



# Parenteral Nutrition in the NICU

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Revised January 2008

*Download article by December 2008*

*Complete examination by December 2009*

**Course ID code: PNN07**

*CDR Suggested Learning Codes: 5000, 5010, 5060, 5070, 5440, 3020*

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## **Learning Objectives:**

*Upon completion of this module, the learner will be able to:*

1. List the indications for parenteral nutrition in the preterm infant.
2. Estimate protein and calories required by a preterm infant to support appropriate fetal weight gain.
3. Determine appropriate fluid and electrolyte needs of preterm infants.
4. Discuss the types of access that can be used for parenteral nutrition in the preterm infant.
5. Determine an appropriate parenteral solution that contains dextrose, amino acids and lipids for a preterm infant.
6. Explain the best way to provide preterm infants vitamins and minerals that meet their specific needs.
7. Develop a monitoring schedule of the preterm infant on parenteral nutrition.
8. Discuss the calcium and phosphorus needs of preterm infants.

**Infants in the neonatal intensive care unit (NICU) often require nutrition support. Parenteral nutrition (PN), the delivery of nutrients into the circulatory system, is often used in the first days of life to maximize caloric intake while oral feedings or enteral feedings (e.g. nasogastric), or a combination of the two methods, are established. This module discusses the assessment and prescription of PN for the preterm infant in the NICU.**

Given that most fetal nutrient stores are deposited during the last three months of pregnancy, premature infants have very minimal caloric reserves. For example, in a preterm infant weighing 1 kg, fat contributes only 1 percent of total body weight, as compared to a term infant (3.5 kg), whose weight is about 16 percent fat (Anderson, 1996).

In situations where adequate nutrition support cannot be achieved and fat and glycogen stores have been exhausted, infants begin to catabolize protein stores for energy. If it is anticipated that an infant will not receive enteral feedings for two to three days, PN should be initiated. Premature infants often do not tolerate enteral feedings due to their small stomach capacity and immature gastrointestinal tract (Anderson, 1996). Gastric emptying and intestinal transit times are significantly delayed as compared to the term infant. “Organized” gut motility does not begin until 32 to 34 weeks gestation (Thureen and Hay, 2001).

## Indications for Parenteral Nutrition

PN should be initiated immediately for medical conditions where enteral feedings are contraindicated until the medical situation allows for safe initiation of enteral feedings. The majority of cases in the NICU requiring PN support are due to either gastrointestinal (GI) malformations or necrotizing enterocolitis (NEC).

GI malformations include omphalecele, gastroschisis, intestinal atresia, volvulus, and Hirschsprung’s disease. An omphalecele is a “congenital herniation of viscera (*e.g.* internal organs) into the base of the umbilical cord, with a covering membranous sac” (Dirckx, 1996). In contrast, gastroschisis is a “defect in the abdominal wall resulting from rupture of the amniotic membrane... usually accompanied by protrusion of viscera (*e.g.* internal organs)” (Dirckx, 1997).

The surgical repair of these malformations is complex, but essentially the bowel and other organs that are outside of the abdominal cavity are reinserted into the abdominal cavity space and the area is sutured closed. Recovery from omphalecele is generally quicker than gastroschisis because the membranous sac protected the bowel during pregnancy. In gastroschisis, the bowel is often quite dilated and inflamed because of exposure to amniotic fluids. Intestinal atresia is the absence of a normal opening; in other words, the intestinal lumen has a closure where it should be a continuous segment. A volvulus is a “twisting of the intestines causing an obstruction” (Dirckx, 1997). Hirschsprung’s disease, a lack of ganglion cells in the affected segment, is also referred to as congenital megacolon.

NEC is defined as inflammation or necrosis of areas of the intestinal tract (Anderson, 1996). Some cases of NEC are classified as “medical” because a period of bowel rest and administration of antibiotics is sufficient to promote a full recovery. Surgical NEC is the term used for cases that require surgical intervention, such as peritoneal drain placement and/or intestinal resection due to bowel perforation. The cause of NEC is unknown and multi-factorial. In the past, rapid titration of feedings was implicated as the cause of NEC, but more recently this association has been questioned (Henderson, *et al.*, 2007; Kamitsuka, *et al.*, 2000; Rayyis, *et al.*, 1999). During acute NEC, feedings are frequently held for seven to 21 days to facilitate recovery.

