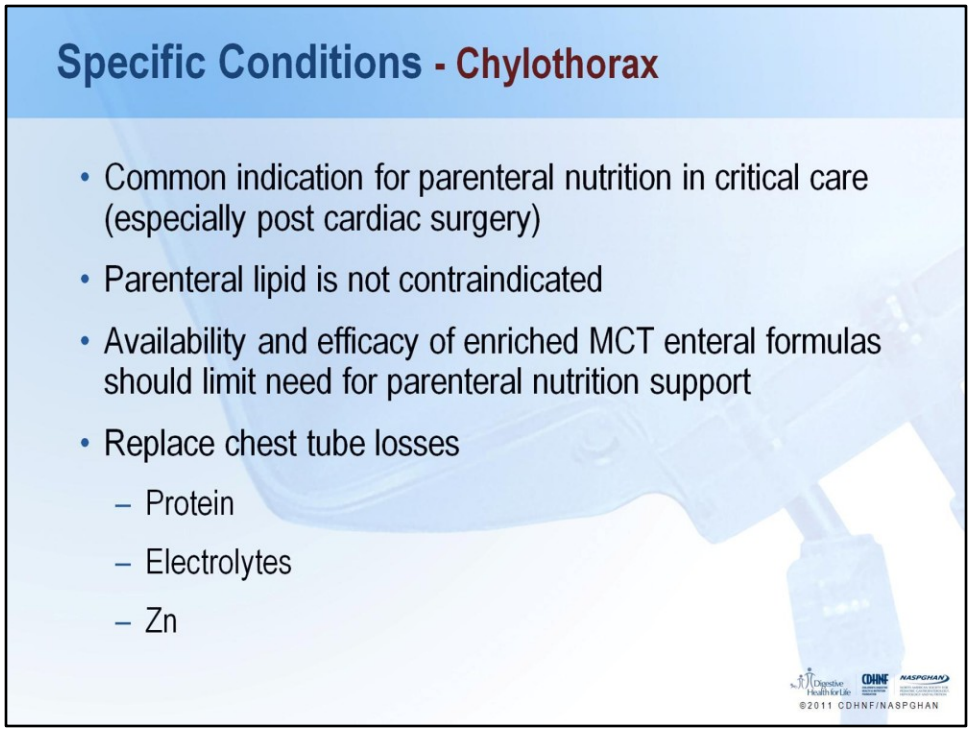
Corcoran TB, O'Neill MP,Webb SA, et al. Inflammation, vitamin deficiencies and organ failure in critically ill patients. Anaesth Intens Care. 2009;37(5):740-7.

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

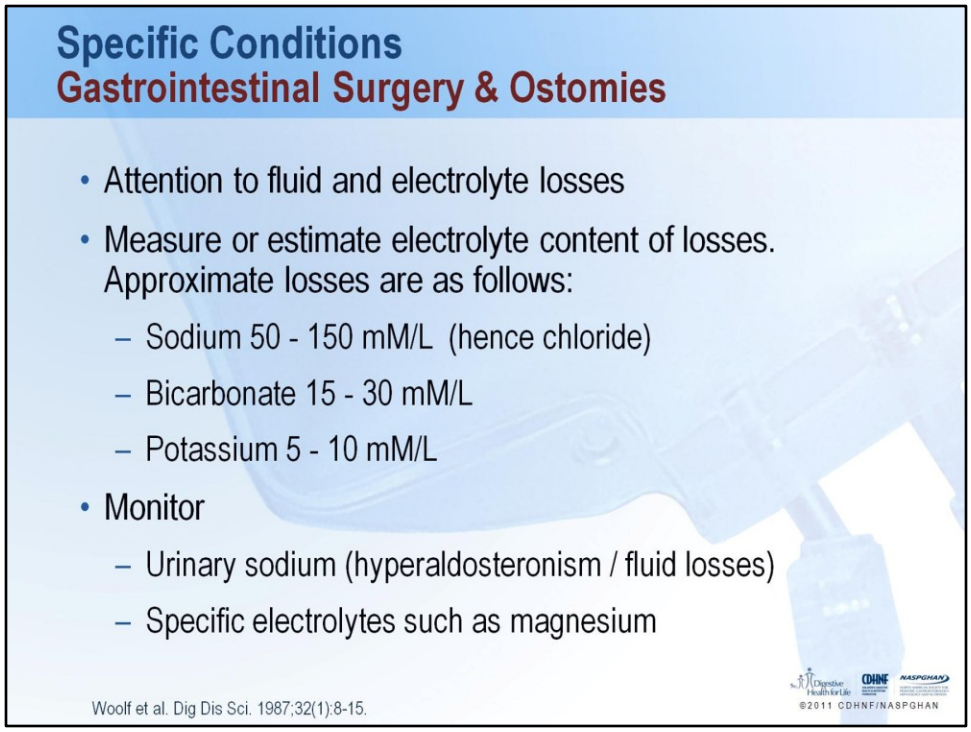


ASPEN Clinical guidelines: nutrition support of neonates supported with extracorporeal membrane oxygenation. Jaksic T, Hull MA, Modi BP, Ching YA, George D, Compher C; American Society for Parenteral and Enteral Nutrition (A.S.P.E.N.) Board of Directors. Children's Hospital Boston, Harvard Medical School, Boston, MA, USA. JPEN J Parenteral 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 quantifiatio of protein metabolism and energy expenditure in enonates 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.



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 prolonge

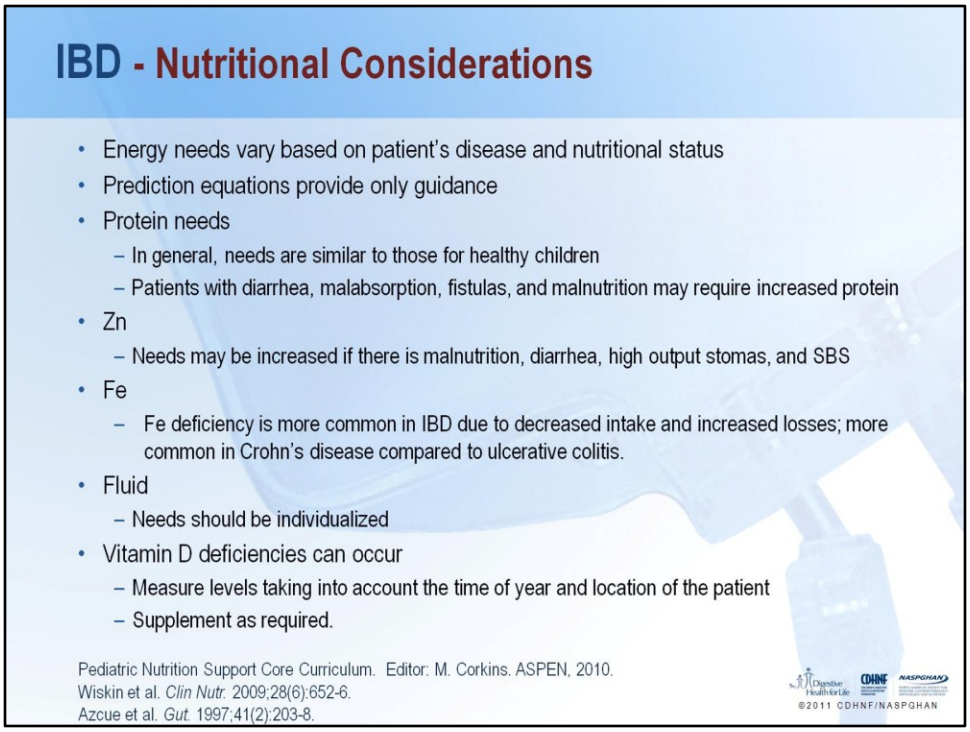


Zn losses are high from ostomies and proximal enterocutaneous fistulas.

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



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.

Trebble 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

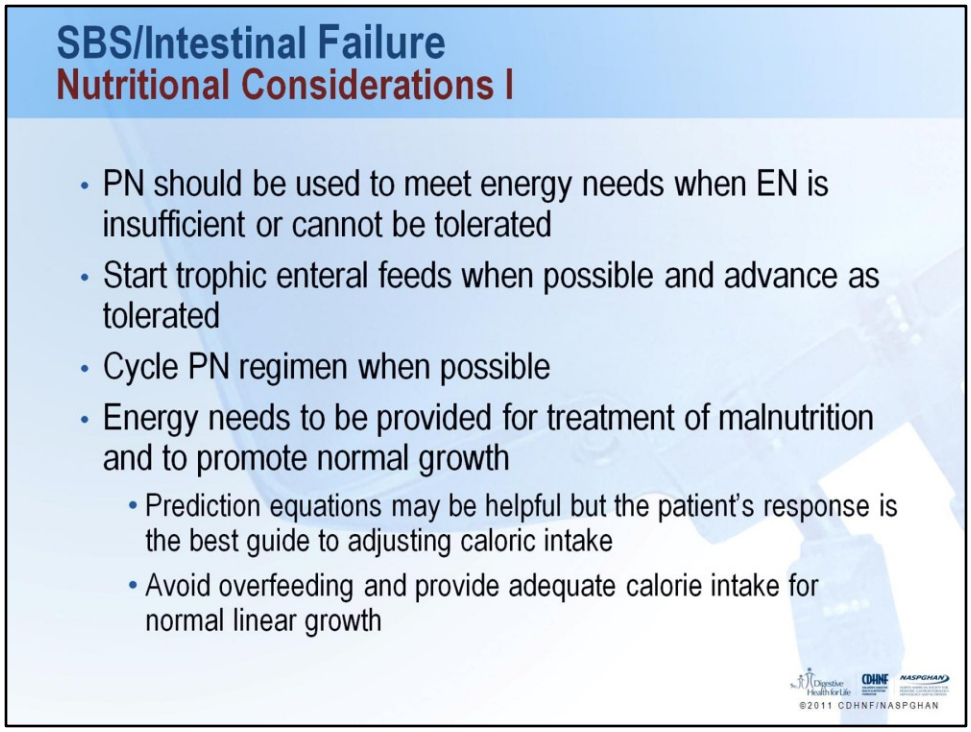
treatment with prednisolone. Gut. 1997 Aug;41(2):203-8.

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.

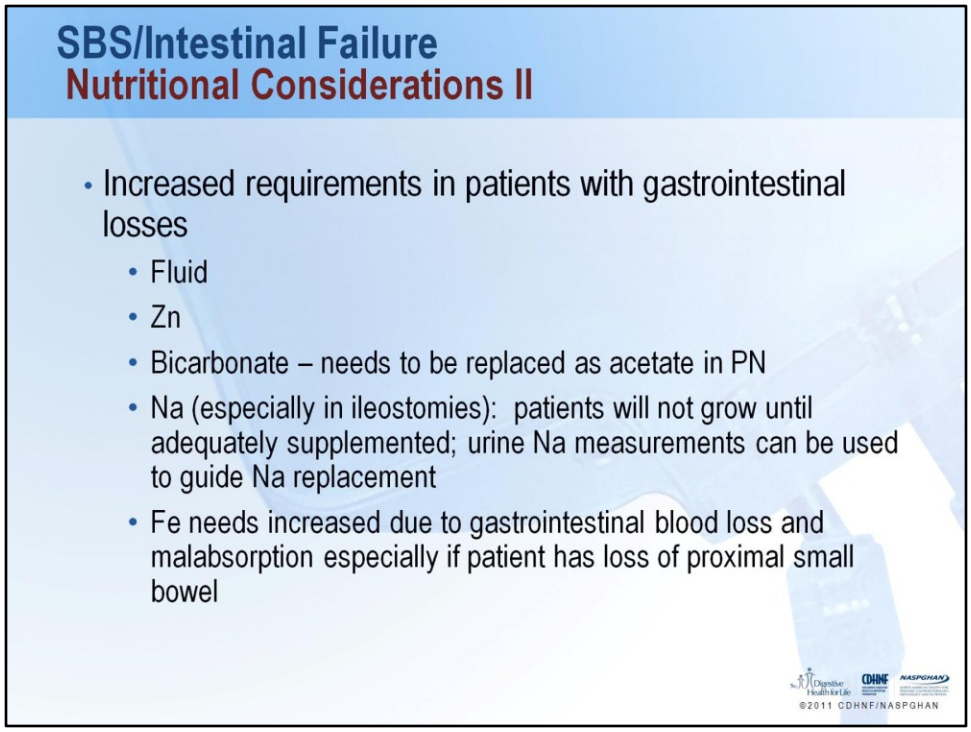
Thomas AG, Taylor F, Miller V. Dietary intake and nutritional treatment in childhood Crohn's disease. J Pediatr Gastroenterol Nutr, 1993; 17(1):75-81.

