Nutritional Support in Pediatric Patients

Topic 10

Module 10.2

Parenteral Nutrition in Pediatric Patients

Berthold Koletzko
Ludwig-Maximilians-University of Munich
Munich, Germany

Learning objectives

- To review basic concepts of parenteral nutrition (PN) in infants, children and adolescents;
- To define indications for and contraindications to PN in paediatric patients;
- To appreciate specific ethical issues of PN in infants, children and adolescents;
- To review parenteral feeding requirements, including water, energy, amino acids, glucose, lipids, minerals and trace elements, and vitamin;
- To understand specific challenges of venous access in infants and children, including placement, care and complications;
- To be able to initiate EN and to wean the patient from continuous tube feeding;
- To review current standards for ordering and monitoring of PN in hospital settings;
- To discuss the advantages of home PN in paediatric patients as well as current concepts for its use;
- To review possible complications of paediatric PN as well as strategies for their prevention and management.

Contents

Key messages

- Parenteral nutrition (PN) is indicated when an adequate energy and nutrient supply cannot be achieved by oral or enteral feeding.

- PN is usually not indicated in patients with adequate small intestinal function who can be enterally (tube) fed.
- PN ordering and monitoring should follow agreed algorithms to improve quality of care.
- Infants, children and adolescents should be evaluated 2-3 times/week to detect consequences of inadequate nutrient supply (e.g. clinical examinations, weight change relative to percentile values, anthropometry, laboratory values, evaluation of parenteral and enteral nutrient supply, as appropriate for the patient).
- The best option for infants and children, depending on long-term PN, that do not need hospitalization for other reasons is home PN (HPN), which often markedly improves the quality of life of these children and their families.
- The establishment of multi-disciplinary paediatric nutrition support teams, which can considerably enhance the quality of PN and of overall nutritional care, is strongly recommended for all treatment centres caring for infants and children.
- The evidence based guidelines on paediatric parenteral nutrition established by ESPGHAN and ESPEN should guide practice, including dosage of substrate supply.

1. Basic concepts of parenteral nutrition (PN) in infants, children and adolescents

1.1 PN in paediatric patients

Parenteral nutrition (PN) is used to treat infants, children and adolescents who cannot receive sufficient oral or enteral feeding due to impaired or immature gastrointestinal function causing severe intestinal failure. Intestinal failure occurs when the gastrointestinal tract is unable to ingest, digest and absorb sufficient macronutrients and/or water and electrolytes to maintain health and growth. The ability to provide sufficient nutrients parenterally to sustain growth in infants and children suffering from intestinal failure or severe functional intestinal immaturity represents one of the most important therapeutic advances in paediatrics over the last three decades. Improvements in techniques for artificial nutritional support now ensure that children in whom digestion and absorption are inadequate, or who are unable to eat normally, no longer need to suffer from the serious consequences of malnutrition including death. Since the 1960s, the wider availability of intravenous amino acid solutions and lipid emulsions has resulted in successful prescription of PN in small infants and children. More recently, techniques have improved the development of more appropriate solutions and delivery systems. PN can now be used not only for patients who require short-term parenteral feeding but also on a long-term basis for patients with chronic intestinal failure. Children with prolonged intestinal failure on PN have the potential to grow and develop normally and to enjoy a good quality of life within the constraints of their underlying disease. Whilst advances in knowledge of nutrient requirements, improved methods of nutrient delivery, and understanding of the prevention and management of complications ensure that paediatric PN can generally be delivered safely and effectively, areas of uncertainty and controversy remain.

The guidance and recommendations provided in this module follow the evidence based guidelines on paediatric parenteral nutrition established by ESPGHAN and ESPEN (1), which are highly recommended for use as a source for more detailed information.

1.2 Indications for PN

PN is generally indicated to correct or prevent malnutrition and to sustain appropriate growth when adequate nutrition cannot be provided orally or enterally. PN should be avoided whenever possible by use of adequate care, specialised enteral nutrition (EN) and artificial feeding devices as appropriate, because PN is more costly and carries higher risks than oral or enteral feeding. PN is not indicated in patients with adequate small intestinal function in whom feeding by oral tube or gastrostomy is possible.