GI malformations and NEC may require surgery that can lead to short bowel syndrome (SBS), also known as short gut syndrome. SBS symptoms include weight loss, muscle wasting, diarrhea, rapid GI transit time, malabsorption, dehydration and hypokalemia (Tyus, 1996). SBS is the primary cause for long-term PN support. A complete discussion of SBS is beyond the scope of this article.

Other medical conditions that may warrant the use of PN support include the following: intractable, non-specific diarrhea; extra corporeal membrane oxygenation (ECMO); congenital diaphragmatic hernia; and vasopressor support (*e.g.* dopamine, dobutamine). ECMO and vasopressor support may not be absolute

contraindications to enteral feedings; however, many neonatologists are hesitant to enterally feed infants with hemodynamic instability due to risk of bowel ischemia. Concerns about NEC and the possible effect of hypoxia on the gut have led to the use of PN as the main source of nutritional support in the neonatal population. However, a study was done in which infant subjects on ECMO received full-strength, continuous enteral feedings administered via either nasogastric or post-pyloric feeding tubes (Pettignano, *et al.*, 1998). There were no documented cases of NEC or intestinal perforation. Although the parenteral group achieved goal calories first (3.07 plus or minus 2.1 days for PN; 4.25 plus or minus 2.6 days for enteral), the benefits of enteral nutrition far outweigh the risks of PN. Pettignano, *et al.* concluded that vasoactive support is not considered to be a contraindication to enteral feeding. Diaphragmatic hernia often requires PN until surgical repair of the hernia occurs, and the stomach and/or intestines are returned to a more anatomically correct place in the abdominal cavity and are functioning (*e.g.* stooling).

## Classification of Premature Infants

Premature infants are born at less than 37 weeks' gestation. Classifications by weight include: Low birth weight (LBW) infants, those weighing less than 2500 gm; Very low birth weight (VLBW) infants weigh less than 1500 gm; Extremely low birth weight (ELBW) infants weigh less than 1000 gm; and micropremies weigh less than 750 gm. (The term "micropremie" is a medically acceptable technical term, but the definition varies from <800 gm to <500 gm. The most recent research uses <750 gm as the standard.)

To evaluate *in utero* growth, it is suggested to plot an infant's birth anthropometrics on the Lubchenco Intrauterine Growth Chart. An infant is "appropriate for gestation age" (AGA) if his/her weight plots between the 10<sup>th</sup> and 90<sup>th</sup> percentiles, small for gestational age (SGA) if below the 10<sup>th</sup> percentile, and large for gestational age (LGA) if above the 90<sup>th</sup> percentile. Anderson (1996) noted:

An SGA infant whose intrauterine weight gain is poor, but whose length and head circumference (HC) are between the 10<sup>th</sup> and 90<sup>th</sup> percentiles on the (Lubchenco) growth chart has experienced asymmetric intrauterine growth retardation (IUGR). An SGA infant whose length and HC are also below or equal to the 10<sup>th</sup> percentile is symmetrically growth retarded... which is more detrimental for later growth and development.

## Estimating Nutrient Needs

Infants have a higher metabolic rate and energy requirement per unit of body weight than children and adults (Pierro, 2002). Energy requirements for infants are broken down as follows: 40 to 70 kcal/kg/day for maintenance metabolism, 50 to 70 kcal/kg/day for growth (tissue synthesis and energy stored), and up to 20 kcal/kg/day to cover losses from excrement (Pierro, 2002). Caloric needs for a newborn infant fed enterally are approximately 100 to 120 kcal/kg/day, whereas those who receive PN require fewer calories (80 to 100 kcal/kg/day) because energy is not needed to cover fecal losses, nor is energy being utilized for the thermogenic effect of food (TEE).

### Estimated Nutrient Intakes Needed for Fetal Weight Gain

Body weight (gm)	500-700	700-900	900-1200	1200-1500	1500-1800
Fetal weight gain (gm/day)	13	16	20	24	26
Fetal weight gain (gm/kg/day)	21	20	19	18	16
Protein (gm/kg/day)					
Parenteral	3.5	3.5	3.5	3.4	3.2
Enteral	4.0	4.0	4.0	3.9	3.6
Energy (kcal/kg/day)					
Parenteral	89	92	101	108	109
Enteral	105	108	119	127	128

Adapted with permission from Ziegler, *et al.* Aggressive nutrition of the VLBW infant. *Clinics in Perinatology* 29;225-244, 2002.