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

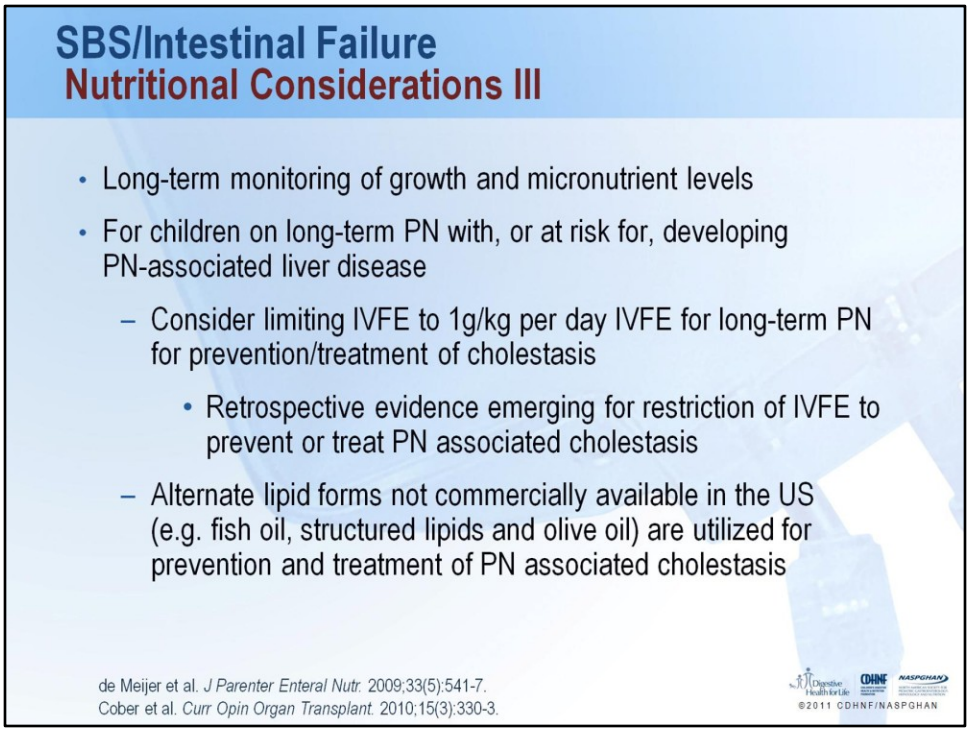
Kirchner et al. Reversal of growth retardation in Crohn's disease with therapy emphasizing oral nutritional restitution. Gastroenterol 1981; 80(1):10-15.



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



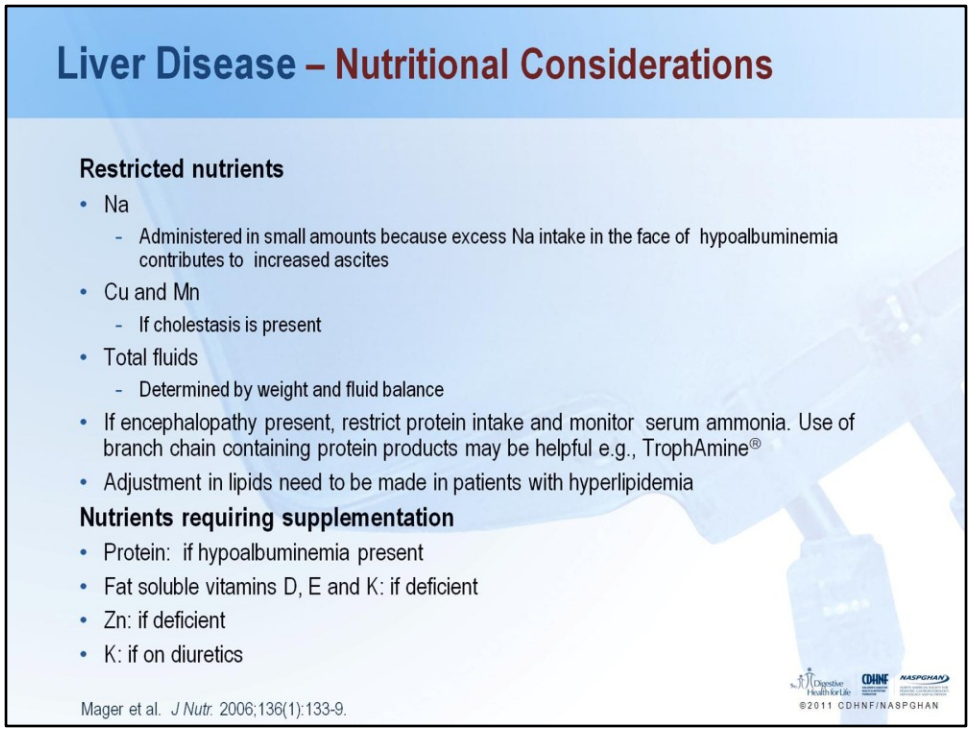
Pediatric Nutrition Support Core Curriculum. Editor: Mark Corkins. American Society for Parenteral and Enteral Nutrition (ASPEN), 2010.



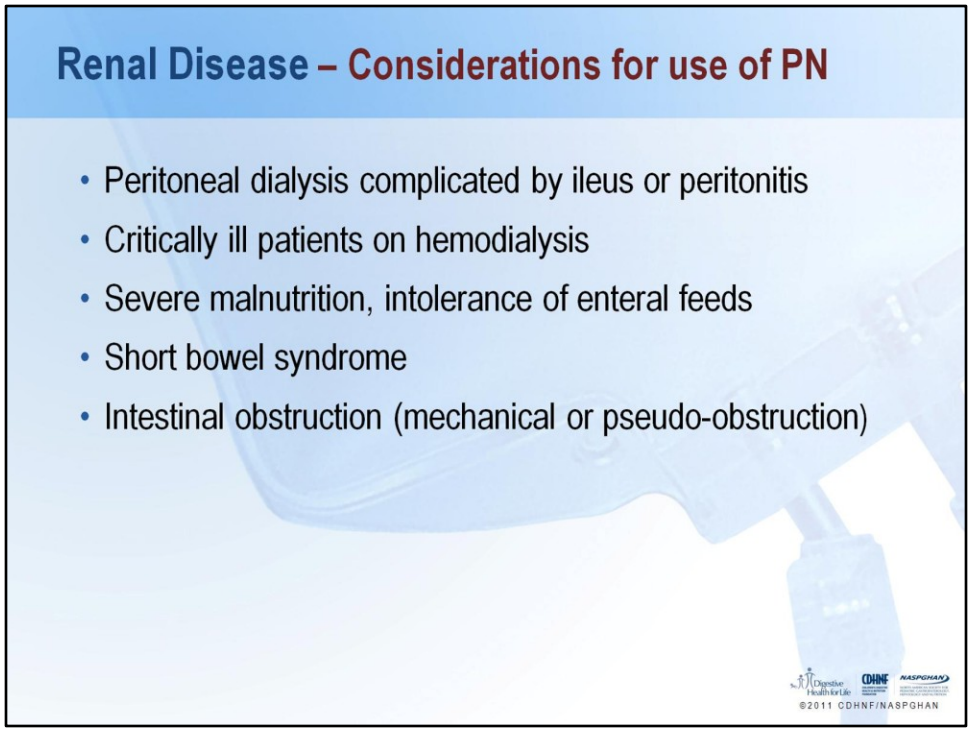
Pediatric Nutrition Support Core Curriculum. Editor: Mark Corkins. American Society for Parenteral and Enteral Nutrition (ASPEN), 2010.

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.

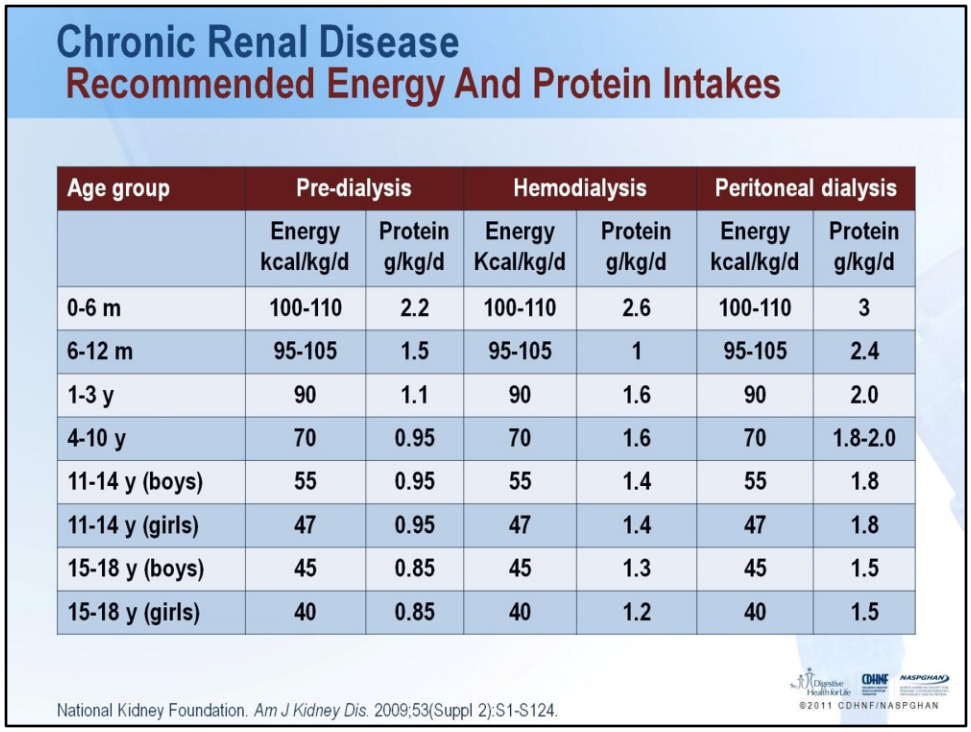


Mager DR, Wykes LJ, Roberts EA, et al. Branched-Chain Amino Acid Needs in Children with Mild-to-Moderate Chronic Cholestatic Liver Disease. J Nutr. 2006;136(1):133-9.



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.



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

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

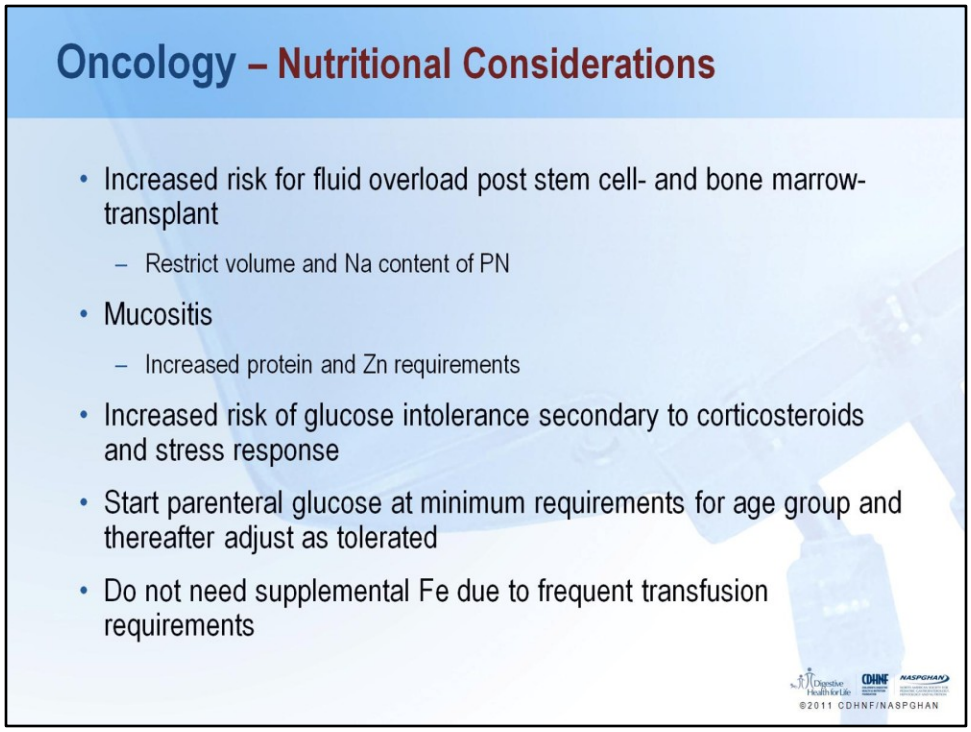
- Total fluids – determined by dialysis settings
- Na, K, Phos (administered in small amounts because excretion is decreased)
- Deduct dialysate dextrose when calculating glucose infusion rate (GIR)
- Lipids in patients with hyperlipidemia of renal failure
- Limit vitamin C to <100 mg per day in patients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