The timing of PN depends both on individual circumstances and the patient's age and size. Generally, the risks and adverse consequences with inadequate energy and nutrient supply increase with decreasing age and body size of children. Infants and children are particularly susceptible to the effects of starvation. The body of a small preterm infant of 1 kg body weight contains only 1 % fat and 8 % protein and has a non-protein caloric reserve of only 110 kcal/kg body weight (460 kJ/kg). As fat and protein contents rise with increasing

size, the non-protein caloric reserve increases steadily to 220 kcal/kg body weight (920 kJ/kg) in a one year old child weighing 10.5 kg (1). In children, malnutrition not only impairs tissue function, e.g. of the immune system, muscle, and cardiorespiratory systems, but also impairs growth and development. Somatic growth exhibits a bi-model pattern, being fastest in infancy, then dropping off and receiving a further spurt around puberty. Other organs of the body may grow and differentiate at only one particular time. This is particularly true with respect to the brain for which the majority of growth occurs in the last trimester of pregnancy and in the first two years of life. Poor nutrition at critical periods of growth results in slowing and stunting of growth which may later exhibit catch-up when a period of more liberal feeding occurs. In adolescence the risk is of failure to achieve growth potential if malnutrition is severe, disease is progressive and nutritional needs are unmet. Sick children are, therefore, at high risk of growth failure and nutritional disorders.

Overall, infants and young children are particularly vulnerable because:

- Due to additional metabolic requirements for rapid growth, their substrate needs per kg body weight are much higher than those of adolescents or adults (2);
- Their ability to compensate for periods of marginal substrate supply is limited because of small body stores of nutrients and immaturity of some absorptive, metabolic and renal conservation functions (3);
- Marginal or deficient substrate supplies during periods of rapid growth and organ development have particularly severe consequences, are more likely to affect disease outcome, and by way of early metabolic programming often have lasting long-term effects on organ function, as well as lifelong health and disease risks (4, 5).

For these reasons, low energy and substrate supplies that do not meet physiological requirements must not be tolerated for any prolonged period of time in paediatric patients, but must be overcome by appropriate nutritional management, including the use of PN. In small preterm infants, starvation for just one day may be detrimental, and PN must be instituted immediately after birth if oral or EN is not tolerated soon. In older children and in adolescence, longer periods of inadequate nutrition up to a maximum of about 7 days may be tolerated, depending on age, nutritional status, the disease, and surgical or medical intervention. Whenever possible, PN should be combined with some (at least minimal) oral or enteral nutrition.

1.3 Ethical aspects

PN enables the child with intestinal failure to survive even if there is little or no chance of recovery of the underlying disease, e.g. intestinal failure. There are situations in which continuing to treat a child with PN might not be beneficial even when medically possible. Ethical issues arise when the suffering imposed with continued administration of PN is greater than any potential benefit. If treatment is continued it may place an intolerable burden of care on the child and family. For example a premature baby may start PN in a neonatal unit with the expectation that it will only be required for a few days or weeks. During the course of treatment the baby may go on to develop major organ failure whilst intestinal failure persists. If intestinal function is not improving and it is likely that long term home PN will be required in a child who also has failure of another major organ, it may be appropriate to change the aims and objectives of treatment. Another situation in which PN might not be beneficial is when a child is dying and other treatment is being withdrawn. It is particularly important to address this problem when parents are administering PN at home. They may find it more distressing to mentally prepare for their child's death when they are continuing to work hard to keep their child alive by administering PN infusions. It is important to address ethical issues by holding a multidisciplinary review meeting with all professionals involved in the child's care. The aim of the meeting is to make the best possible treatment plan for the individual child and to ensure that all professionals understand the reasons for any alteration in management. A smaller group of just two or three professionals can then discuss the issues with parents. Only then can an appropriate management plan be made. If treatment is to be withdrawn, it may be necessary to involve a palliative care team particularly since parents often wish to take their child home.

2. Parenteral substrate supply

2.1 Fluid and electrolytes

Fluid needs vary markedly and must be adapted to the individual patient's condition. For example, some renal or cardiac disorders require lower water intakes, whereas higher intakes are needed with enhanced fluid

losses, e.g. due to fever, hyperventilation, diarrhea or from wounds or fistulae. Monitoring of fluid status is vital, recording the patient's clinical status, body weight, and possibly water intake and excretion, blood electrolytes, acid base status, haematocrit, urine specific gravity and urine electrolytes.

After birth, fluid supply should be gradually increased over the first 3 - 6 days after birth, i.e. in the transition phase when contraction of the extracellular fluid compartment occurs (Table 1).

Table 1 Recommended gradual increase of fluid intake (ml/kg body weight per day) for term and preterm infants during first days after birth, i.e. the transition phase when contraction of the extracellular fluid compartment occurs.