The caloric needs of premature infants are even higher than the caloric needs of full-term newborn infants. It is suggested that VLBW neonates require a daily minimum of 60 kcal/kg/day, including 2.5 gm/kg/day of amino acids (AA) to prevent catabolism, and at least 80 to 90 kcal/kg/day, including 2.7 to 3.5 gm AA/kg/day to maintain growth rates similar to those observed *in utero* (Ibrahim, *et al.*, 2004).

Research previously described preterm newborns as minimally anabolic with parenteral intakes of 2 gm AA/kg/day and 50 to 60 kcal/kg/day (Thureen and Hay, 2001). However, a new study has revealed that provision of as low as 1.1 to 1.5 gm AA/kg/day and 30 kcal/kg/day can change protein balance from substantially negative to zero or slightly positive (Donovan, *et al.*, 2006).

Metabolic rates vary widely in neonates over time and among neonates on ECMO, with a mean of 57 plus or minus 11 kcal/kg/day, and a range of 38 to 80 kcal/kg/day (Cilley, *et al.*, 1988). An evaluation of nutrition support in neonates on ECMO demonstrated that a surplus in caloric intake does not improve protein catabolism and merely increased CO<sub>2</sub> production (Shew, 1999). Therefore, calorie goals for infants on ECMO and PN will be lower than expected for most infants in the NICU.

Enterally fed premature infants require approximately 110 to 130 kcal/kg/day. Premature infants receiving PN require an estimated 90 to 110 kcal/kg/day. Some medical circumstances may require even higher caloric intakes to support adequate growth (*e.g.* bronchopulmonary dysplasia or congenital heart disease).

## Fluid and Electrolytes

It is essential to re-evaluate an infant's fluid status daily at minimum, for at least the first week of life. In the first day of life, a full-term infant will require as little as 60 ml/kg/day to meet fluids needs. As the infant matures, fluid needs will increase to 120 to 150 ml/kg/day to allow for increases in renal solute load, stool water output, and infant growth.

Fluid Needs (ml/kg/day)			
Birth weight (gm)	Day 1-2	Day 3	DOL 15-30
750-1000	105	140	150
1001-1250	100	130	140
1251-1500	90	120	130
1501-1700	80	110	130
1701-2000	80	110	130
Term infant	70	80	100

Anderson D and Pittard WB. Parenteral Nutrition for Neonates. In: Baker R, Baker S and Cavis A eds. *Pediatric Parenteral Nutrition International* Thomson Publishing: New York 3001-314, 1997.

In preterm infants, fluid needs are 80 ml/kg/day on Day of Life 1 (DOL1), increasing by 10 to 20 ml/kg/day to 120 to 160 ml/kg/day as the infant matures (Groh-Wargo, *et al.*, 2000). Preterm infants have increased insensible water losses due to the immaturity of their skin and respiratory losses.

Close monitoring of electrolyte status is essential. The addition of electrolytes to PN may be deferred until the second day of life in some cases. Potassium is generally added once normal kidney status and good urine output are established, and sodium is often added once diuresis begins (Groh-Wargo, *et al.*, 2000). Daily adjustments to electrolyte intake are often necessary. Electrolyte requirements of preterm and full-term infants are generally similar, with the exception of calcium and phosphorus.

Daily Electrolyte Requirements for Pediatric Patients		
Electrolyte	Preterm Neonates	Infants/Children
Sodium	2-5 mEq/kg	2-5 mEq/kg
Potassium	2-4 mEq/kg	2-4 mEq/kg
Calcium	2-4 mEq/kg	0.5-4 mEq/kg
Phosphorus	1-2 mmol/kg	0.5-2 mmol/kg
Magnesium	0.3-0.5 mEq/kg	0.3-0.5 mEq/kg
Acetate	As needed to maintain acid-base balance	As needed to maintain acid-base balance

Mirtollo J, Canada T, Johnson D, *et al.* Safe practices for parenteral nutrition. *JPEN* 28(6): S39-S70, 2004.

## Access for Administering PN

PN can be administered through a peripheral vein, as peripheral parenteral nutrition (PPN). PPN requires a relatively large volume to allow for adequate administration of nutrients. In the ill infant, nutrient requirements often cannot be met with PPN due to fluid restriction. It is recommended to limit dextrose concentration to 10 to 12.5 percent with a final osmolality of 900 mOsm/kg to minimize risk of phlebitis and infiltration (Committee on Nutrition, 1983).

