Parenteral Nutrition

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ABSTRACT

Nutritional insufficiency, leading to early growth deficits has long-lasting effects, including short stature and poor neurodevelopmental outcomes. Early enteral feeding is commonly limited by immaturity of gastrointestinal motor function in preterm neonates.   To ensure that a stressed premature infant receives an adequate but not excessive amount of glucose, the amount of carbohydrate delivered in the form of dextrose is commonly initiated at the endogenous hepatic glucose production and utilization rate of 4 to 6 mg/kg/min; and 8 to 10 mg/kg/min in ELBW infants. The early provision of protein is critical to attain positive nitrogen balance and accretion as premature babies lose ~1% of their protein stores daily. Aminoacid can be used at concentrations of 3-3.5g/kg/day and lipid at 3.5-4g/kg/day as long as the fat intake remains less than 60% of nonprotein calories. Sodium, potassium, chloride, calcium, magnesium and phosphorus need to be provided in PN solution as per their daily needs. Hospital-acquired infection (HAI) is a major complication of PN. All efforts should be made to avoid it. **[Indian J Pediatr 2008; 75 (4) : 377-383]** *E-mail: ashokdeorari_56@hotmail.com*

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The goal of nutrition management in neonates, especially very low birth weight (VLBW) infants is the achievement of postnatal growth at a rate that approximates the intrauterine growth of a normal fetus at the same postconceptional age. Although, this is best achieved with optimal enteral nutrition, early enteral feeding is commonly limited by immaturity of gastrointestinal motor function, manifested principally as delayed stomach emptying, gastro-esophageal reflux, abdominal distension, and infrequent stooling. Nutritional insufficiency, leading to early growth deficits has long-lasting effects, including short stature and poor neurodevelopmental outcomes (Table 1)[1]. Likewise, establishing an alternative source of nutrition becomes a life-sustaining intervention in surgical neonates with congenital or acquired disease causing gastrointestinal failure. Parenteral nutrition (PN), first introduced in the late 1960s, has been used extensively in neonatal intensive care units (NICU) of developed countries. With improving survival of extremely premature neonates and increasing number of NICUs in India, need of parenteral nutrition is being widely recognized among health care providers. This recognition of need is accompanied by the fact that with availability of optimum nutrient sources, early administration of PN is now both safe and efficacious.

Indications

PN should be considered in neonates who are not on significant enteral feeds for more than 3-5 days or are anticipated to be receiving less than 50% of total energy requirement by day 7 of life (Table 2).

Energy

Determination of appropriate energy and nutritional requirements of a newborn infant is the first step in formulating PN. Preterm infants have very low energy reserves due to low amounts of fat as well as low glycogen reserves. Cessation of placental nutrient supplies and low reserves results in 'metabolic shock' and protein catabolism if appropriate amounts of energy and proteins are not provided soon after birth.[2] A daily energy intake of 120-130 kcal/kg is needed to meet the metabolic demands of a healthy premature neonate and to allow for growth rate comparable to intrauterine growth rate (Table 3)[3]. Energy requirement of term neonate is 100-120 kcal/kg/day. Energy intake of sick neonates (*e.g.,* acute respiratory illness, chronic lung disease, necrotizing enterocoliltis) is not exactly known but is likely to be near upper limits of the energy requirement of preterm infant.[3]

10% dextrose solution provides 0.34 kcal/ml. 10% lipid

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solution provides 0.9 kcal/ml and 20% lipid solution provides 1.1 kcal/ml. If sufficient amount of non-protein energy is not provided, amino acids are catabolised for energy production. Adequate balance between nitrogen and non-protein energy sources (Protein/Energy ratio: 3-4 gm/100 kcal) is needed to promote protein accretion.[2] Balance between carbohydrates and fat is needed to prevent excessive fat deposition and excessive production of CO_2. The ideal distribution of calories should be 50-55% carbohydrate, 10-15% proteins and 30-35% fats.