Days after birth	**1st day**	**2nd day**	**3rd day**	**4th day**	**5th day**	**6th day**
Term neonate	60 - 120	80 - 120	100 - 130	120 – 150	140 - 160	140 – 180
Preterm neonate >1500 g	60 - 80	80 - 100	100 - 120	120 - 150	140 - 160	140 - 160
Preterm neonate <1500 g	80 - 90	100 - 110	120 -130	130 - 150	140 - 160	160-180

Na^+ supply may start within the first 2 days controlled by monitoring of serum electrolytes levels, and K^+ supply is started after the onset of diuresis (Table 2).

Table 2 Recommended Na^+, K^+ and Cl^- supply (mmol/kg body weight per day) during first 3 - 6 days after birth, i.e. the transition phase when contraction of the extracellular fluid compartment occurs. K^+ supplementation should usually start after onset of diuresis

***Na^+**	0 – 3 (5)
****K^+**	0 – 2
Cl^-	0 - 5

The stabilisation phase after the extracellular fluid compartment contraction is completed may vary in duration from about 5-15 days and is completed when birth weight is regained and the kidneys produce more concentrated urine. Higher intakes of water and electrolytes are provided during this phase (Table 3).

Table 3 Recommended fluid and electrolyte supply to term and preterm infants during the stabilisation phase when extracellular fluid compartment contraction is completed (may vary in duration from about 5-15 days and is completed when birth weight is regained and the kidneys produce more concentrated urine; the expected weight gain is 10–20 g/kg body weight per day).

Birth weight	**Fluid intake** (ml/kg body weight per day)	**Na^+ intake** (mmol/kg body weight per day)	**K^+ intake** (mmol/kg body weight per day)	**Cl^- intake** (mmol/kg body weight per day)
Term neonate	140 - 170	2.0 - 5.0	1.0 - 3.0	2.0 - 3.0
Preterm >1500 g	140 - 160	3.0 – 5.0	1.0 – 3.0	3.0 – 5.0
Preterm <1500 g	140 - 180	2.0 – 3.0 (5)	1.0 – 2.0	2.0 – 3.0

During the next or third phase when stable growth is established, the aim is to match physiological growth rates. Recommended intakes of water, Na^+ and K^+ are given in Table 4.

Table 4 Recommended fluid and electrolyte supply to term and preterm infants during the phase of stable growth. Chloride supply may follow sodium and potassium intakes.

	Fluid intake (ml/kg body weight per day)	**Na^+ intake** (mmol/kg body weight per day)	**K^+ intake** (mmol/kg body weight per day)
Term neonate	140 - 160	2.0 – 3.0	1.5 – 3.0
Preterm neonate	140 - 160	3.0 - 5 .0 (7.0)	2.0 - 5.0

Chloride supply may follow sodium and potassium intakes. Recommended fluid and electrolyte intakes for infants after the neonatal period, and for children and adolescents are shown in Table 5 and Table 6, respectively.

Table 5 Recommended fluid supply to infants after the neonatal period, and to children and adolescents.

Age	**Fluid Intake** (ml/kg body weight per day) (maximal volumes in brackets)
Term infants from the second month of life	120 – 150 (180)
1-2 years	80 – 120 (150)
3-5 years	80 – 100
6-12 years	60 – 80
13-18 years	50 – 70

Table 6 Recommended electrolyte supply to infants after the neonatal period, and to children and adolescents. Chloride supply may follow sodium and potassium intakes.

Electrolyte	**Infants**	**Children > 1 year**
Na^+ (mmol/kg body weight per day)	2.0 – 3.0	1.0 – 3.0
*K^+ (mmol/kg body weight per day)	1.0 – 3.0	1.0 – 3.0

2.2 Energy

Energy supply should aim to cover the nutritional needs of the patient (basal metabolic rate, physical activity, growth and correction of pre-existing malnutrition) including the support of anabolic functions. Excessive energy intake may result in hyperglycaemia, increased fat deposition, fatty liver and other complications, whereas underfeeding may result in malnutrition, impaired immunological responses and impaired growth. In general, parenteral energy requirements are lower than enteral requirements, particularly if there is significant enteral malassimilation as is usually the case in immature infants. Energy supply can be divided into protein and non protein (carbohydrate and lipid) calories. Reasonable estimates for basal metabolic rate (equivalent to resting energy expenditure) can be derived from formulae, such as Schofield equations based on body weight and height Schofield (Table 7). Total energy need via PN is calculated by multiplying basal metabolic rate by a factor reflecting additional needs including physical activity. In most parenterally fed hospital patients energy needs are met by 100-120 % of resting energy expenditure, whereas children who are underweight and need to regain weight (catch up growth) may need up to 130-150 % of BMR.