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

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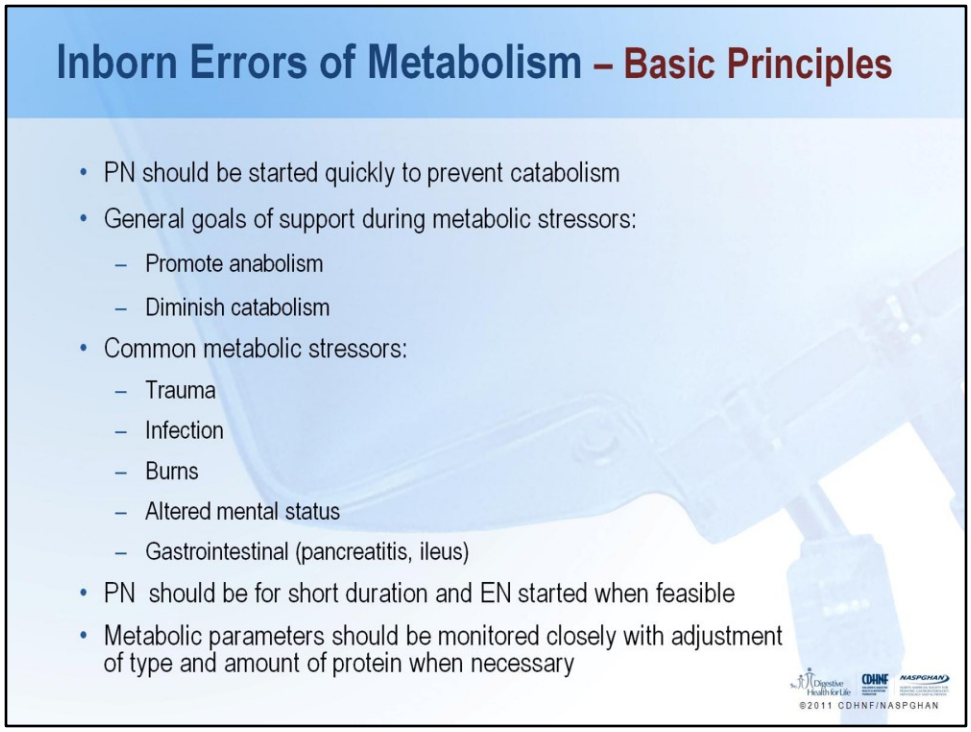
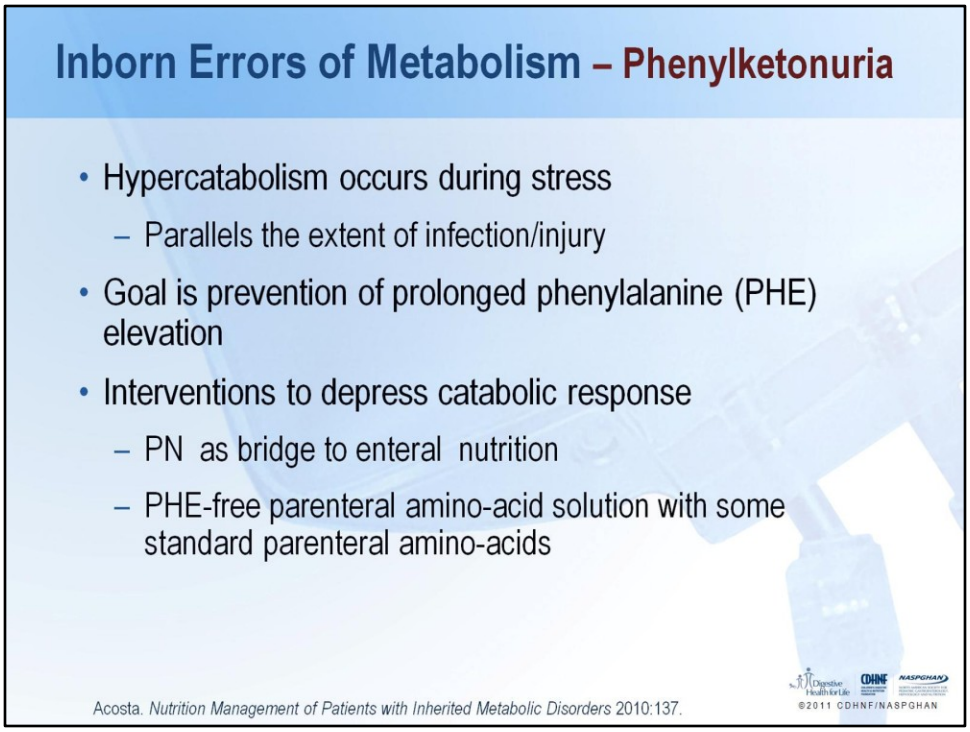
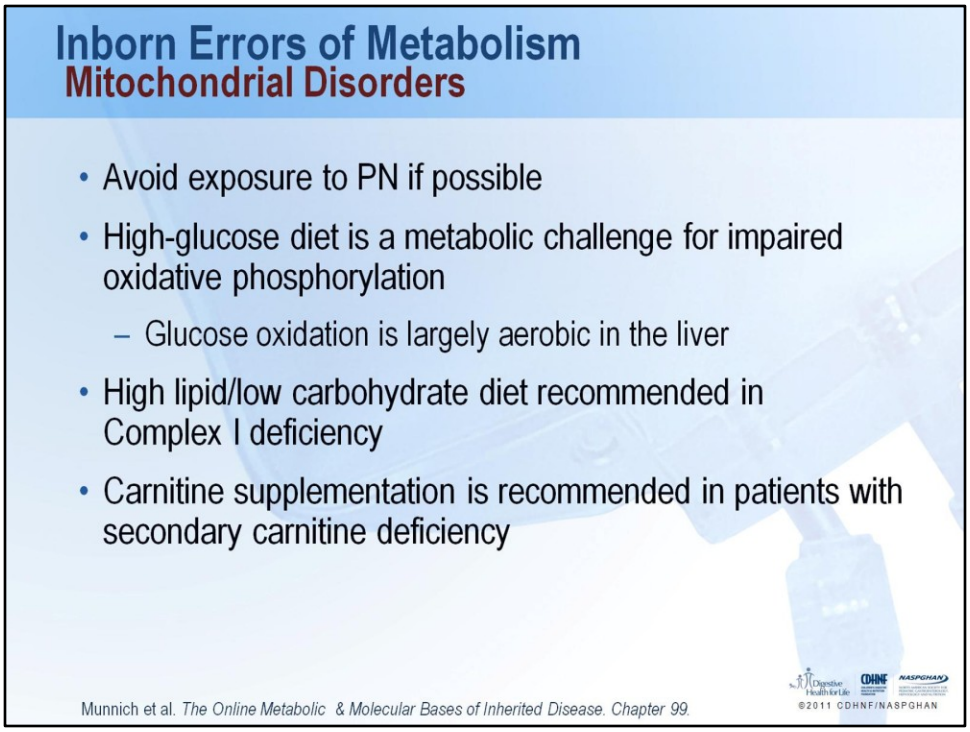


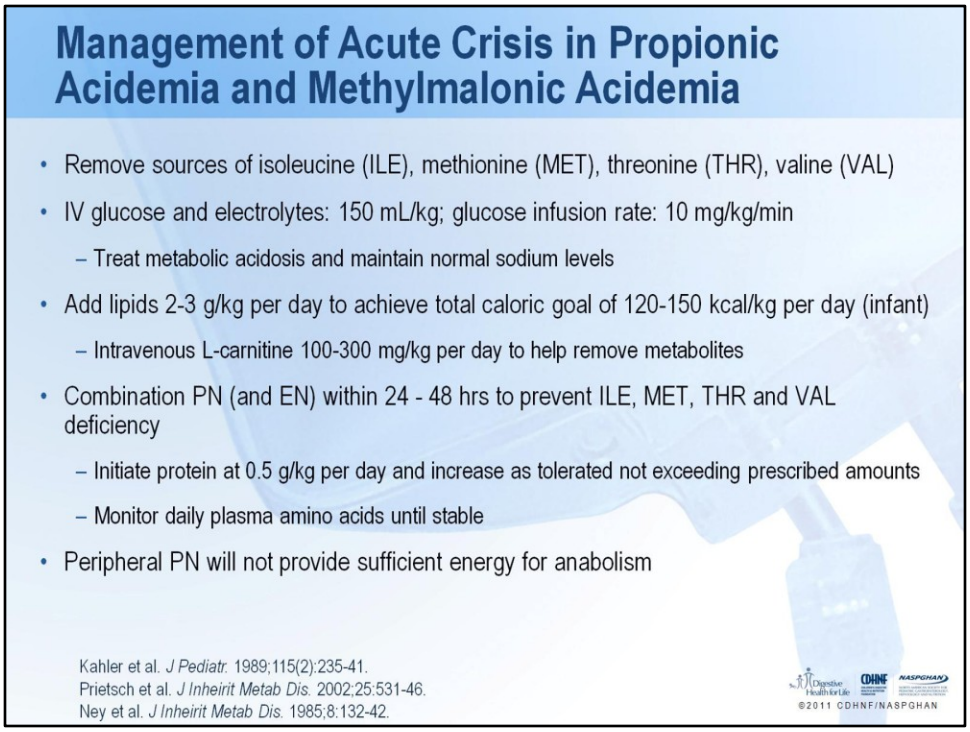
This slide reviews the basic principles of PN support in metabolic disease. The following slides will go over principles of management in select metabolic disorders



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



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



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. On needs to minimize fasting because catabolism increases propionate metabolites.

Strategies employed during ketoacidosis include withdraw 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

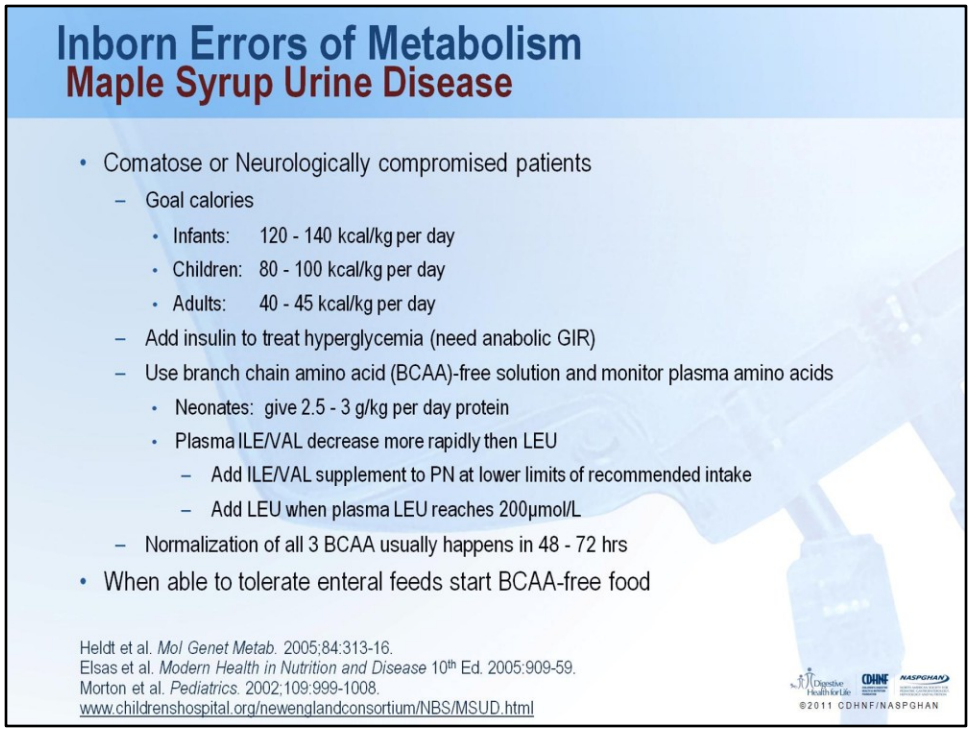
Parenteral nutrition in propionic and methylmalonic acidemia

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)

31month 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 propionyi- 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