Amino acids

Amino acids (AA) are building blocks of the body. The amount needed, calculated using 'factorial approach' is 3.0-3.5 gm/kg/day (0.3 gm/kg/d to mimic intrauterine changes in body composition + 2.2 to 2.5 gm/kg/d for normal growth + 1 gm/kg/d obligatory urinary and dermal protein loss). An optimal AA solution should contain essential (valine, leucine, isoleucine, methionine, phenylalanine, threonine, lysine and histidine) and conditionally essential (cysteine, tyrosine, glutamine, arginine, proline, glycine and taurine) AAs, should not have excess of glycine and methionine and should not contain sorbitol. AA infusion can be started between 0 and 36 h of birth. The amount started on day 1 of PN has varied from 0.5 to 3.0 gm/kg/d in different studies. To avoid negative protein balance, one should start with at least 1 to 1.5 gm/kg/d and then increase by 1 gm/kg/d to maximum of 3.5 gm/kg/d. With this regimen, there have been no reports of side effects like metabolic acidosis, hyperaminoacidemia, azotemia or hyperammonaemia.[1] Studies in preterm babies who receive TPN suggest that protein accretion occurs by amino acid stimulation of protein synthesis rather than by suppression of protein breakdown.[4, 5] Protein requirements for the neonate tend to be inversely related to gestational age and size due to more rapid growth rates and greater protein losses in the smaller, more premature infants.[6] The early provision of protein is critical to attain positive nitrogen balance and accretion, as premature babies lose ~1% of their protein stores daily.[7] Benefits include improvement in nitrogen balance, stable plasma AA profile and better growth in neonatal period. AA solutions are available as 10% and 20% preparations (appendix).

Carbohydrates

Carbohydrates are the main energy substrate for the neonates receiving PN. Although, glucose is routinely administered to VLBW infants beginning soon after birth, the main objective of this established practice is to maintain euglycemia. During PN, glucose infusion rate is gradually advanced and objective is the achievement of higher energy intake. Glucose is available as 5%, 10%, 25% and 50% solutions.

To ensure that a stressed premature infant receives an adequate but not excessive amount of glucose, the amount of carbohydrate delivered in the form of dextrose is commonly initiated at the endogenous hepatic glucose production and utilization rate of 4 to 6 mg/kg/min; and 8 to 10 mg/kg/min in ELBW infants. It provides 40 to 50 kcal/kg/d and preserves carbohydrate stores.

Frequently smaller, more unstable premature infants

TABLE 1. Consequences of Suboptimal Nutrient Intake[1]

Short term	Long term
• Increased vulnerability to infections • Free-radical mediated damage • Greater need of ventilator support	• Poor growth • Poor neurodevelopment outcome • Susceptibility to cardiovascular diseases • Reduced cell growth in specific organ systems (heart, kidney, pancreas)

TABLE 2. Indications of Parenteral Nutrition

Indications of parenteral nutrition

• Birth weight less than 1000 gm
• Birth weight 1000-1500 gm and anticipated to be not on significant feeds for 3 or more days
• Birth weight more than 1500 gm and anticipated to be not on significant feeds for 5 or more days
Surgical conditions in neonates: Necrotizing enterocolitis, Gastroschisis, Omphalocele, Tracheo-esophageal fistula, Intestinal atresia, Mal-rotation, Short bowel syndrome, and Meconium ileus

TABLE 3. Daily Energy Intake Recommended for Preterm Infants[3]

Committee	Recommended energy intake (kcal/kg/day)
American Academy of Pediatrics	105-130
Canadian Pediatric Society	105-135
European Society of Gastroenterology and Nutrition	98-128
Life Sciences Research Office	110-135

develop hyperglycemia due to decreased insulin production and insulin resistance. Glucose infusion rates (GIR) for these babies may need to be limited to 4 mg/kg/min or less, while larger preterm infants or term infants can often tolerate up to 8 mg/kg/min initially.[8, 9] Once the GIR supports acceptable serum glucose values, it is advanced in a gradual, stepwise fashion (0.5 to 1 mg/kg/min) to a suggested maximum glucose oxidative rate for neonates of 12 to 13 mg/kg/min to support growth and maintained there unless serum glucose values change significantly.