Table 7 Schofield equations for estimating basal metabolic rates (BMR, kcal/day) from weight (Wt = body weight in kilograms) and height (Ht = body height in meters). Total energy expenditure is modified by physical activity level and other factors. In most parenterally fed hospital patients energy needs are met by 100-120 % of BMR, while patients who are underweight and need to regain weight may need 130 to 150 % of BMR.

Males, 0-3 years	BMR = 0.167 x Wt + 1517.4 x Ht - 617.6
Males, 3-10 years	BMR = 19.6 x Wt + 130.3 x Ht + 414.9
Males, 10-18 years	BMR = 16.25 x Wt + 137.2 x Ht + 515.5
Females, 0-3 years	BMR = 16.25 x Wt+ 1023.2 x Ht - 413.5
Females, 3-10 years	BMR = 16.97 x Wt + 161.8 x Ht + 371.2
Females, 10-18 years	BMR = 8.365 x Wt + 465 x Ht + 200

Recommended average total energy intakes with PN (including energy from amino acids) are shown in Table 8. In the individual patient, energy supply may need to be adjusted depending on the patient's clinical condition.

Table 8 Recommended average parenteral energy and substrate supply to infants, children and adolescents. Supply in the individual patient may need to be adjusted depending on the patient's condition.

Age group in years	**Energy** (kcal/kg)	**Amino acids** (g/kg)	**Glucose** (g/kg)	**Lipids** (g trigl/kg)	**Sodium** (mmol/kg)	**K** (mmol/kg)	**Ca** (mmol/kg)	**Ca** (mmol/kg)	**Mg** (mmol/kg)
Preterm	110-120	1.5-4	18	up to 3-4	3-5 (-7)	2-5			
Neonate 1st. month	90-100	1.5-3	18	up to 3-4	2-3	1.5-3			
0-1 yrs	90-100	1-2.5	16-18	up to 3-4	2-3	1-3	0-6mon: 0.8 7-12mon: 0.5	0.5	0.2
1-2 yrs	75-90	1-2	12-14	up to 2-3	1-3	1-3	0.2	0.2	0.1
3-6 yrs	75-90	1-2	10-12	up to 2-3	1-3	1-3	0.2	0.2	0.1
7-12 yrs	60-75	1-2	<12	up to 2-3	1-3	1-3	0.2	0.2	0.1
13-18 yrs	30-60	1-2	<10	up to 2-3	1-3	1-3	0.2	0.2	0.1

Most studies indicate that major operations e.g. abdominal surgery, are not accompanied by a lasting increase in energy expenditure, so that energy intakes should not usually be increased after uncomplicated surgery. However, energy intakes usually need to be adjusted in patients with disease states that increase resting energy expenditure, such as pulmonary (e.g. cystic fibrosis) and cardiac (e.g. some congenital heart disease) disorders. Energy supply should be adjusted according to change in weight or in parameters reflecting body composition. Therefore, parenterally fed patients should be weighed daily if possible, particularly during acute illness or during periods of instability, remembering of course that short term weight change reflects fluid balance as well as changes in tissue mass.

2.3 Amino acids

Infants and young children should receive paediatric amino acid solutions with adequate amounts of cysteine, taurine and tyrosine which are considered conditionally essential at a young age (Table 9). For cysteine the minimum advisable intake in infants and young children lies between 200 and 350 μmol/kg per day (approx. 30-55 mg cysteine-HCl/kg per day). The advisable tyrosine intake for term infants is 520 μmol/kg per day (≈ 94 mg tyrosine/kg per day). Taurine provision to infants should reach approx. 22 μmol/ gram amino acids or 2.8 mg/g amino acids. There is no conclusive evidence for the need to provide glutamine to either preterm or term infants.

Table 9 Amino acids considered essential, non-essential and conditionally essential in infants and young children

Essential	Non-essential	Conditionally essential
Histidine	Alanine	Arginine
Isoleucine	Aspartic acid	Cysteine
Leucine	Asparagine	Glycine
Lysine	Glutamic acid	Proline
Methionine	Glutamine	Tyrosine
Phenylalanine	Serine	
Threonine		
Tryptophan		
Valine		

Amino acid requirements are lower by the parenteral than the enteral route, because PN bypasses intestinal amino acid uptake and utilization. Recommended intakes of amino acids are shown in Table 8. Effective amino acid utilisation requires an energy supply of ≈30-40 kcal/1 g amino acids. Amino acids should usually be given to both preterm and term infants from the first day after birth. Higher intakes may be advisable for critically ill children and adolescents (up to 3 g/kg per day).