Total parenteral nutrition (TPN) requires central vein access and allows for administration of a solution with a higher osmolality (>900 mOsm/kg). Venous access is not defined by the initial point of entry, but by the position of the catheter tip. With central lines (CVL) the catheter tip terminates in the superior vena cava (SVC) or the right atrium of the heart. Examples of CVL that are found in infants include umbilical venous catheters (UVC), non-tunneled lines, and tunneled lines. UVC are generally placed after birth and are removed within two weeks due to increased risk of infection (Pereira, 1995).

Non-tunneled lines include femoral, jugular, subclavian and peripherally/percutaneously inserted central catheters (PICC). PICC lines are generally placed when a long-term intravenous (IV) access is needed, and duration may vary from several days to months. PICC lines may be central or peripheral, depending on the placement of the catheter tip. If the PICC line terminates in the SVC it is considered central, and termination in other vessels needs to be individually evaluated as to determine the maximum dextrose concentration that can be safely infused.

A Broviac line is the tunneled line typically used in pediatric patients, comparable to a Groshong or Hickman in adults. Broviac lines are often placed when an infant is expected to be discharged on home PN support, as with SBS patients. X-ray confirmation of central line placement is essential prior to administration of a solution with a high osmolality. Dextrose concentration of PN solution administered via a central line is generally limited to a maximum of 25 to 30 percent.

## Macronutrients

Parenterally, carbohydrates are administered in the form of dextrose, which provides 3.4 kcal per gram. Protein is administered as a crystalline amino acid solution, which provides 4 kcal/gm. TrophAmine and Aminosyn PF are amino acid solutions most appropriate for use in infants because of the addition of taurine, N-acetyl-L-tyrosine, glutamic acid and aspartic acid (Groh-Wargo, *et al.*, 2000).

TrophAmine is formulated to promote growth in neonates and young infants and to achieve a plasma amino acid pattern similar to that of normal post-prandial breast-fed infants. Research has shown a potential decrease in PN-associated cholestasis with TrophAmine (Wrught, *et al.*, 2003). Another benefit of TrophAmine is that when L-cysteine is added, there is an increased solubility of calcium and phosphorus.

Parenteral fat is a lipid emulsion of either soybean oil or a combination of safflower and soybean oil. Intravenous lipids provide 10 kcal/gm regardless of the product concentration, and are available in 10 percent (1.1 kcal/ml) and 20 percent (2 kcal/ml) concentrations. For infants the 20 percent concentration is preferred over the 10 percent product because it allows adequate lipid intake in less volume.

Also, as Groh-Wargo *et al.* noted, the “10 percent solution has a higher phospholipid/triglyceride weight ratio than the 20 percent solution, and this higher ratio may affect the activity of lipoprotein lipase, the primary enzyme for lipid clearance, resulting in higher triglycerides and other plasma lipids in infants” (Groh-Wargo, *et al.*, 2000).

Not only are lipids a concentrated source of calories, but they also provide essential fatty acids (EFA) for cell membrane integrity and brain development. Lipids also help to prolong the integrity of peripheral lines

because of their lower osmolality. It is crucial to provide a minimum of 0.5 to 1.0 gm lipids/kg/day to prevent EFA deficiency, which can develop in premature infants during the first week of life and as early as the second day of life (Groh-Wargo, *et al.*, 2000). EFA deficiency is defined as a triene-to-tetraene ratio equal to or greater than 0.4 (Kerner, 1996).

## Initiating and Titrating Parenteral Nutrition

Dextrose infusions initially are provided at 4 to 6 mg/kg/minute/day and increased gradually, as long as serum glucose is within normal ranges ( $>70$  mg/dl and  $<120$  mg/dl) (Pereira, 1995). It is recommended to increase dextrose infusion by 1 to 2 mg/kg/minute/day to a maximum of 12 mg/kg/minute/day (Lee and Werlin, 1997). This equates to increases of approximately 2.5 to 5 percent dextrose daily and is generally well tolerated. Daily increments in dextrose concentrations should not exceed 5 percent because of hyperglycemia risk (Pereira, 1995).

Occasionally, it may be necessary to administer insulin to facilitate blood sugar control if a dextrose infusion of 4 to 6 mg/kg/minute/day is not tolerated due to hyperglycemia, thus facilitating provision of sufficient dextrose for the infant's brain and meeting basal caloric requirements.

Historically it was felt that there needed to be a titration of not only dextrose, but also AA and lipids when initiating PN to facilitate tolerance and minimize the risk of metabolic disturbances (*i.e.* acidosis, hypertriglyceridemia). Recent studies have demonstrated that it is appropriate to practice a more aggressive introduction of PN in order to promote positive nitrogen balance and growth (Ibrahim, *et al.*, 2004). Minimal protein intake is the amount needed to prevent breakdown of protein stores (Thureen and Hay, 2001).