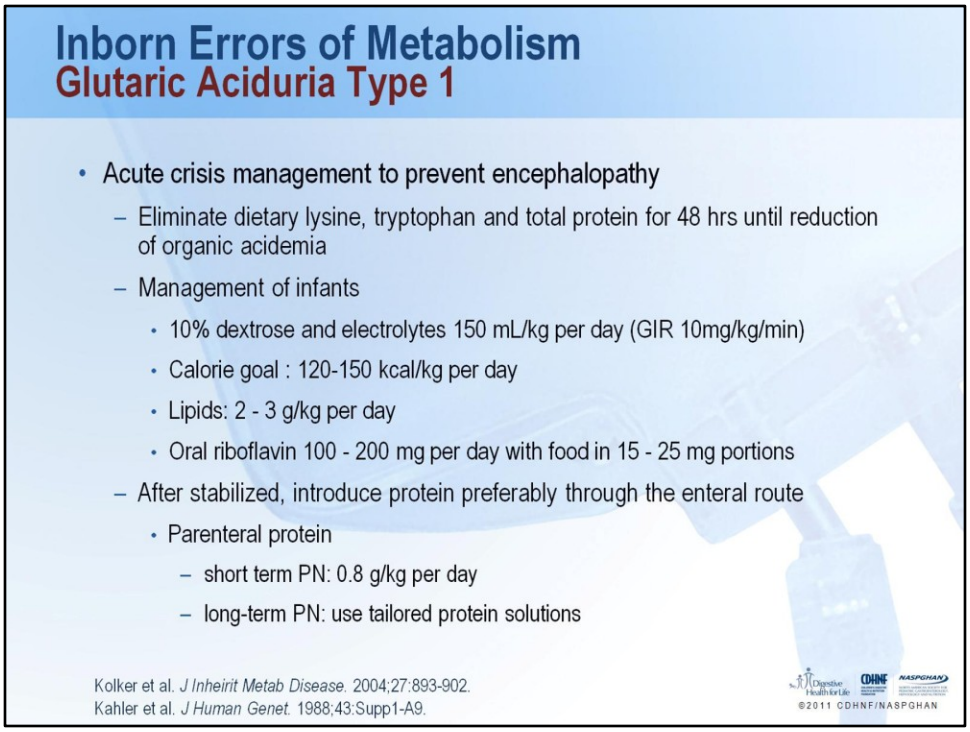
Kahler SG, Millington DS, Cederbaum SD, Vargas J, Bond LD, Maltby DA, Gale DS, Roe CR. Parenteral nutrition in propionic and methylmalonic acidemia. J Pediatr. 1989

Aug;115(2):235-41.
Prietsch V, Lindner M et al. Emergency Management of Inheirited Metabolic Diseases. J Inheirit Metab Di 2002;25:531-46.
Ney D, Bay C, Saudubray J-M et al. An Evaluation of Protein Requirements in Methylmalonic Acidaemia. J Inheir Metab Dis 1985;8:132-42

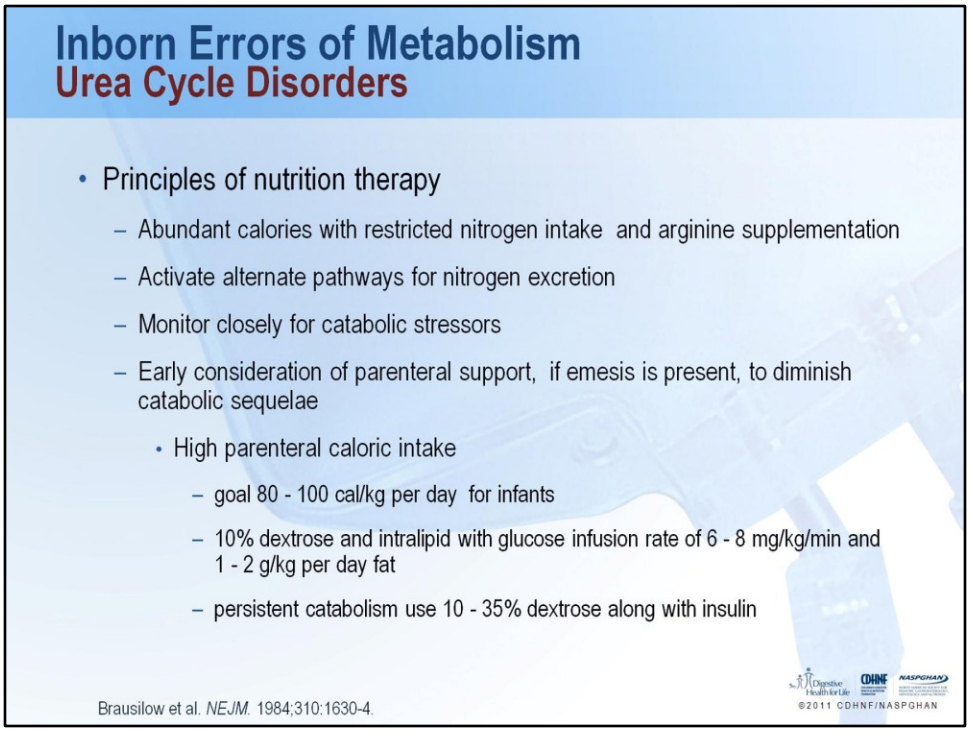


In MSUD metabolic issues and toxicity are tied to plasma leucine status. There is little toxicity with increased levels of isoleucine or valine. L1 neutral transporter allows brain update of Paa, Trypt, Leu, Meth, Isol, tyr, hist, val, thr and in cases of leucinosis, leucine is taken up by the L1 transporter at the expense of other L-neutral amino acids especially in the brain. The sequealae 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. Inheirited 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



Kolker S, Greenberg D, et al. Emergency Treatment in Glutaryl Co Dehydrogenase Deficiency. J Inheirit Metab Disease 2004;27:893-902.
Kahler SG, Iaofolla AK. Effect of Dietary Alteration and Parenteral Nutrition in Glutaric Aciduria Type 1. J Human Genet 1988;43:Supp1- A9.

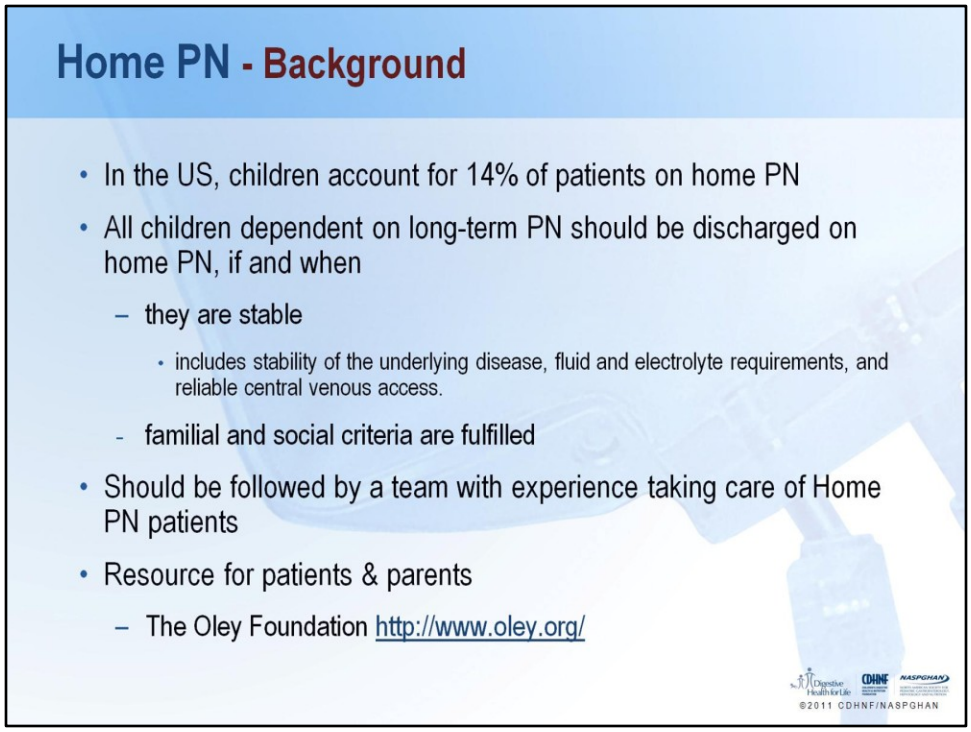


This slide covers the aims of nutritional therapy in patients with urea cycle disorders. The goal should be to restrict nitrogen intake and minimize catabolism as well as activate pathways aside from urea for nitrogen excretion. Arginine, which is downstream in the pathway requires supplementation.

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.

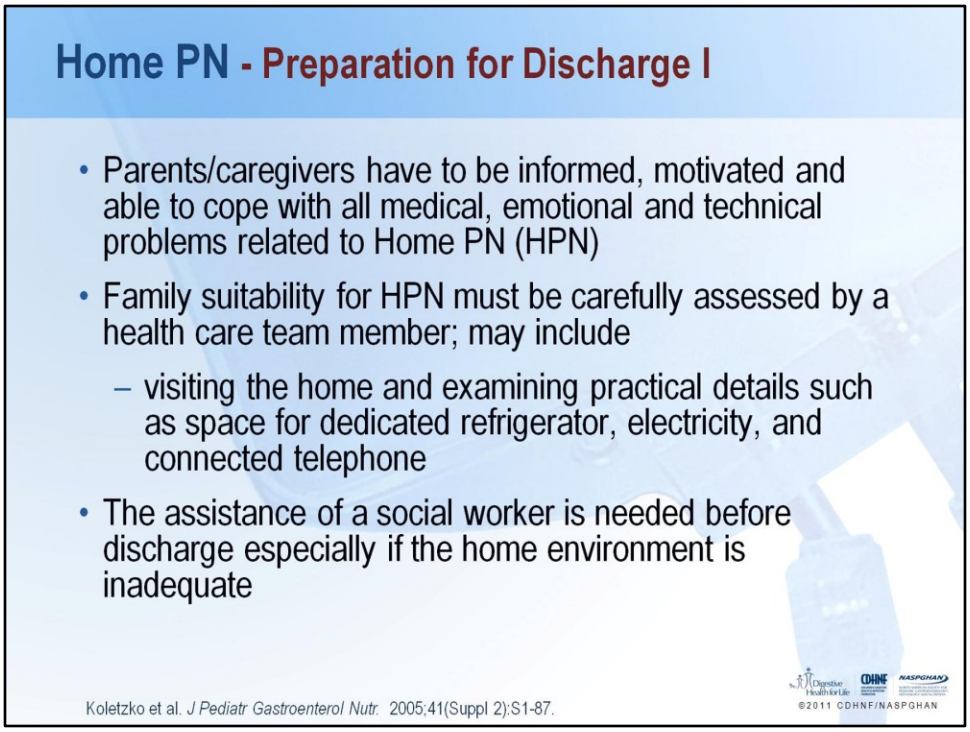
Brausilow SW, Danney M, Waber LJ, Batshaw M, et al. Treatment of Episodic Hyperammonemia in Children with Inborn Errors of Urea Synthesis. NEJM 1984;310:1630-4.