2.4 Glucose

Glucose is the only carbohydrate recommended for paediatric PN and should provide 60-75% of non-protein calories. During the first few days of PN, the amount of glucose in the feed should usually be gradually increased (Table 10) until desirable final dosages are achieved (Table 8). In preterm infants glucose intake should begin at 4-8 mg/kg & min (5.8-11.5 g/kg & day) and be increased gradually. In critically ill children glucose intake should be ≤5 mg/kg & min (7.2 g/kg & day). Glucose infusion for term neonates and children ≤2 years should not exceed 18 g/kg & day (13 mg/kg & min). Glucose intake should be also be adjusted if drugs which impair glucose metabolism are also being administered (e.g. steroids, somatostatin analogues, tacrolimus). Very high glucose intakes and marked hyperglycaemia should be avoided because they may induce increased lipogenesis and tissue fat deposition, liver steatosis, enhanced CO_2 production, impaired protein metabolism, and possibly increased infectious-related morbidity and mortality. In critically ill and unstable patients, glucose dosage should be lower and increased according to the patient's condition and blood glucose levels.

Table 10 Suggested increase of intravenous glucose supply over the first 4 days of PN (g/kg body weight and day)

	Day 1	Day 2	Day 3	Day 4
Up to 3 kg	10	14	16	18
3-10 kg	8	12	14	16-18
10-15kg	6	8	10	12-14
15-20kg	4	6	8	10-12
20-30kg	4	6	8	<12
>30kg	3	5	8	<10

2.5 Lipids

Lipid emulsions are an integral part of paediatric PN that should generally be provided with all PN, because they provide a high energy density in isosmolar solutions without inducing carbohydrate overload, and they also supply essential fatty acids. Lipids should generally provide 25-40 % of non-protein PN calories. Parenteral lipid intake should usually not exceed 3-4 g/kg & day (0.13-0.17 g/kg & h) in infants and 2-3 g/kg & day (0.08-0.13 g/kg & hour) in children.

In young infants lipid emulsions should usually be administered continuously over about 24 h. If cyclic PN is used, for example in home PN, lipid emulsions should be given over the same duration as the other PN components. The widely used practice of a stepwise increase in lipid infusion rates by 0.5-1 g/kg & day has not been shown to improve tolerance although it allows monitoring for hypertriglyceridaemia. Regular plasma triglyceride measurements are recommended during PN particularly in critically ill or infected patients. Dosage reduction should be considered if triglyceride concentrations during infusion exceed 250 mg/dl in infants or 400 mg/dl in children, but a minimum linoleic acid intake to prevent EFA deficiency should always be given (preterm infants $\geq$0.25 g linoleic acid/kg & day, term infants / children $\geq$0.1 g/kg & day). In critically ill or infected patients receiving lipid emulsions, more frequent monitoring of plasma triglyceride concentration and dose adjustments in cases of hyperlipidaemia are recommended. In patients with severe unexplained thrombocytopenia serum triglyceride concentrations should be monitored and a reduction in parenteral lipid dosage be considered. Although there is no firm evidence of the effects of lipid emulsions in children with severe acute respiratory failure with or without pulmonary hypertension, it appears prudent to avoid giving lipid emulsions in high dosages under these conditions. However, lipid intake should generally be continued, at least in amounts which are sufficient to supply the minimal essential fatty acids requirements. In severe, progressive PN associated cholestasis, a decrease or transient interruption of intravenous lipids should be considered.

Heparin does not improve utilisation of intravenous lipids and should not be added to lipid infusion on a routine basis, unless indicated for other reasons.

In newborn infants who cannot receive sufficient enteral feeding, intravenous lipid emulsions should be started no later than the third day of life, but may be started on the first day. Early administration of intravenous lipids in the first days of life does not increase the incidence of chronic lung disease or death in premature infants when compared to late administration of intravenous lipids. However, there are concerns about potential adverse effects of the early administration of lipid emulsions in very low birth weight infants weighing less than 800 g. Lipid emulsions have not been demonstrated to have a significant effect on hyperbilirubinaemia in premature infants. In parenterally fed infants at risk of hyperbilirubinaemia, serum triglyceride and bilirubin levels should be monitored and lipid infusion rate be adjusted if deemed necessary. During phototherapy, validated light-protected tubing for lipid emulsions is recommended to decrease hydroperoxide formation.

Decreased levels of carnitine occur during prolonged PN without carnitine supplementation. There is no documented benefit of parenteral carnitine supplementation on lipid tolerance, ketogenesis or weight gain in neonates requiring PN. Carnitine supplementation should be considered on an individual basis in patients receiving PN for more than 4 weeks.