Excessive carbohydrate delivery above the amount that can be oxidized for energy and glycogen storage will lead to an increase in basal metabolic rate,[10] fat deposition, cholestasis,[11] hepatic steatosis,[12] or overfeeding.

Insulin has been used along with glucose to serve two distinct purposes. One is to manage hyperglycemia if infant is developing high glucose levels despite glucose infusion rate of 4-6 mg/kg/minute. In this case, insulin is stopped as soon as euglycemia is achieved. Second objective is to achieve higher glucose infusion rate and promote growth. Later approach does not result in increased AA accretion, can induce lactic acidosis and is therefore not recommended.[13]

Lipids

Lipids are essential components of parenteral nutrition for preterm infants to provide essential fatty acids (EFAs) and to meet high energy needs. Parenteral lipids are an attractive source of nutrition in the first postnatal days because of their high energy density, energy efficiency, isotonicity with plasma, and suitability for administration through a peripheral vein. Parenteral lipid emulsions enable the delivery of fat-soluble vitamins. Even a short delay of 3 to 7 days in supplying lipids to parenterally fed preterm infants leads to biochemical EFA deficiency.[14] Such deficiency increases antioxidant susceptibility in preterm infants. EFA deficiency can be prevented with introduction of as little as 0.5 to 1.0 g/kg per day of lipid infusion. Fluid-restricted, growth-compromised patients or those limited to peripheral line access may require as high as 3.5 to 4 grams fat/kg/d to achieve adequate energy for growth and protein sparing. This intake is appropriate as long as the fat intake remains less than 60% of nonprotein calories.[15]

The routine use of intravenous lipid (IVL) emulsions has not been universally accepted in critically ill, ventilated VLBW infants because of potential complications like adverse effects on gas exchange and displacement of bilirubin from albumin. Proper use of IVL emulsions includes slow infusion rates ($\leq$0.15 g/kg per hour), slow increases in dosage, and avoidance of unduly high doses (>3.0 g/k per day). Studies have shown that administration of IVLs, beginning on day 1 at a dose of 1.0 g/kg per day and increasing in stepwise fashion to 3.0 g/

kg per day by day 4, has been well tolerated without noticeable adverse effects. Consider avoiding lipids for a short period in the unstable, late preterm infant who has evidence of increased PVR. Lipids may be restricted in patients with hyperbilirubinemia in minimum amounts that will provide only the essential fatty acids. Because both lipids and bilirubin are transported in the blood by albumin, lipids competing for binding sites on albumin may result in insufficient binding of bilirubin to facilitate excretion.[16] Persistently high bilirubin values may increase the risk of kernicterus from the deposition of bilirubin in brain cells. A free fatty acid to albumin ratio (FFA:albumin) greater than 6:1 is thought to be clinically significant.

IVL emulsions are aqueous suspensions containing neutral triglycerides derived from soybean, safflower oil, egg yolk to emulsify and glycerine to adjust tonicity. Hydrolysis of triglycerides by hepatic and lipoprotein lipase results in formation of free fatty acids. IVL emulsions are available in two strengths: 10% and 20% (Appendix). Use of 20% lipid emulsion is preferable to a 10% solution to decrease the risk of hypertriglyceridemia, hypercholesterolemia, and hyperphospholipidemia (Fig. 1). When lipids are exposed to light, they form potentially toxic lipid hydroperoxides. Hence lipid
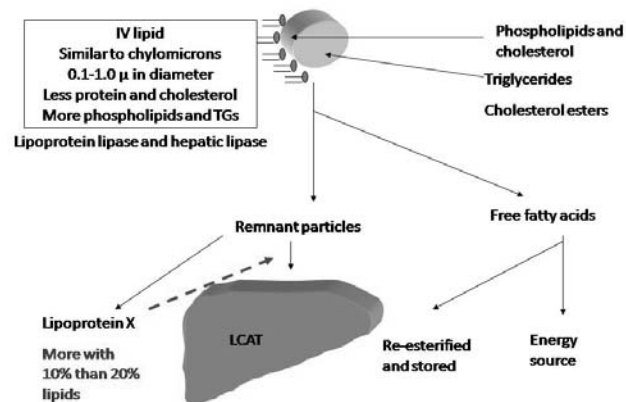