Protein restriction may be warranted in certain instances, such as renal or hepatic failure; however “... protein restriction should be done with caution and consideration should be given to the need for adequate protein to support growth and development” (Mirtallo, *et al.*, 2004).

Ibrahim, *et al.*, 2004 demonstrated that VLBW infants tolerated the initiation of PN with 3.5 gm AA/kg/day and 3 gm/kg/day of 20 percent Intralipid,<sup>TM</sup> starting within one hour of birth. Nitrogen retention was significantly greater in infants who received early aggressive PN support (Ibrahim, *et al.*, 2004). Many neonatologists hesitate to initiate PN this aggressively, especially in micropremies. Dietitians may find that a “conservative” PN initiation may be more readily accepted within 24 hours of birth, assuming normal renal function — *e.g.*, initiating with 2 to 3 gm AA/kg/day and 2 to 3 gm/kg/day of 20 percent Intralipid<sup>TM</sup>.

For infants weighing less than 1 kg, it is best to initiate lipids at 2.0 gm/kg/day and advance by 0.5 to 1.0 gm/kg/day to a goal of 3.0 gm/kg/day. Lipids can usually be well tolerated when initiated at 3.0 gm/kg/day for infants weighing more than 1 kg. Serum triglycerides (TG) should be measured at baseline, with each lipid increase, and weekly thereafter. Serum TG  $<150$  mg/dl indicate satisfactory tolerance and the lipid rate may be increased. Many clinicians tolerate levels up to 200 mg/dl (Groh-Wargo, *et al.*, 2000). To avoid hyperlipidemia, the rate of lipid infusion should not exceed 0.15 gm/kg/hour. Infusion of 3 gm/kg/day over 24 hours would result in a rate of 0.125 gm/kg/hour (Groh-Wargo, *et al.*, 2000).

Some NICU are now utilizing “stock” amino acid and dextrose solution (*e.g.* “starter PN”) to facilitate the timely initiation of PN, which now may be started in the delivery room or on the first day of life. The composition of this type of PN varies from D5 to D10 percent, and from 2 to 5 percent neonatal amino acids. Some institutions have added electrolytes (*e.g.* calcium gluconate), but many have chosen not to. Generally, administration of “stock PN” is limited to 60 to 80 mL/kg/day to minimize the risk of excessive protein and dextrose administration.

Additional intravenous fluids and electrolytes may be administered as needed. Suggested contraindications for the use of “stock PN” include patients with possible metabolic disorders, renal or hepatic failure.

## Vitamins, Minerals and Trace Elements

Available pediatric parenteral multivitamins do not meet the vitamin needs of preterm infants (Greene, *et al.*, 1988). The available formulations provide higher amounts of thiamin, riboflavin, pyridoxine and cyanocobalamin, and lower amounts of fat-soluble vitamins (*e.g.* vitamin A), than recommended (Greene, *et al.*, 1988).

Recommendations for Pediatric Multiple Vitamins*			
Manufacturer		AMA-NAG	
Weight (kg)	Daily Dose (ml)	Weight (kg)	Daily Dose
<1	1.5	<2.5	2 ml/kg
1-3	3.25	>2.5	5 ml
>3	5		

\* Pediatric multiple vitamin formulation (5 ml): vit A 2300 IU; vit D 400 IU; vit E 7 IU; vit K 200 mcg; vit C 80 mg; vit B<sub>1</sub> 1.2 mg vit B<sub>2</sub> 1.4 mg; niacin 17 mg; pantothenic acid 5 mg; vit B<sub>6</sub> 1 mg; vit B<sub>12</sub> 1 mcg; biotin 20 mcg; folic acid 140 mcg.

Mirtollo J, Canada T, Johnson D, *et al.* Safe practices for parenteral nutrition. *JPEN* 28(6): S39-S70, 2004.

Available trace element products do not adequately meet the needs of preterm neonates either. Specifically, if sufficient zinc is administered, manganese is provided in excessive amounts. However, short-term use of a standard neonatal trace element product is considered safe. Many institutions with NICUs have begun developing their own trace element mixtures from individual trace element products to better meet the needs of their smallest patients. In cases of specific medical conditions, such as renal or hepatic disease, some units will use “custom” trace elements.