Home Parenteral Nutrition

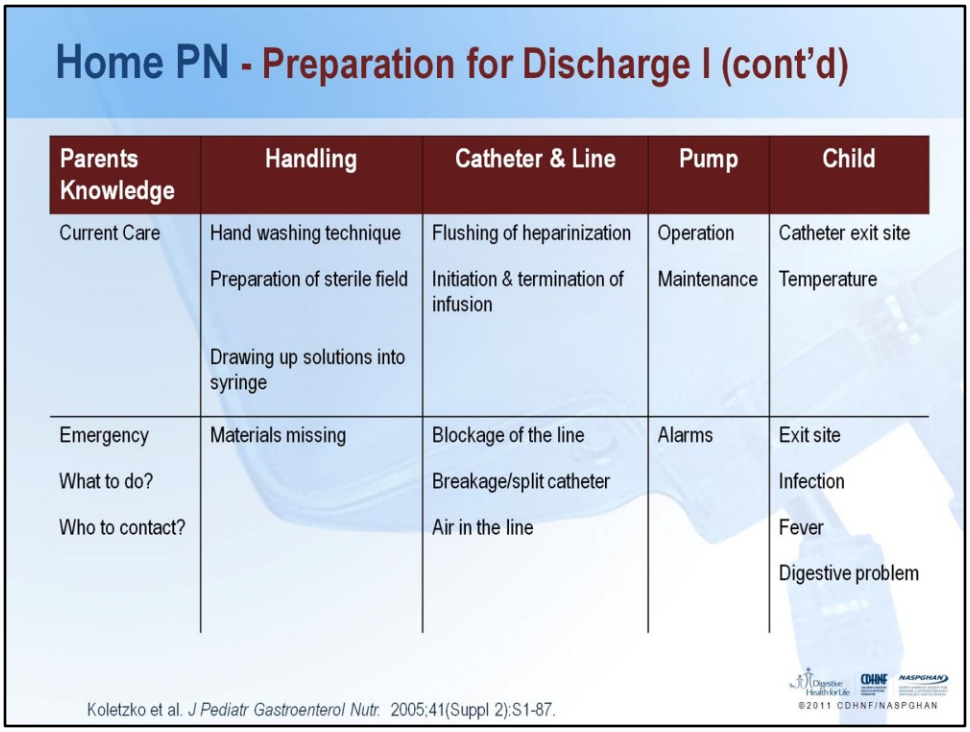


Founded in 1983 by Lyn Howard, MD and her patient, Clarence "Oley" Oldenburg, the Oley Foundation is a national, independent, non-profit 501(c)(3) organization that provides information and psycho-social support to consumers of home parenteral and enteral nutrition , helping them live fuller, richer 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/

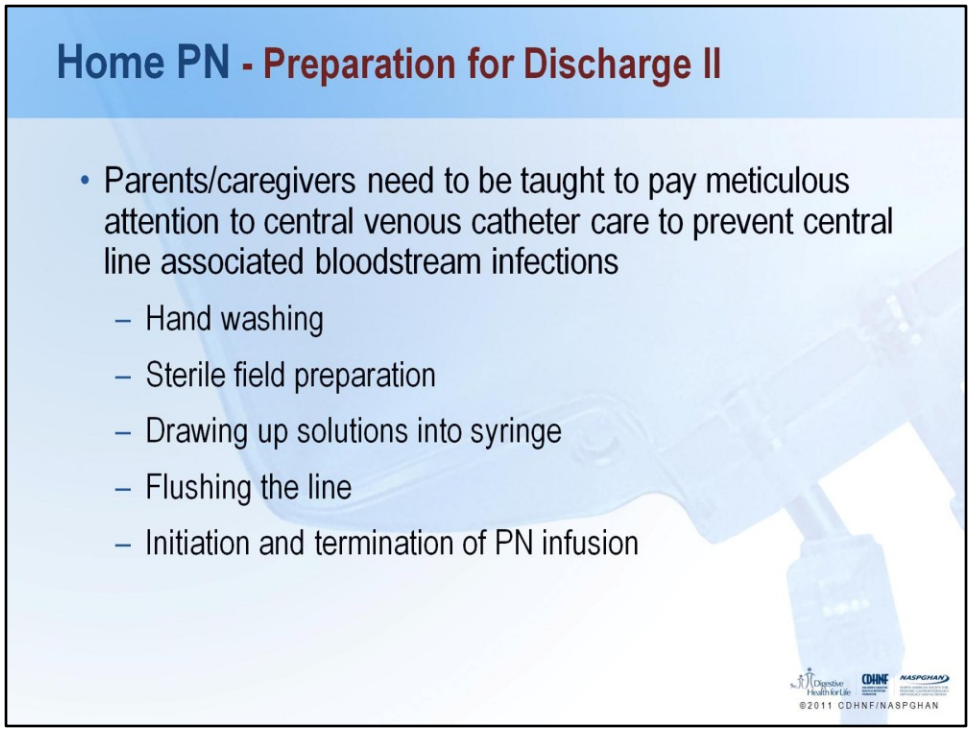
Koletzko B, Goulet O, Hunt J, Krohn K, Shamir R; Guidelines on Paediatric Parenteral Nutrition of the European Society of Paediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN) and the European Society for Clinical Nutrition and Metabolism (ESPEN), Supported by the European Society of Paediatric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



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.



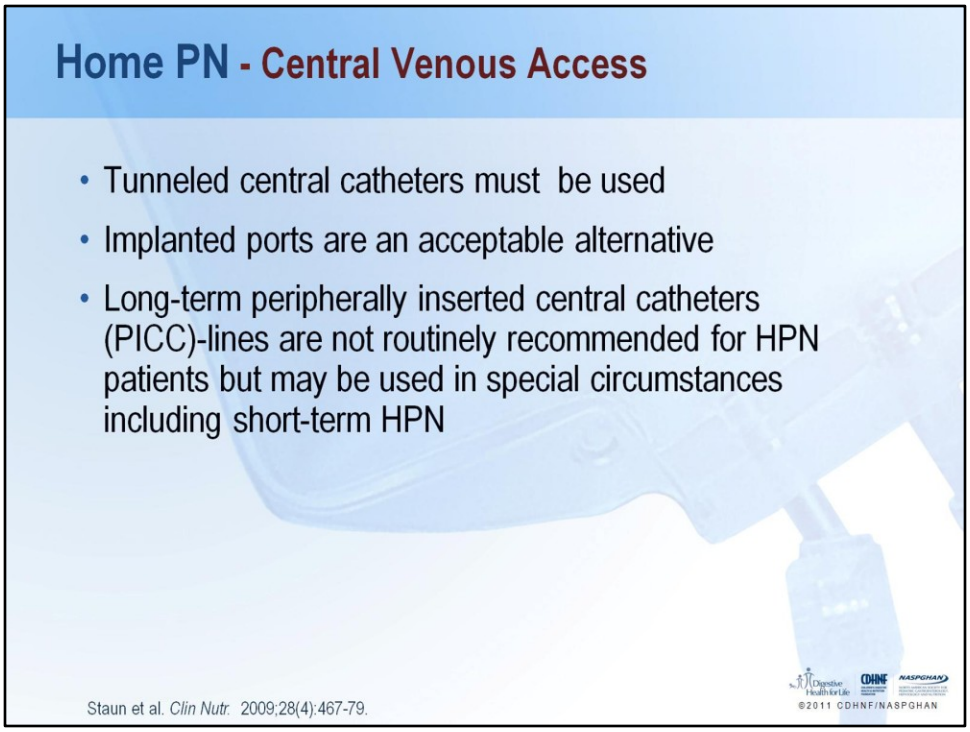
Koletzko B, Goulet O, Hunt J, Krohn K, Shamir R; Guidelines on Paediatric Parenteral Nutrition of the European Society of Paediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN) and the European Society for Clinical Nutrition and Metabolism (ESPEN), Supported by the European Society of Paediatric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



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

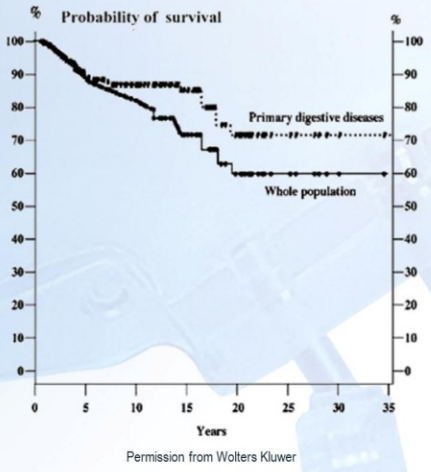
- Parents/caregivers also need to be taught to recognize common central venous catheter problems
  - Occlusion
  - Damage
  - Accidental removal
  - Infection e.g., fever
- They should be aware of whom to contact and how to provide first aid
- They should also be able to recognize and manage the symptoms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



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

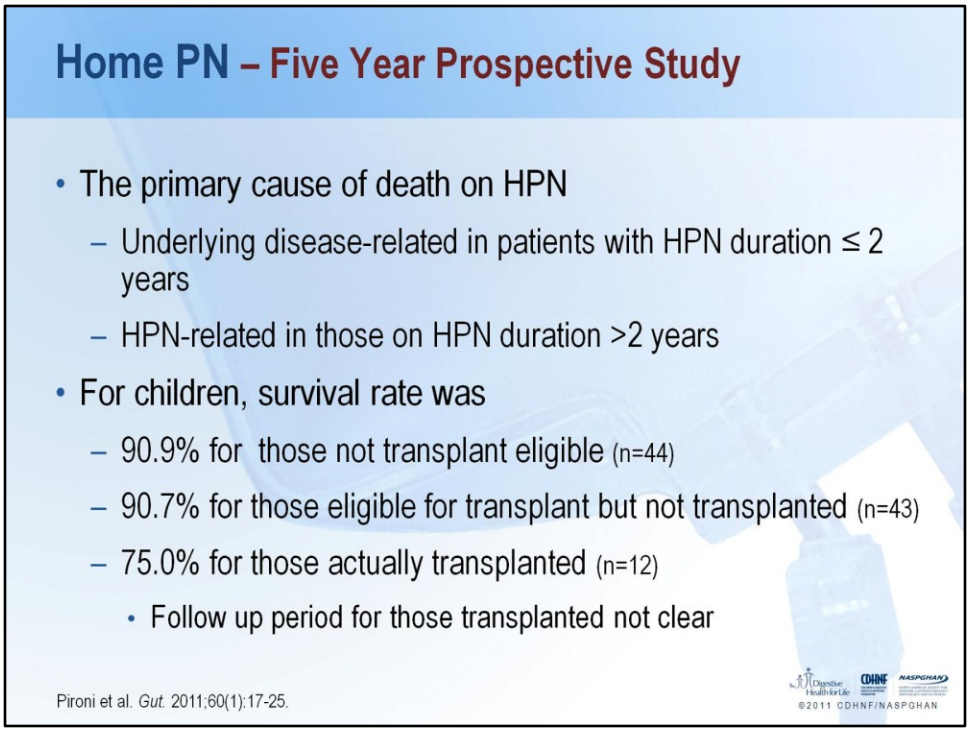


Permission from Wolters Kluwer

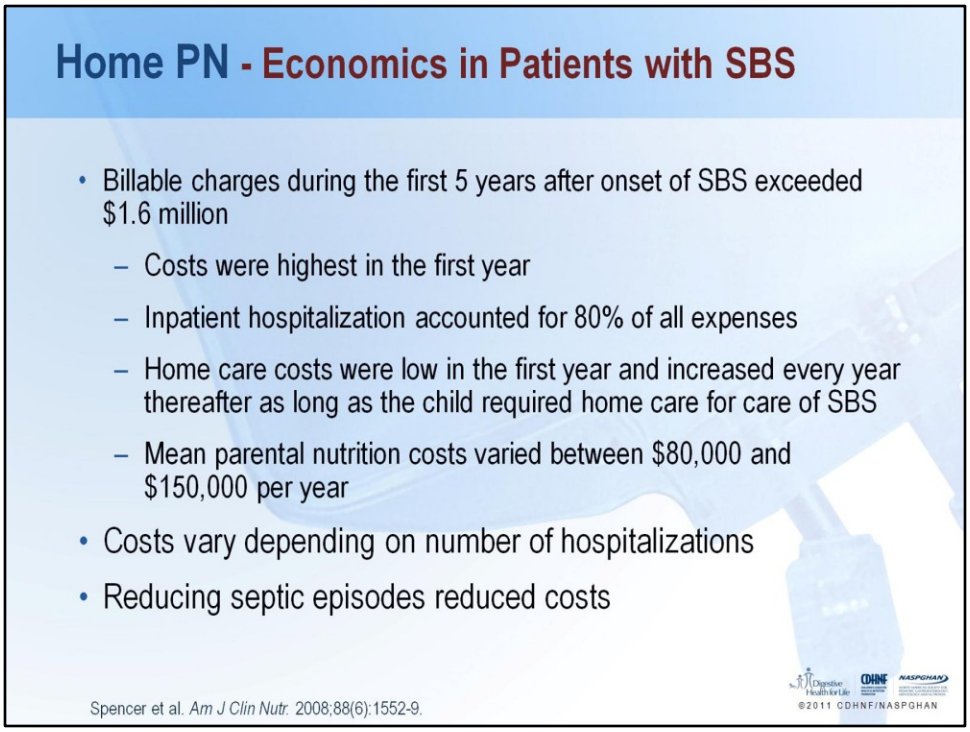
Colomb et al. *J Pediatr Gastroenterol Nutr.* 2007;44:347-53.

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.