Fig. 1. Metabolism of intravenous lipid emulsions. Lipoprotein X inhibits the clearance of remnant particles

Appendix
Sources of Parenteral Solutions

Component	Source	Concentration
Proteins	Aminoven Primene	6% and 10%
Lipids	Intralipid	10%, 10% PLR (phospholipids reduced), 20%
Glucose	Dextrose	5%, 10%, 25%, 50%
NaCl	NaCl	0.9%, 3%
KCl	KCl	15%
Calcium	Calcium gluconate	10%
Multivitamin	Adult MVI	-
Trace elements	Celcel TMA	-
Magnesium sulfate	Magnesium sulfate	50%

syringes and tubing should be covered by wrapping it in aluminum foil.

Lipids may be restricted in patients with hyperbilirubinemia in minimum amounts that will provide only the essential fatty acids. Some clinicians will reduce or withhold lipids if rising bilirubin trends approach levels requiring exchange transfusions. Because both lipids and bilirubin are transported in the blood by albumin, lipids competing for binding sites on albumin may result in insufficient binding of bilirubin to facilitate excretion.[16] Persistently high bilirubin values may increase the risk of kernicterus from the deposition of bilirubin in brain cells. A free fatty acid to albumin ratio (FFA:albumin) greater than 6:1 is thought to be clinically significant.

Minerals

Sodium, potassium, chloride, calcium, magnesium and phosphorus need to be provided in PN solution as per their daily needs (Table 4). Except phosphate, all these minerals are easily available in India. Sodium, potassium, and chloride are essential to life and requirements are dependent on obligatory losses, abnormal losses, and amounts necessary for growth. Estimated and advisable intakes are based on accretion studies and urinary and fecal losses from balance studies completed in the late 1970s.[17]

Calcium, phosphorus, and magnesium are the most abundant minerals in the body. They are closely interrelated to each other in metabolism, the formation of tissue structure, and function.

Vitamins

Vitamins are added in PN solution to meet the daily requirement (Table 5). Separate preparations of fat-soluble and water-soluble vitamins suitable for neonates are not available in India. Multivitamin injection (MVI), when added in a dose of 1.5 ml/kg to AA-glucose solution meets the need of vitamin A and most other vitamin. Furthermore, intravenous vitamin delivery may be less due to photodegradation of vitamins A, D, E, K, B_2, B_6, B_{12}, C, and folic acid and adsorption of vitamins A, D, and E into the vinyl delivery bags and tubing. Vitamin K needs to be given separately as weekly intramuscular injections. Although vitamin B_{12} is not present in MVI, its deficiency is not manifested unless the neonate is on long-term PN.

Trace elements

Trace elements like zinc, copper, manganese, selenium, fluorine and iodine should be provided in PN solutions. Zinc is universally recommended from day one of TPN, whereas the other trace minerals are generally provided after two, four, or 12 weeks of TPN without any appreciable enteral feeding. Copper, selenium, molybdenum, and iron can be delivered separately also.

TABLE 4. Daily Requirement of Minerals

Mineral	Requirement
Sodium	0-3 meq/kg/d (1st week of life)
	3-6 meq/kg/d (beyond 1st week)
Potassium	0-2 meq/kg/d (1st week of life)
	1-3 meq/kg/d (beyond 1st week)
Chloride	2-3 meq/kg/d
Calcium	150-200 mg/kg/day
Magnesium	15-25 mg/d
Phosphate	20-40 mg/kg/d

TABLE 5. Recommended Vitamin Intake

Vitamin	Term (daily dose)	Preterm (dose/kg/day)
Vitamin A (IU)	2300	1640
Vitamin D (IU)	400	160
Vitamin E (IU)	7	2.8
Vitamin K (µg)	200	80
Vitamin B6 (µg)	1000	180
Vitamin B12 (µg)	1	0.3
Vitamin C (mg)	80	25
Biotin (µg)	20	6
Folic acid (µg)	140	56
Niacin (mg)	17	6.8
Pantothenic acid (mg)	5	2
Riboflavin (µg)	1400	150
Thiamin (µg)	1200	350

Dosage of zinc to be provided is 150-400 microgram/kg/d even with short-term PN, but a suitable preparation is difficult to find in Indian market.