Commercial lipid emulsions based on soybean oil, physical mixtures of olive and soybean oils, or MCT and soybean oil are considered safe for paediatric PN, but emulsions based only on soybean oil are not recommended because of their very high content of polyunsaturated fatty acids. Lipid emulsions should not contain a higher phospholipid/triglyceride ratio than standard 20% lipid solutions in order to decrease the risk of hyperlipidaemia.

2.6 Minerals and trace elements

Minerals need to be supplied with all PN given for over several days or more, and trace elements need to be supplied with long-term parenteral nutrition. Mineral and trace element status should be monitored periodically in patients on long-term PN.

Calcium (Ca) is the most abundant mineral in the body, with approximately 99% in the skeleton. Approximately 1 kg of calcium is deposited in the skeleton between birth and adulthood, with average accretion rates for boys and girls of approximately 150 and 200 mg calcium/day, respectively. However, since growth is not uniform, accretion rates may be as high as 400 mg calcium/day during infancy and puberty. The dietary calcium intake needed to satisfy the demand for skeletal growth and mineralization is greater than the accretion rate because of incomplete calcium absorption (in case of enteral supply) and losses from skin, urine and gastrointestinal tract. The amount of intravenous calcium that can be administered with PN is limited by solubility and interactions with other components.

Phosphorus (P) is a major intracellular mineral and also crucial for bone mineralization. Total body phosphorus increases from around 16 g in a newborn infant to 600-900 g in an adult, with 80% in bone and 9% in skeletal muscle. Hypercalcaemia and hypercalciuria may result from phosphate deficiency, whereas excess phosphate intake may lead to hyperphosphataemia, hypocalcaemia and secondary hyperparathyroidism. Deficiency of phosphate results in bone demineralisation and rickets. Extreme hypophosphataemia can be precipitated by nutritional restitution ('refeeding syndrome') and may result in muscle paralysis, cardiac dysfunction and respiratory failure.

Magnesium is the fourth most abundant metal in the body and the second most abundant intracellular electrolyte. Total body content of Mg is about 0.8 g in the newborn infant, rising to 25 g in an adult, with 60 % in bone. Plasma Mg represents only 0.3 to 11 % of total body stores and total plasma Mg concentration does not estimate the biologically active ionized fraction. Inadequate intakes of Mg, Ca and P may induce rickets, fractures, impaired bone mineralization and reduced linear growth.

Intravenous supply. Parenterally administered Ca cations may precipitate with inorganic phosphate anions. This can be avoided to some degree by mixing Ca and phosphate with amino-acids and glucose but even more so by using organic phosphorus compounds, such as the glycerophosphate available as a di-sodium salt.
Growing newborn infants should usually receive 1.3 – 3 mmol calcium/kg per day and 1 – 2.3 mmol phosphorus /kg per day, with a Ca:P ratio (mol/mol) in the range of 1.3 – 1.7. The adequacy of Ca and P intakes in young infants should be adjusted until both are excreted simultaneously with low urine concentrations (1-2 mmol/L) indicative of a slight surplus. Recommended intakes for infants beyond the neonatal period, children and adolescents are shown in Table 11.

Table 11 Recommended parenteral daily supply of calcium, phosphorus and magnesium for infants, children and adolescents. Growing newborn infants should usually receive 1.3 – 3 mmol calcium/kg per day and 1 – 2.3 mmol phosphorus /kg per day, with a Ca:P ratio (mol/mol) in the range of 1.3 – 1.7.

Age	Ca: mg (mmol)/kg	P: mg (mmol)/kg	Mg: mg (mmol)/kg
0-6 m	32 (0.8)	14 (0.5)	5 (0.2)
7 – 12 m	20 (0.5)	15 (0.5)	4.2 (0.2)
1 – 13 y	11 (0.2)	6 (0.2)	2.4 (0.1)
14 – 18 y	7 (0.2)	6 (0.2)	2.4 (0.1)

Iron should be supplied to all very low birth weight infants receiving PN, and to other paediatric patients receiving long-term PN (> 3 weeks). In children who receive long-term iron supplementation in PN, the risk of iron overload necessitates regular monitoring of iron status using serum ferritin. The recommended dose of iron for infants and children of 50-100 μg/kg per day is based on calculations extrapolated from studies showing that lower doses may not be sufficient to maintain iron balance. Premature infants may need 200 μg/kg per day. The preferred modality of iron administration is as regular daily doses. Which formulation (dextran, citrate etc) is optimal has not been adequately evaluated, but data in adults regarding iron dextran show it to be safe and efficacious.