**Zinc** is important for the maintenance of cell growth and development. When PN is supplemental to enteral nutrition or of short duration, zinc is the only trace element that requires supplementation. Some conditions that require additional zinc intake include elevated urinary zinc excretion (*e.g.* high output renal failure) and increased GI excretion (*e.g.* high volume stool loss and fistula/stoma losses).

**Copper** is an essential constituent of many enzymes. Current daily recommendations are adequate to prevent deficiency in preterm infants. Copper deficiency is more likely to occur with high dose zinc therapy, due to their inverse relationship. Clinical manifestations of copper deficiency include hypochromic anemia that is unresponsive to iron therapy, neutropenia and osteoporosis. Rapid growth in VLBW infants increases the risk of deficiency.

Conditions requiring higher copper intake include increased biliary losses due to jejunostomy and losses via external biliary drainage. These conditions may require an additional 10 to 15 mcg/kg/day. Historically, copper was withheld in PN for patients with cholestasis; however, cases of copper deficiency have recently been

reported when copper was withheld in PN (Hurwitz, *et al.*, 2004). In patients with cholestasis, it is recommended to reduce supplementation by 50 percent (*i.e.* 10 mcg/kg/day), monitor monthly serum copper levels and ceruloplasmin, and adjust supplementation accordingly.

**Manganese** is an important component of several enzymes (Reifen, 1993). Manganese deficiency has not been documented in humans. However, manganese toxicity has been reported. Manganese supplementation in PN should be withheld in patients with cholestasis or other liver function impairment (Reifen, 1993; Fok, *et al.*, 2001). Fok, *et al.*, provided evidence suggesting that high manganese intake contributes to the development of cholestasis. Manganese should therefore be used with caution in PN provided to infants because they are more susceptible to cholestasis (Fok, *et al.*, 2001). It is recommended to monitor monthly serum manganese levels and adjust supplementation as needed.

**Selenium** is a component of the enzyme glutathione peroxidase, which is involved in protecting cell membranes from peroxidase damage through detoxification of peroxides and free radicals (Reifen, 1993). Supplementation with selenium is recommended in long-term PN (*i.e.* longer than one month). It is recommended to decrease selenium intake when renal dysfunction is present.

**Chromium** potentiates the action of insulin and is required for growth in light of its role in glucose, protein and lipid metabolism (Reifen, 1993). It is also recommended to decrease chromium intake with renal dysfunction.

**Molybdenum** supplementation is recommended in cases when exclusive PN exceeds four weeks. Deficiency of molybdenum has not been reported in premature infants; however, one adult case of deficiency has been documented (Reifen, 1993).

**Iodine** is often omitted from PN given that iodine-containing disinfectants and detergents are used on the skin and absorbed. The Committee on Clinical Practice Issues of the American Society of Clinical Nutrition recommended parenteral intakes of iodine at 1.0 mcg/kg/day for the preterm infant (Reifen, 1993).

**Iron** supplementation should be considered only among long-term PN-dependent patients who are not receiving frequent blood transfusions. Iron supplementation of 100 mcg/kg/day may be safely delayed until three months of age in term infants. Preterm infants not receiving blood transfusions may benefit from iron supplementation of 100 to 200 mcg/kg/day at two months of age (Reifen, 1993). Monitoring iron status is imperative with iron supplementation as there is a risk of iron overload (Mirtallo, *et al.*, 2004).

Trace Element Daily Requirements		
Trace Element	Preterm Neonates <3 kg (mcg/kg/day)	Term Neonates 3-10 kg (mcg/kg/day)
Zinc	400	50 - 250
Copper	20	20
Manganese	1	1
Chromium	0.05 - 0.2	0.2
Selenium	1.5 - 2	2

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## Calcium and Phosphorus

Fetal accretion rates of calcium and phosphorus reach their peak during the third trimester, with upwards of 80 percent of fetal skeletal mineralization taking place during this time period. Therefore, premature infants are at an increased risk of osteopenia simply due to their prematurity. Ideally, the goal is to achieve intrauterine rates of bone mineralization; however, there are many barriers to this including the delayed establishment of full enteral feeds, prolonged PN, and the chronic use of medications that increase mineral excretion (*e.g.* furosemide, aldactone, sodium bicarbonate, corticosteroids).