Fluids

Intravenous fluid is the carrying medium for PN. It is started at 60-80 ml/kg/d and advanced by 15-20 ml/kg/d to maximum of 150 ml/kg/d by end of first week of life. Fluid therapy is regulated by monitoring hydration status of the infant (weight gain/loss, serum sodium, urinary specific gravity, urine output and osmolality of plasma and urine.

Evidence-based recommendations

Evidence-based recommendations for use of PN constituents are summarized in Table 6.

Dispensing PN solution

In developed countries PN solution is prepared by central pharmacy and delivered ready to be used. But this facility is usually not available in most of Indian hospitals and physicians and nurses have to chart and prepare PN. Steps for calculation and preparing PN are as follows (a PN chart is provided in appendix):

- Determine total fluid requirement for the day
- Subtract amount of fluid to be used for medications (*e.g.,* diluting and infusing antibiotics) and enteral feeds
- Plan AA, IVL and glucose to be given over 24 h

TABLE 6. Evidence-based Recommendations for Parenteral Nutrition

Component	Recommendations
Fluids	Day 1: 60-80 mL/kg/d.
	Postnatal weight loss of 5% per day to a maximum of 15% is acceptable. This is achieved by progressively increasing the fluid intake to 120-150 mL/kg/d by one week of age.
Energy	An intake of 50 kcal/kg/d is sufficient to match ongoing expenditure, but it does not meet additional requirements of growth.
	The goal energy intake is 120 kcal/kg/d (higher in infants with chronic lung disease)
Protein	Optimal parenteral amino acid intake is 3.5 g/kg/d.
	Parenteral amino acids can begin from day 1 at 1-1.5 gm/kg/d
Carbohydrates	From day 1, 6 mg/kg/min can be infused, increased by 2 mg/kg/min/d to 12-14 mg/kg/min and adjusted to maintain euglycemia
	Insulin is only used in infants who continue to have hyperglycemia associated with glycosuria and osmotic dieresis even after the glucose intake has been reduced to 6 mg/kg/min. Insulin is given as a continuous infusion commencing at a rate of 0.05 units/kg/h, increasing as required for persistent hyperglycemia.
Fat	Intravenous fat, 1 g/kg/d can be started from day 1, at the same time as when intravenous amino acids are started. This is increased to 2 g/kg/d and 3 g/kg/d over the next two days.
	It is delivered as a continuous infusion of 20% intravenous fat via a syringe pump, separate from the infusate containing the amino acids and glucose. The syringe and infusion line should be shielded from ambient light.
Minerals and Trace Elements	Minerals should include: sodium, chloride, potassium, calcium, phosphorus, magnesium.
	Trace elements should include: zinc, copper, selenium, manganese, iodine, chromium, and molybdenum.
Vitamins	Vitamins must be added to the fat emulsion to minimize loss during administration due to adherence to tubing and photo-degradation.

- Take IVL suspension in one syringe and add MVI in to it.
- In second syringe mix AA, dextrose, electrolytes and trace elements
- IVL+MVI suspension is infused separately from AA-Glucose-Minerals solution, although they can be mixed at the site of infusion using a three-way adapter.
- For calculating amount of each PN component, use following formula:

$$\text{Amount of component} = \frac{\text{Amount to be given per kg body weight} \times \text{Body weight}}{\text{Strength of solution}}$$

For example, for a baby weighing 1.5 kg to be given 3 meq/kg of sodium, amount of 3% NaCl to be used is:

$$\text{Amount of 3\% NaCl} = \frac{3 \text{ meq/kg} \times 1.5 \text{ kg}}{0.5 \text{ meq/ml}} = 9 \text{ ml}$$

Route of administration

PN can be delivered through peripheral or central venous lines. The limiting factor in deciding route of delivery is osmolarity of the AA-glucose solution which is dependent on dextrose concentration. A dextrose concentration greater than 12.5% has an acidic pH and can be irritating to the peripheral veins. In addition to dextrose, electrolytes and minerals added to the solution increase the osmolarity of the solution. Hypertonic solution need to be administered through central venous line. Increasing use of peripherally inserted central catheters (PICC) has facilitated administration of PN while avoiding many potential complications of surgically inserted central lines.