Zinc should be supplied parenterally in daily dosages of 450–500 μg/kg per day for premature infants, 250 μg/kg per day for infants less than 3 months, 100 μg/kg per day for infants aged 3 months or older, and 50

μg/kg per day (up to a maximum of 5.0 mg/day) for children. Excessive cutaneous or digestive losses of zinc require additional supplementation.

Copper should be given with PN to infants and children in a dosage of 20 μg/kg per day. Plasma copper and coeruloplasmin concentrations should be monitored in patients receiving long term PN and in parenterally fed patients with cholestasis, and adjustment of copper supply be considered accordingly.

Iodine should be given to parenterally fed infants and children in a daily dose of about 1 μg/day.

Manganese: In children receiving long-term PN, a low dose supply of no more than 1.0 μg (0.018 μmol)/kg per day (maximum of 50 μg/day for children) is recommended.

Molybdenum: For low birth weight infants, an intravenous molybdenum supply of 1 μg/kg per day (0.01 μmol/kg per day) seems adequate and is recommended. For infants and children an intravenous molybdenum supply of 0.25 μg/kg per day (up to a maximum of 5.0 μg/day) is recommended.

Selenium: An intravenous selenium supply of 2 to 3 μg/kg per day is recommended for parenterally fed low birth weight infants.

Chromium contaminates PN solutions to a degree that satisfies requirements, therefore, additional supplementation of Cr is considered unnecessary.

2.7 Vitamins

Vitamins should be supplied with all PN given for several days or longer. Parenteral vitamins are usually given as a mixture of different vitamins and pose particular pharmacological problems, since some may adhere to the tubing, be degraded by light, or be affected by admixture and "ingredients". Therefore the actual amount of vitamins delivered to the patient may be much lower than the intended dose, particularly in the case of retinol (vitamin A) and in premature infants who receive solutions with slow infusion rates. The optimal parenteral vitamin dosages for infants and children have never been determined. There is also little data on vitamin needs of children with acute and chronic diseases whose requirements might differ.

While there are several parenteral vitamin preparations for adults and older children, there are just a few multivitamin preparations available for preterm infants and neonates. The available products for infants contain the same relative amount of lipid soluble vitamins despite different pharmacological properties in different preparations (combined water and fat soluble vitamin solution versus only fat soluble vitamin preparation). Adult formulations containing propylene glycol and polysorbate additives are not recommended for use in infants because of concerns about potential toxicity.

Current recommendations are based on the composition of specific products. Given the lack of adequate evidence, it is recommended that, for the time being, we should continue to use parenteral vitamin dosages that have been previously recommended and have been used for a number of years without apparent harmful effects. The one possible exception is thiamine where needs may be higher than previously assumed (Table 12).

- Infants and children receiving PN should receive parenteral vitamins.
- When possible water and lipid soluble vitamins should be added to the lipid emulsion or a mixture containing lipids to increase vitamin stability.
- Intermittent substitution twice or three times a week has not been studied. There is a hypothetical risk of adverse effects by transient high levels. Present recommendations are based on daily infusion. An exception is Vitamin K, which can be given weekly.
- Optimal doses and conditions of infusion for vitamins in infants and children have not been established, therefore, recommendations in Table 12 are based on expert opinion and experience.
- Measurement of vitamin concentrations may be needed in some children on long term PN or with particular clinical indications. For the majority, however, routine monitoring is not recommended because of the lack of evidence of any benefit.

Table 12 Recommended parenteral vitamin supply for infants and children

	Infants (Dose /kg body weight per day)	**Children** (Dose per day)
Lipid soluble vitamins		
Vitamin A (µg)*	150-300	150
Vitamin D (µg)	0,8 (32 IU)	10 (400 IU)
Vitamin E (mg)	2,8-3,5	7
Vitamin K (µg)	10 (recommended, but currently not possible)**	200
Water soluble vitamins		
Ascorbic acid (mg)	15-25	80
Thiamine (mg)	0.35-0.50	1,2
Riboflavin (mg)	0.15-0.2	1,4
Pyridoxine (mg)	0.15-0.2	1,0
Niacin (mg)	4.0-6.8	17
B12 (µg)	0.3	1
Pantothenic acid (mg)	1.0-2.0	5
Biotin (µg)	5.0-8.0	20
Folic Acid (µg)	56	140

* 1 µg RE (retinol equivalent) = 1 µg all-trans retinol = 3.33 IU vitamin A.
** Current multivitamin preparations supply higher vitamin K amounts without apparent adverse clinical effects

3. Venous access

While peripheral venous access may be used in infants and children for providing parenteral nutrients for a limited period of time, prolonged total or near total PN usually requires the use of central venous catheters (CVCs). Since their insertion and usage is associated with complications, insertion and care of such catheters should be confined to personnel trained and experienced with CVCs in paediatric patients , The importance of providing aseptic conditions in handling the catheter and of maintaining appropriate skin hygiene around the catheter cannot be exaggerated.