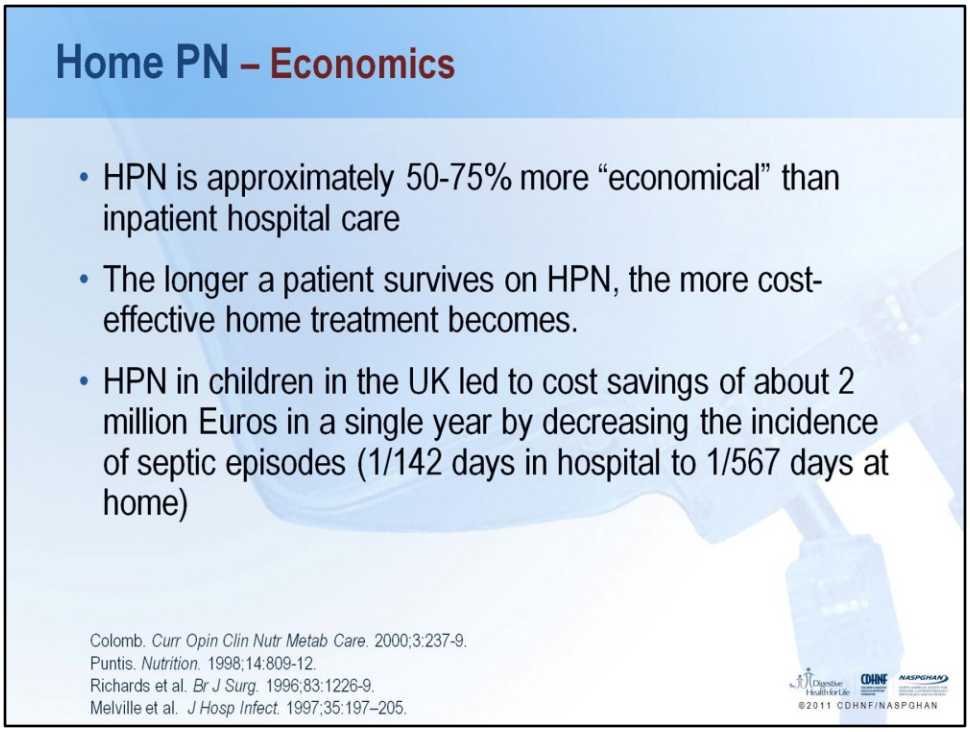
Colomb V, Dabbas-Tyan M, Taupin P, et al. Long-term outcome of children receiving home parenteral nutrition: a 20-year single-center experience in 302 patients. J Pediatr Gastroenterol Nutr. 2007 ;44:347-53



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.



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.



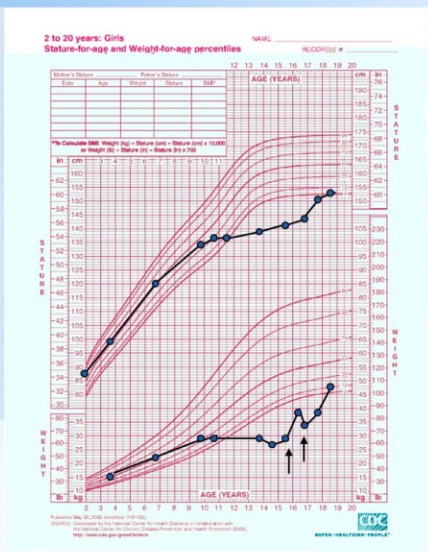
Colomb V. Economic aspects of paediatric home parenteral nutrition. Curr Opin Clin Nutr Metab Care. 2000;3(3):237-9.
Puntis JW. The economics of home parenteral nutrition. Nutrition. 1998;14(10):809-12.
Richards DM, Irving MH. Cost-utility analysis of home parenteral nutrition. Br J Surg. 1996;83(9):1226-9.
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 - Growth in Children

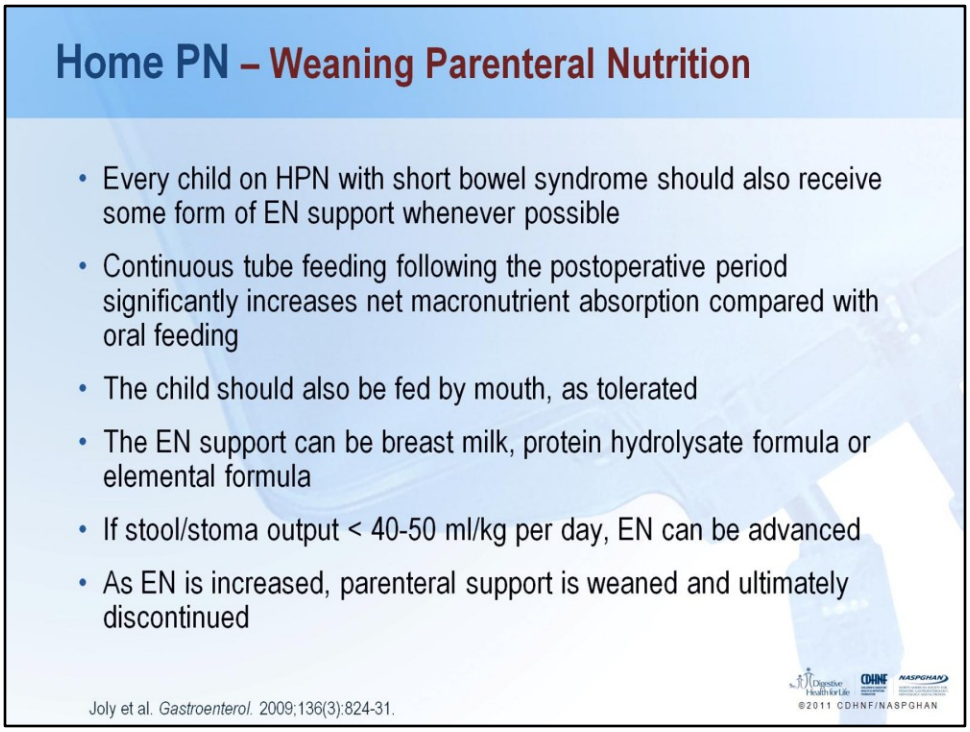
- HPN is successful in maintaining adequate nutritional status
- Most children with short bowel syndrome will grow along their own percentiles and some children will exhibit some degree of catch up growth



Torres et al. *J Pediatr Gastroenterol Nutr.* 2007;45:204-12.

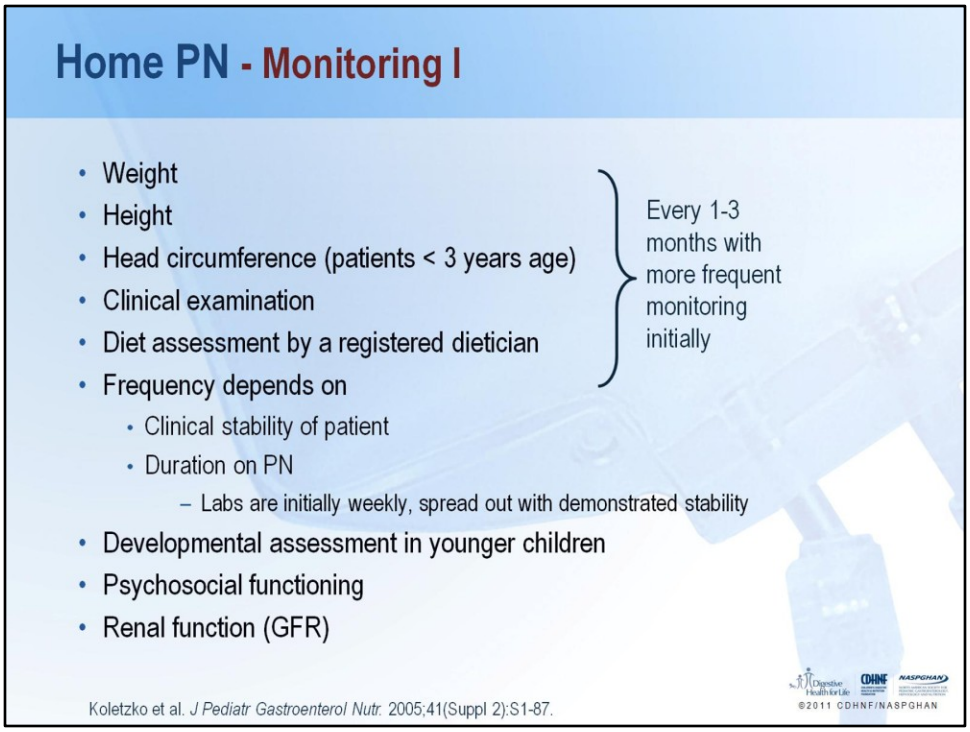
The inserted growth chart is of a patient on home PN with acquired SBS due to surgical resection for Crohn's disease. The first arrow indicates the start of PN. Because of good weight gain, PN was weaned. The second arrow indicates the restarting of PN.

Torres C, Sudan D, Vanderhoof J, et al. Role of an intestinal rehabilitation program in the treatment of advanced intestinal failure. J Pediatr Gastroenterol Nutr. 2007;45:204-12.

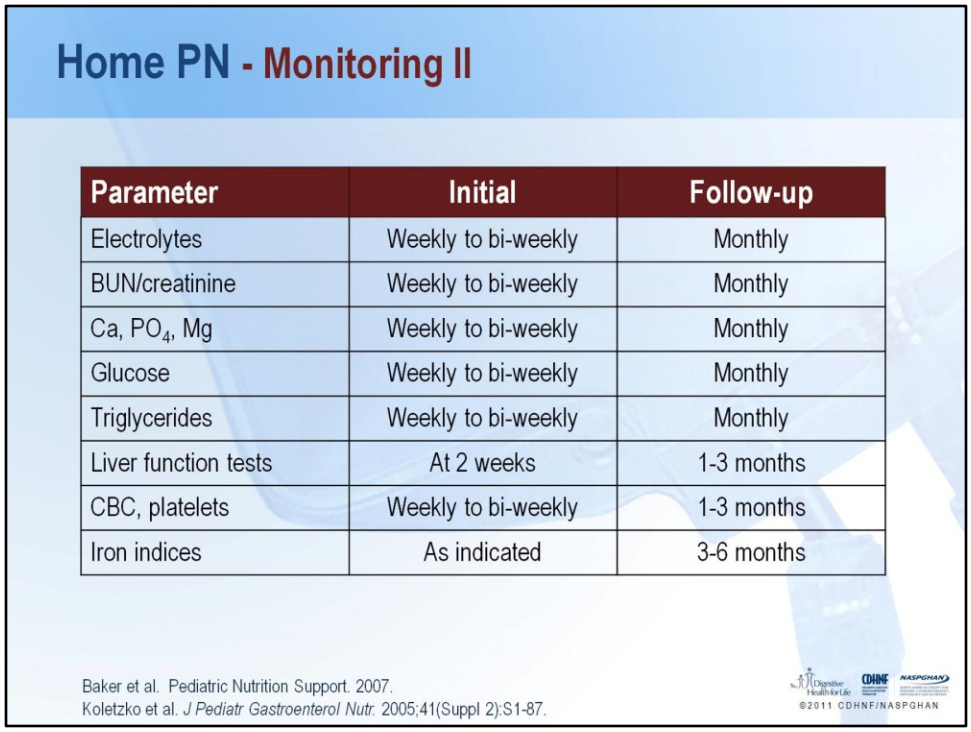


EN support should be tailored based on the patient.

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.



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.

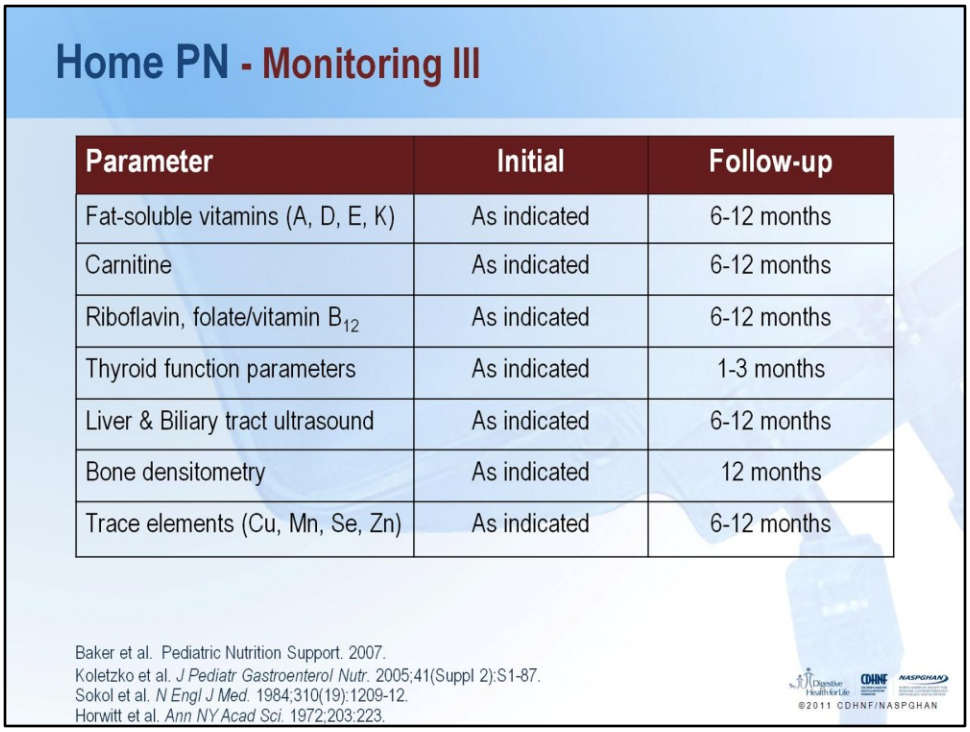


The above are suggested, however there may be variation in certain populations e.g. adult and adolescents.