Short-term PN can be given through peripheral venous line. Another attractive option in neonates is central line inserted through umbilical vein. Position of central line should be confirmed by X-ray before starting infusion through it. The venous access used for PN should not be interrupted for giving antibiotics or other medications. For this a separate intravenous line should be established.

Peripheral access offers the advantage of a lower risk of infection due to the greater distance of the catheter from the central circulation as well as a smaller risk of mechanical complications. However, nutrition delivery is limited with peripheral lines due to constraints created by a solution's osmolarity. Osmolality refers to the number of particles per weight of water in kilograms and is typically used to describe enteral feedings and a standard in describing blood.[18] Osmolarity refers to the number of millimoles of liquid or solid in a liter of solution and is the preferred term for TPN. The sample worksheet of TPN is shown in Table 7. In peripheral access concentration greater than 900-1000 mOsm/ L are to be avoided. With central access, solutions greater than 1,000 mOsm/L are acceptable.

Monitoring and complications

Meticulous monitoring is needed in a neonate receiving PN. Monitoring protocol and its rationale is summarized in Table 8. Monitoring should be more frequent in the initial stages. Once a steady metabolic stage has been achieved, monitoring can be reduced to once a week.

Complications of PN can be nutrient-related or venous access-related. Nutrient related complications include hypoglycemia (plasma sugar < 54 mg%), hyperglycemia (plasma sugar > 150 mg%) (glucose related); azotemia,

TABLE 7. TPN Worksheet

Name		Date of birth		Age		
B. wt		Weight		Gain/loss		
Total fluid rate(ml/kg/day)			Net fluid(ml)			
Feed volume(ml)		Other medications (ml)				
Parenteral fluid (ml)						
	Strength (%)	gm/kg/day		mEq/kg/d	Strength	
Lipid planned			Sodium			
Amino acid planned			Potassium			
GIR planned						
		Multiply with 1.2 for overfill				
Lipid volume required (ml)						
MVI (ml)						
Total lipid solution (ml)						
Fluid rate (ml/hr)						
Amino acid (ml)						
10% Calcium gluconate (ml)						
Sodium chlroride						
Potassium chloride						
TMA						
Magnesium						
Others			Energy	Kcal/kg		
			Carbohydrate			
			Protein			
Net (ml)			Fat			
			Total			
Fluid left for Glucose						
Total grams of glucose to be given						
5% dextrose (ml)						
10% dextrose (ml)						
25% dextrose (ml)						
50% dextrose (ml)						
Net (ml)						
Glucose fluid rate						

TABLE 8. Monitoring Schedule for a Neonate on Parenteral Nutrition

Parameter	Frequency
Blood sugar	2-3 times a day while increasing glucose infusing rate Once a day while on stable glucose infusion rate
Urine sugar	Each urine sample ideally
Serum electrolytes	Twice a week initially, then weekly
Blood urea	Twice a week initially, then weekly
Calcium, magnesium and phosphorous	Weekly
Serum albumin	Weekly
Packed cell volume	Weekly
Liver function tests	Weekly
Serum triglycerides	Weekly
ANTHROPOMETRY	
Weight	Daily at the same time
Length	Weekly
Head circumference	Weekly
FLUID	ml/kg/day - Daily
Nutrient Intake Calculation	Energy in Kcal per kg day Protein in grams per kg per day

metabolic acidosis (protein-related); hypertriglyceridemia (triglyceride > 200 mg/dl) (lipid-related), cholestasis and trace element deficiency. Most of these complications can be avoided by proper monitoring and provision of nutrients. PN-related cholestasis is usually complication of long-term PN and can be avoided by provision of at least minimal-enteral nutrition. Catheter-related complications include dislodgement and infection.