When maximizing calcium and phosphorus in PN, there is a risk of precipitation. It is essential to collaborate with a pharmacist to review solubility curves to identify safe, yet maximum levels of calcium and phosphorus. Maximal retention can be accomplished when providing between 1.3 to 1 and 1.7 to 1 calcium/phosphorus by weight, or 1.1 to 1.3 to 1 by molar ratio. Calcium/phosphorus ratios <1 to 1 by weight (0.8 to 1 by molar ratio) and alternating daily infusions of calcium and phosphorus are not recommended. (Groh-Wargo, *et al.*, 2000). Calcium supplementation is usually provided as calcium gluconate and phosphorus in the form of sodium phosphate. Potassium phosphate is generally not used because of its high aluminum content.

Maximizing Calcium and Phosphorus in PN					
mEq CaGluc/kg	mg Ca/kg (elemental)	mMol Ca/kg	mEq NaPhos/kg	mMol Phos/kg	mg Phos/kg
3	60	1.5	2	1.5	46
3.5	70	1.75	2.33	1.75	53.6
4	80	2	2.67	2	61.4
4.5	90	2.25	3	2.25	69

\*Choose one calcium and one phosphorus column within the same horizontal row  
Adapted from information by Donna Pryor, RD, CSP, CNSD and Margaret Begany, RD, CSP, LDN

## PN Additives: Heparin, Carnitine and Cysteine

Addition of heparin to PN solutions “reduces the formation of a fibrin sheath around the catheter, may reduce phlebitis... and increases the duration of catheter patency” (Groh-Wargo, *et al.*, 2000). Heparin also stimulates the release of lipoprotein lipase, which may improve lipid clearance. It is recommended to add 0.25 to 1.0 units heparin/mL of PN solution (Groh-Wargo, *et al.*, 2000). There is an increased risk of anti-coagulation with the higher doses of heparin.

Carnitine is essential for optimum oxidation of fatty acids in the mitochondria, according to Groh-Wargo, *et al.* (2000). Impaired fatty acid oxidation can present as hypertriglyceridemia. Carnitine synthesis and storage are not optimal at birth, when compared to older children and adults. Premature infants less than 34 weeks gestation receiving PN without carnitine can develop carnitine deficiency 6 to 10 days after birth (Schmidt-Sommerfield, *et al.*, 1982). Carnitor™ (Sigma-Tau Pharmaceuticals) is available for intravenous supplementation. An initial, safe dose to consider for infants on exclusive PN for more than four weeks is 8 to 10 mg/kg/day

(Groh-Wargo, *et al.*, 2000). A recent study revealed that parenteral supplementation of 20 mg/kg/day carnitine resulted in plasma total carnitine concentrations that exceeded the reference range, which supports the use of smaller doses of carnitine supplementation (Crill, *et al.*, 2006). It is now recommended to monitor monthly carnitine levels and titrate supplementation from 8 to 10 mg/kg/day, up to a maximum of 20 mg/kg/day.

Cysteine, a conditionally essential amino acid, is not a component of crystalline amino acid solutions because it is unstable and will form an insoluble precipitate (Groh-Wargo, *et al.*, 2000). In adults, cysteine can be synthesized from methionine; however, preterm infants lack adequate hepatic cystathionase to facilitate this conversion. Commonly recommended dosing for L-cysteine hydrochloride is 40 mg per gram of amino acids. Current practice suggests supplementation with L-cysteine hydrochloride for the first year of life, although practice varies widely (Mirtallo, *et al.*, 2004).

One benefit of the addition of L-cysteine hydrochloride to PN is the decrease in the pH of the solution, which increases the solubility of supplemental calcium and phosphorus. It should be noted though that the addition of cysteine to PN warrants close monitoring of an infant's acid-base status as it may predispose infants to acidosis, and acetate may need to be added to the solution.

## Complications of PN

Short-term potential adverse effects of PN include the following: infection, hyperglycemia, electrolyte abnormalities, disturbance of acid-base balance, hypertriglyceridemia, bacterial translocation and compromised gut integrity. With long-term PN support adverse effects may include: infection, PN-cholestasis, metabolic complications, disturbance of acid-base balance, osteopenia, risk of vitamin/mineral deficiency or toxicity, and continued risk of bacterial translocation. Nosocomial infections appear to result either from improper care of the catheter and/or frequent use of the catheter for purposes other than delivery of nutrients (*e.g.* blood draws, medication administration) (Reifen, 1993).