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.



Trace elements

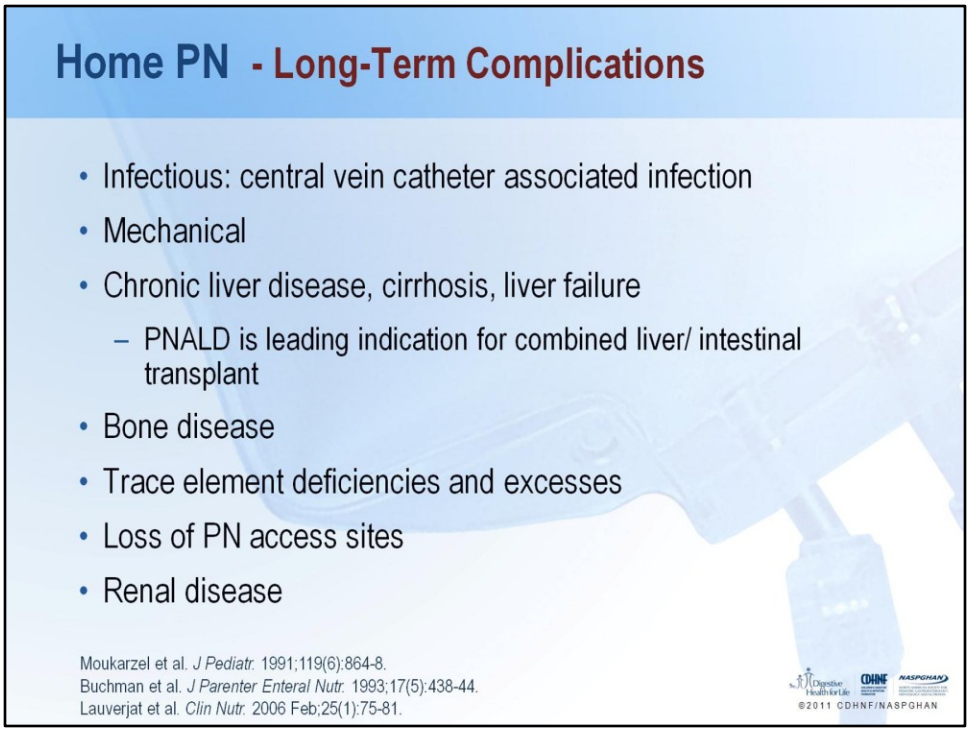
- Mn: follow whole blood levels although ideal may be a MRI of brain
- Zn: serum zinc is not an accurate marker of zinc deficiency
- Cu: serum copper and ceruloplasmin
- Se: serum or whole blood selenium
- Fe: hemoglobin, serum ferritin or iron, transferrin saturation

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, PIVKAII
- Vitamin D: 25-hydroxy vitamin D; both 1,25-Dihdroxy- 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.

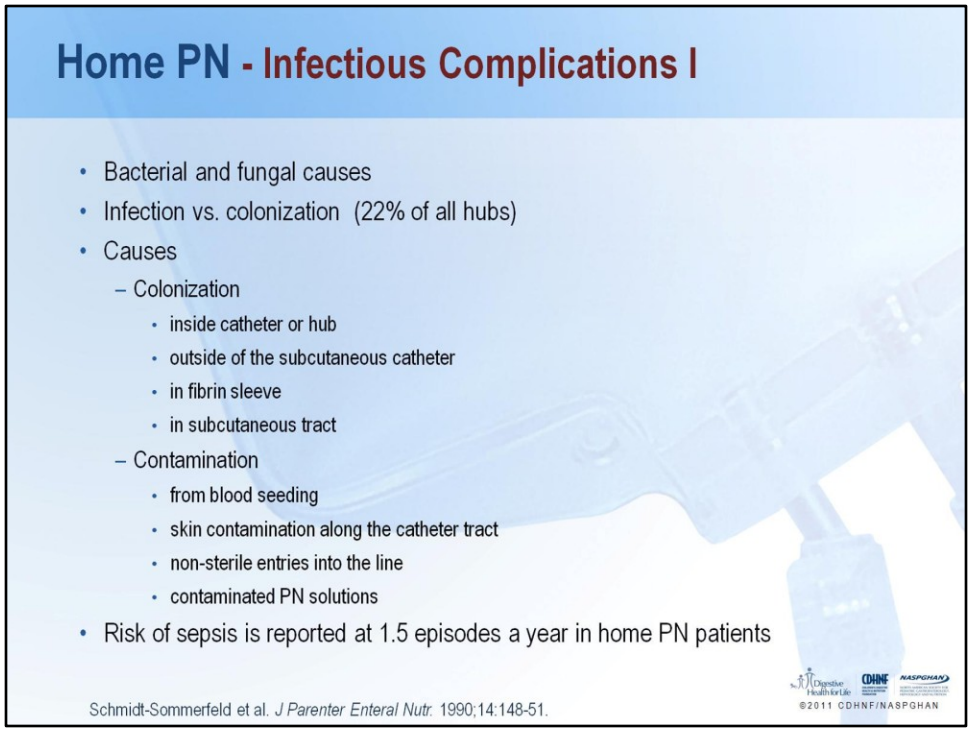


Patients at risk for renal disease should have GFR monitored.

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.

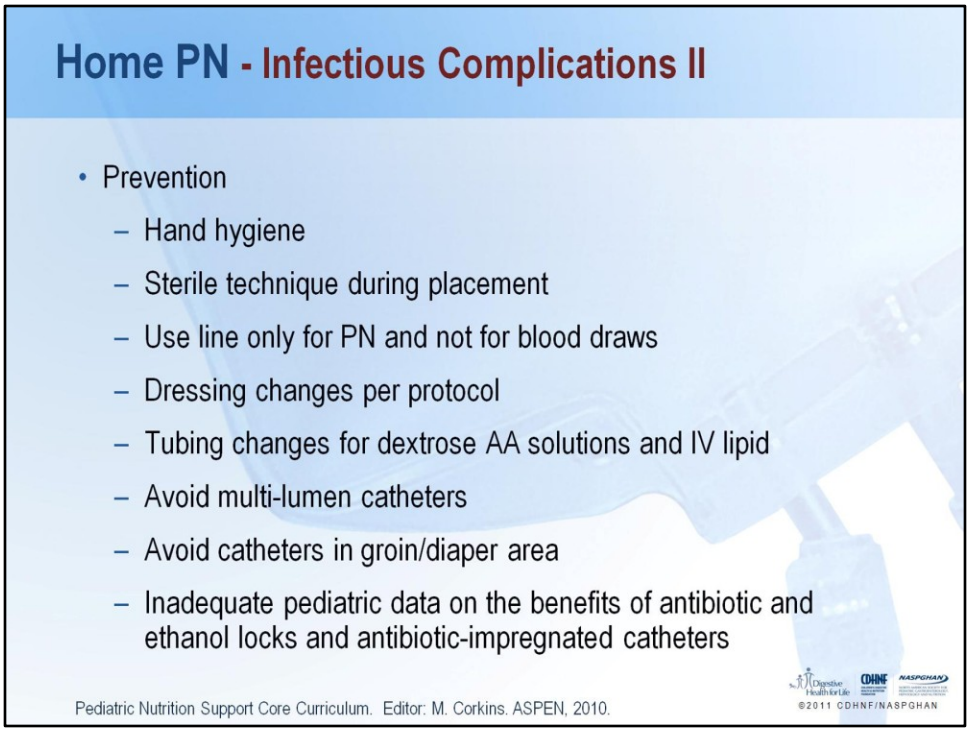
Moukarzel AA, Ament ME, Buchman A, Dahlstrom KA, Vargas J. Renal function of children receiving long-term parenteral nutrition. J Pediatr. 1991 Dec;119(6):864-8.
Buchman AL, Moukarzel A, Ament ME, Gornbein J, Goodson B, Carlson C, Hawkins RA. Serious renal impairment is associated with long-term parenteral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



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.



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

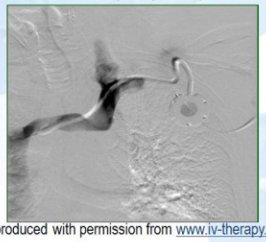
Pediatric Nutrition Support Core Curriculum. Editor: Mark Corkins. American Society for Parenteral and Enteral Nutrition (ASPEN), 2010.

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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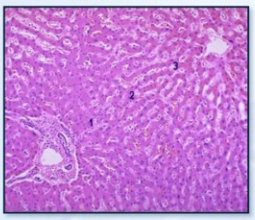
Non-thrombotic occlusions are caused by calcium phosphate precipitates, medication precipitates, lipid residue, or mineral precipitates. Thrombotic catheter occlusions are usually treated with thrombolytics. The use of 0.1N hydrochloric acid is most effective for clearing catheter occlusions due to precipitation 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.