Prevention of infection

Hospital-acquired infection (HAI) is a major complication of PN. All efforts should be made to avoid HAI.

- Aseptic precautions during preparation of PN
- Use of laminar flow
- No compromise on disposables
- Trained staff
- No reuse of the PN solutions
- No interruption of the venous line carrying PN
- Use of bacterial filter in AA-glucose line

REFERENCES

1. te Braake FW, van den Akker CH, Riedijk MA, van Goudoever JB. Parenteral amino acid and energy administration to premature infants in early life. *Semin Fetal Neonatal Med* 2007; 12 : 11-18.
2. Ziegler EE, Thureen PJ, Carlson SJ. Aggressive nutrition of the very low birthweight infant. *Clin Perinatol* 2002; 29 : 225-44.
3. Hulzebos CV, Sauer PJ. Energy requirements. *Semin Fetal Neonatal Med* 2007; 12 : 2-10.
4. Thureen P, Melara D, Fennessey P. Effect of low versus high intravenous amino acid intake on very low birth weight infants in the early neonatal period. *Pediatr Res* 2003; 53: 24-32.
5. Denne S, Karn C, Alrichs J. Proteolysis and phenylanine hydroxylation in response to parenteral nutrition in extremely premature and normal newborns. *J Clin Invest* 1996; 97: 746-754.
6. Heird W. Amino acid and energy needs of pediatric patients receiving parenteral nutrition. *Pediatr Clin North Am* 1995; 42: 765-789.
7. Heird W, Discoll J. Total parenteral nutrition. *Neo Reviews* 2003; 4 : e137-e139.
8. Denne S, Poindexter B, Leitch C. Nutrition and metabolism in the high-risk neonate. Part 2: Parenteral Nutrition. In Fanaroff A, Martin R, eds. *Neonatal-Perinatal Medicine,* St. Louis, MO: Mosby; 2002; 598-617.
9. Lifshitz C. *Carbohydrate Needs in Preterm and Term Infants*, Vol 122, Philadelphia, PA: Hanley and Belus; 1988.
10. Kanarek K, Santeiro M, Malone J. Continuous infusion of insulin in hyperglycemic low-birth weight infants receiving parenteral nutrition with and without lipid emulsion. *J Parenter Enteral Nutr* 1991; 15 : 417-420.
11. Henry B. Pediatric Parenteral Nutrition Support. In Nevin-Folino N, eds. *Pediatric Manual of Clinical Dietetics*, Faulhabes; 2003; 495-514.
12. Shulman R. New developments in total parenteral nutrition for children. *Curr Gastroenterol Rep* 2000; 2 : 253-258.
13. Poindexter BB, Karn CA, Denne SC. Exogenous insulin reduces proteolysis and protein synthesis in extremely low birth weight infants. *J Pediatr* 1998; 132 : 948-953.
14. Gutcher GR, Farrell PM. Intravenous infusion of lipid for the prevention of essential fatty acid deficiency in premature infants. *Am J Clin Nutr* 1991; 54 : 1024-1028.
15. Diamond R. Parenteral nutrition in the critically ill infant and child. In Baker R, Baker S, Davis A, eds. *Pediatric Parenteral Nutrition*, New York, NY: Chapman and Hall; 1997; 273-300.
16. Aba-Sinden A, Bollinger R. Challenges and controversies in the nutrition support of the preterm infant. *Support Line* 2002; 2 : 2-15.
17. Ziegler E, O'Donnell A, Nelson S. Body composition of the reference fetus. *Growth* 1976; 40 : 320-341.
18. Fuhrman M. Management of complications of parenteral nutrition. In Matarese L, Gottschlich M, eds. *Contemporary Nutrition Support Practice: A Clinical Guide,* Philadelphia, PA: Saunders; 1998; 236-237. 249, 252-253.