## Monitoring

Prior to initiation of PN support, it is recommended to check the following biochemical indices: basic metabolic panel (BMP), calcium, magnesium, phosphorus, liver function tests (*i.e.* Alk Phos, ALT, AST, GGT), total bilirubin, conjugated or direct bilirubin, pre-albumin, albumin and triglyceride. The BMP, calcium, magnesium, phosphorus and triglyceride levels should be checked daily for three days after the initiation of PN support, or until indices are stable. Weekly LFTs, total bilirubin, conjugated or direct bilirubin, pre-albumin, albumin and triglyceride should be monitored.

Other biochemical studies (*e.g.* iron status, vitamin levels, ionized calcium, serum zinc, copper, manganese) may be warranted on an individual basis. Patients on long-term PN, such as those with SBS, need monthly monitoring of vitamin and mineral status.

## Emerging Issues

It has come to light that various products utilized during PN compounding have a high aluminum content, which can be especially dangerous for infants and children. Preterm infants are extremely vulnerable to aluminum toxicity due to immature renal function and the likelihood for long-term PN (Mirtallo, *et al.*, 2004).

Since July 2004, FDA mandates that products used in compounding PN should note the aluminum content on the label. The FDA identified 5 mcg/kg/day as the maximum amount of aluminum that can be safely toler-

ated and amounts exceeding this limit may be associated with central nervous system or bone toxicity (Mirtallo, *et al.*, 2004).

It is essential for pharmacists, dietitians, physicians, and nurses to collaborate to reduce the use of higher aluminum content products. However, it is difficult to achieve the recommended aluminum intake level set by the FDA when patients are receiving multiple medications and PN. A reasonable goal for clinicians is to minimize aluminum exposure.

In summary, providing PN is wrought with unique potential risks and complications to these fragile infants and calls for a diligent interdisciplinary team approach. Early enteral nutrition as soon as medically appropriate is the key to minimizing the potential adverse effects of PN support.

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## Examination for PNN07

1. PN is most often administered to infants in the NICU with which of the following:
  - a. Respiratory distress
  - b. Necrotizing enterocolitis
  - c. Renal insufficiency
  - d. Intrauterine growth retardation
  
2. A low birth weight (LBW) infant weighs:
  - a. Less than 1000 gm
  - b. Less than 1500 gm
  - c. Less than 2500 gm
  - d. Less than 3000 gm
  
3. If an infant's weight plots between the 10<sup>th</sup> and 90<sup>th</sup> percentiles, s/he is classified as:
  - a. SGA (small for gestational age)
  - b. IUGR (intrauterine growth retardation)
  - c. LGA (large for gestational age)
  - d. AGA (appropriate for gestational age)
  
4. When given exclusive parenteral nutrition support, preterm infants generally require:
  - a. 50 to 60 kcal/kg
  - b. 70 to 80 kcal/kg
  - c. 90 to 110 kcal/kg
  - d. 120 kcal/kg
  
5. Preterm infants have increased *insensible* water losses due to:
  - a. Immaturity of their skin and respiratory losses
  - b. Increased urinary output and increased fecal output
  - c. Respiratory losses and increased fecal output
  - d. Increased tissue growth and increased urinary output
  
6. The maximum osmolality of a PN solution infused via a peripheral vein (PPN) is:
  - a. 500 mOsm
  - b. 900 mOsm
  - c. 1200 mOsm
  - d. none of the above
  
7. A PICC may be considered central or peripheral access, depending on the position of the catheter tip.
  - a. True
  - b. False

8. The minimum amount of lipids that should be provided to prevent EFA deficiency is:
- 4 gm/kg
  - 2 to 3 gm/kg
  - 0.125 gm/kg/hr
  - 0.5 to 1.0 gm/kg
9. Which of the following is the appropriate initial infusion rate for dextrose and the appropriate daily increase in dextrose administration?
- Begin at 1 to 2 mg/kg/minute and increase by 1 to 2 mg/kg/minute/day
  - Begin at 3 to 4 mg/kg/minute and increase by 2 to 3 mg/kg/minute/day
  - Begin at 4 to 6 mg/kg/minute and increase by 1 to 2 mg/kg/minute/day
  - Begin at 5 to 6 mg/kg/minute and increase by 2 to 3 mg/kg/minute/day
10. Preterm infants, not receiving blood transfusions, should receive which of the following iron supplementation:
- No iron is needed, as supplemental iron is unsafe for preterm infants
  - 100 to 200 mcg/kg/day beginning at two months of age
  - 200 to 300 mcg/kg/day beginning at three months of age
  - Limit iron supplementation to 100 mcg/kg/day and start when indicated



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