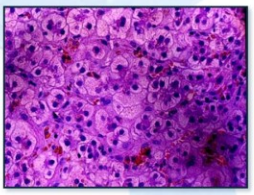
Home PN - Liver Disease I

- 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



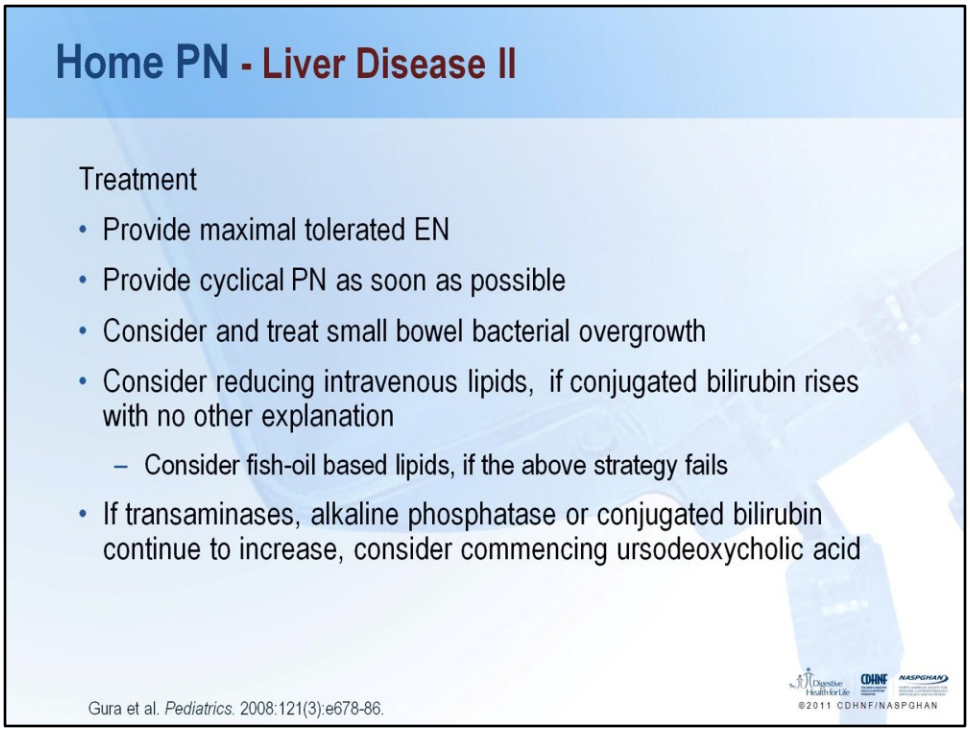
Cholestasis



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

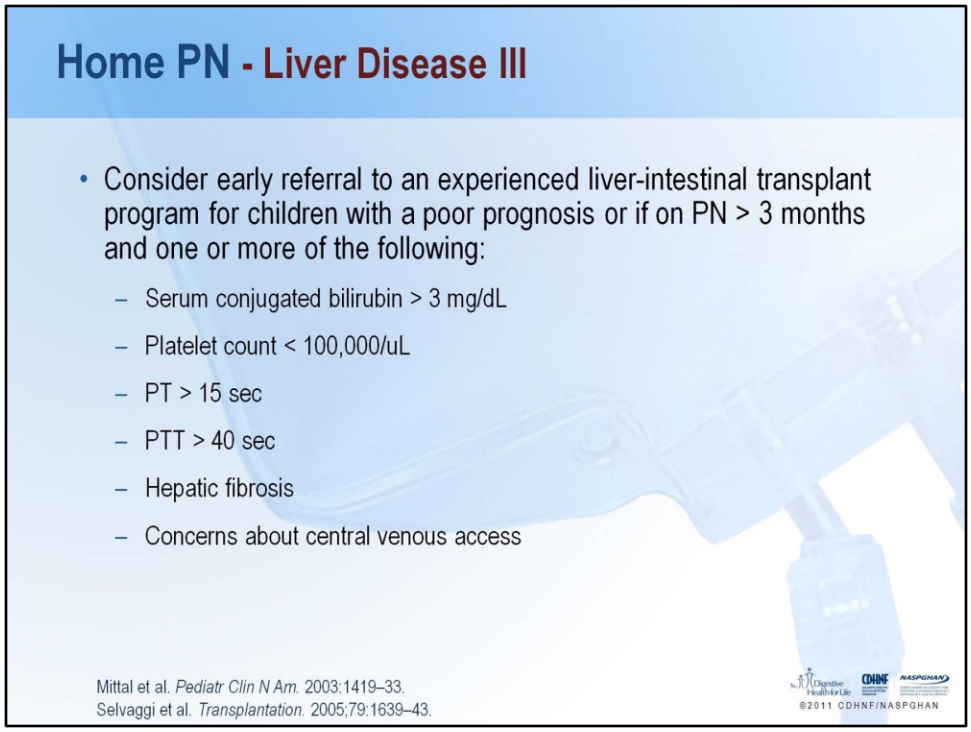
Treatment considered decreasing IV fat emulsion, start EN if only trophic, wean PN or adjust PN components.

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



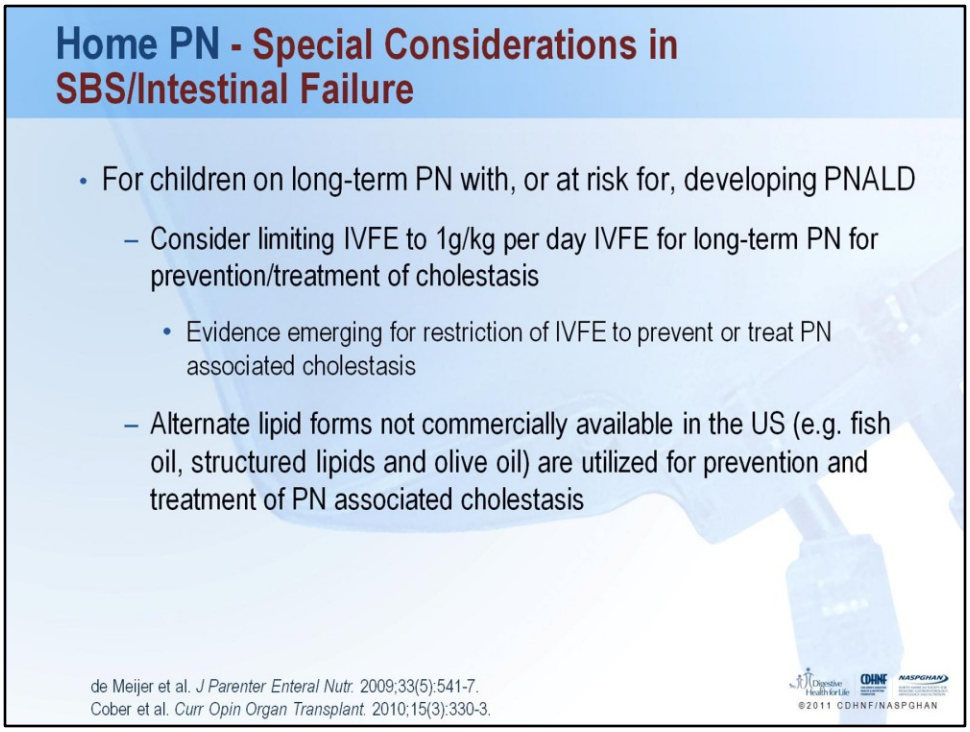
Ursodeoxycholic acid often used but limited data on its effectiveness if given enterally.

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.

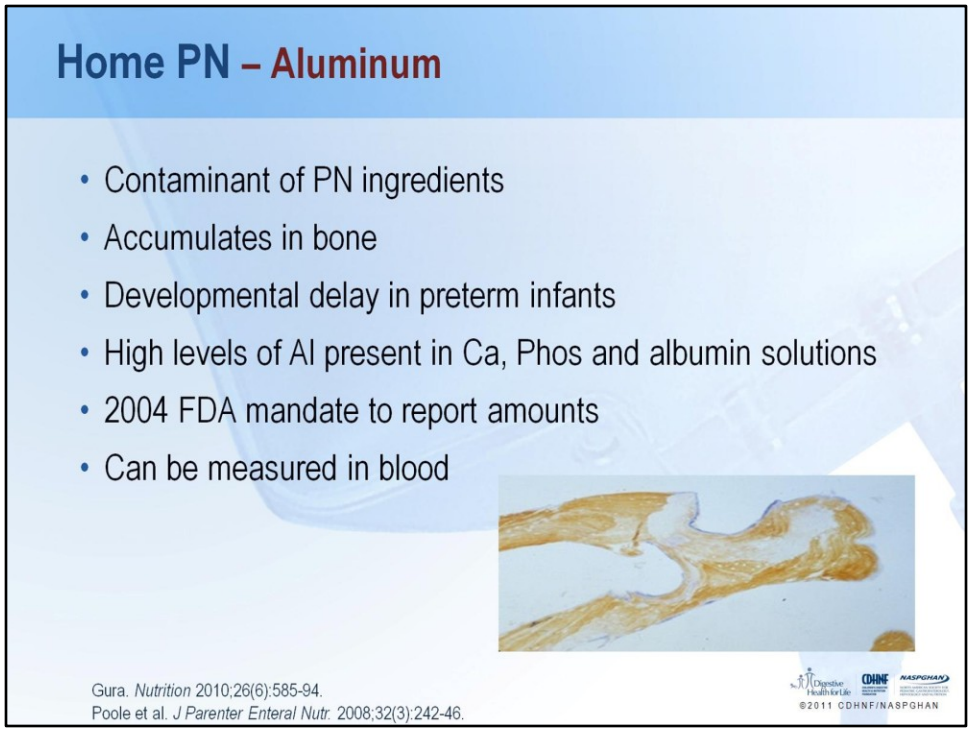


Early referral to an transplant or intestinal rehabilitation program may allow for avoidance of a liver transplant.

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.

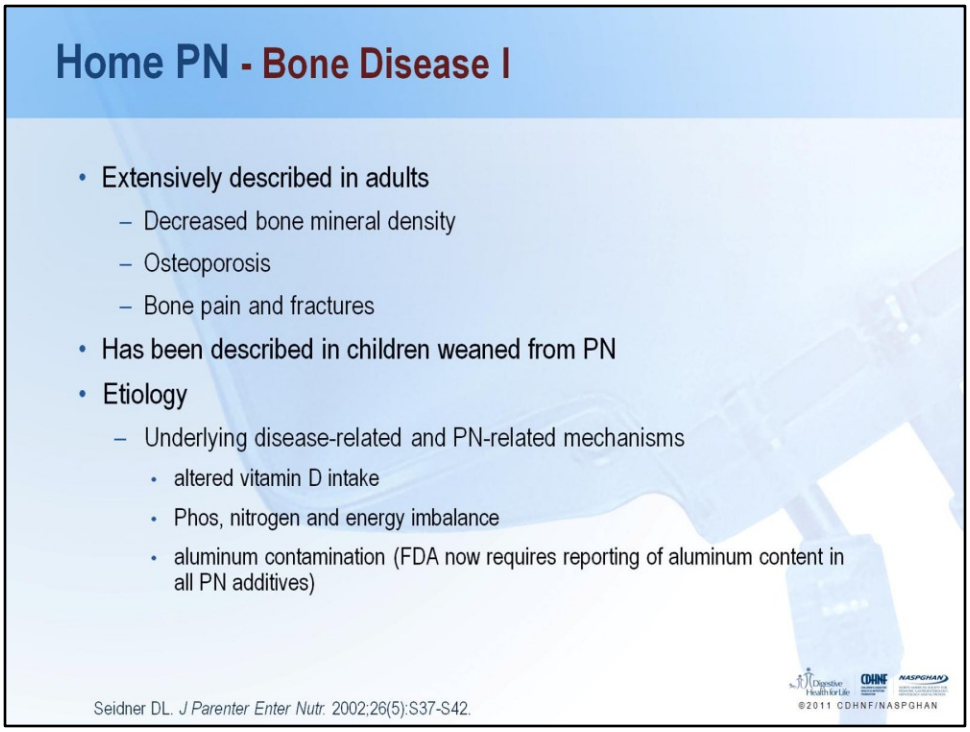


de Meijer VE, Gura KM, Le HD, et al. Fish oil-based lipid emulsions prevent and reverse parenteral nutrition-associated liver disease: the Boston experience. *J Parenter Enteral Nutr.* 2009;33(5):541-7.
Cober MP, Teitelbaum DH. Prevention of parenteral nutrition-associated liver disease: lipid minimization. *Curr Opin Organ Transplant.* 2010;15(3):330-3.



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.



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 osteomlacia, reduced bone aposition 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.

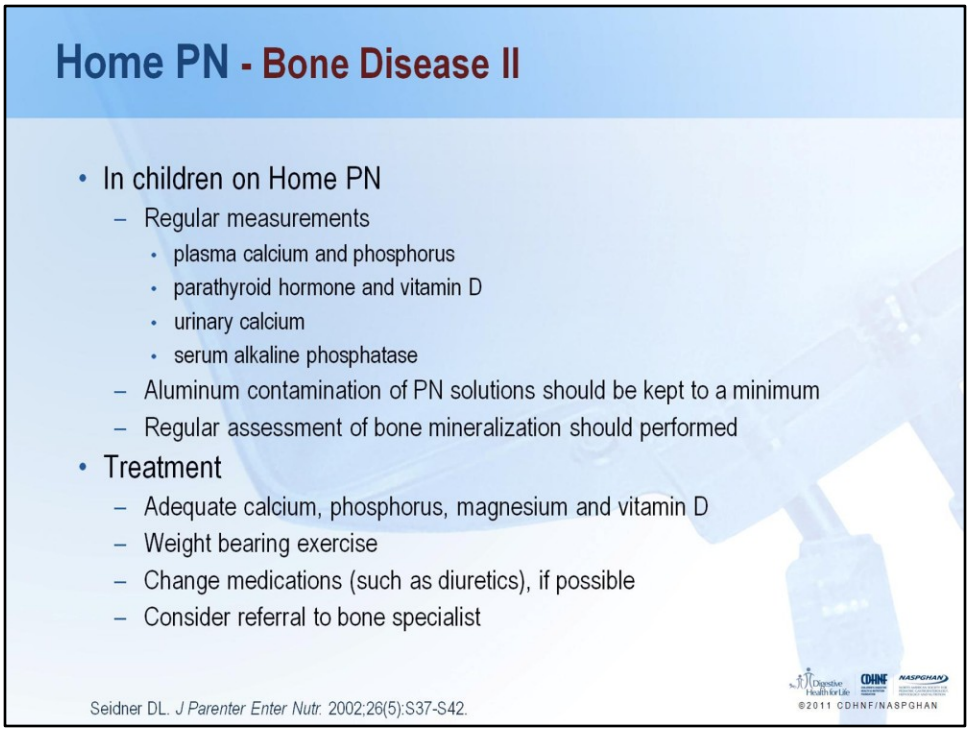
Seidner DL. Parenteral nutrition-associated metabolic bone disease. JPEN 2002; 26(5):S37-S42

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.



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

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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.