Peripherally inserted central catheters (PICC's) and tunnelled central venous catheters (CVCs) should be used preferentially to provide central venous access in neonates and children receiving prolonged PN. Catheters made of stiffer material (polyvinylchloride, polypropylene, polyethylene) are easier to insert, but have been associated with more infectious and mechanical complications. Softer catheters made of silicone or polyurethane coated with hydromers, are preferable for long-term PN since they are less thrombogenic and less traumatic.

With respect to insertion sites, femoral catheters in infants and children, in contrast to adults, are not associated with higher incidence of mechanical and infectious complications than those inserted via the jugular or subclavian routes. In children, the risk of mechanical complications of subclavian venous access does not exceed that of other insertion sites under appropriate conditions of insertion.

The position of the CVC tip should lie outside the pericardial sac to avoid the risk of pericardial tamponade. In small infants the catheter tip of a jugular or subclavian CVC should lie at least 0.5 cm outside the cardiac outline on a chest x-ray, while in older / larger infants that distance should be at least 1.0 cm. The catheter tip of a femoral catheter should lie above the renal veins. In older children, as in adults, positioning above the carina suggests that the catheter tip lying in the superior vena cava is likely to be outside the pericardial

sack. The risk of perforation increases with the acute angle of the catheter and the vessel wall. The catheter should therefore be parallel with the long axis of the vein. Ultrasound guidance may help in reducing complications during internal jugular venous catheterization in children and in newborns. Percutaneous, radiologically controlled insertion is equally as effective as surgical cut-down, and carries less risk of damaging the vein. CVC placement should be done under strict aseptic conditions, in infants and children preferably under general anesthesia, and by a team experienced in paediatric CVC insertion.

Umbilical vessels can be used for CVC placement in neonates. The risk of complications increases if umbilical artery catheters are left in place for more than 5 days, and umbilical venous catheters for more than 14 days. Umbilical artery catheters placed above the diaphragm are associated with a lower incidence of vascular complications.

Routine replacement of functioning CVC's and PICC's is not recommended. Malfunctioning non-tunelled CVCs can be replaced by using a guide-wire exchange technique if there is no evidence of bacteraemia or catheter related infection.

To reduce the risk of catheter related infections, a central venous line should be dedicated to the administration of PN where possible. If a CVC is used to administer PN, a catheter with the minimal number of ports or lumens essential for the management of the patient should be used in infants and children. If a multi lumen catheter is used to administer PN, one port should be exclusively designated for PN. Blood administration and central intravenous pressure monitoring from the designated line should be avoided. If single lumen catheters are used, the risk of complications increases with blood sampling from the catheter. However, to improve the quality of life of infants and children on long-term or home PN, blood sampling may need to be performed from single lumen catheters depending on the situation of the individual child, provided that the procedure is aseptic and conducted by an appropriately trained person.

The use of heparin has not been shown to be useful in the prevention of complications related to peripherally placed percutaneous CVCs in neonates. Also, the routine use of heparin with CVC's under regular use in children has no proven benefit for the prevention of thrombotic occlusion. The routine use of heparin with regularly used CVCs is not therefore recommended. With respect to CVC's not in regular use, flushing with 5 to 10 U/ml of heparinised saline once to twice weekly is recommended for maintaining CVC potency.

For skin disinfection before insertion of an intravascular device and for post-insertion site care, a clean skin should be disinfected preferably with 2% chlorhexidine, rather then 10% povidone-iodine or 70% alcohol. The antiseptic solution should remain on the insertion site and air dry before catheter insertion or application of any dressing. Organic solvents (acetone, ether, etc.) should not to be applied on the skin before insertion of a catheter or during dressing changes.

Dressings are used to secure the CVC and to prevent dislodgement and trauma. Sterile gauze and tape or various transparent polyurethane film dressings can be used for the catheter site. If the catheter site is bleeding or oozing, a gauze dressing is preferable to a transparent, semi-permeable dressing. The catheter-site dressing should be replaced when it becomes damp, loosened, or when inspection of the site is necessary. On short term CVC sites dressings should be replaced every 2 days in the case of r gauze dressings and at least every 7 days for transparent dressings, except in those paediatric patients in whom the risk of dislodging the catheter outweighs the benefit of changing the dressing. Topical antimicrobial ointments should not be used routinely at the insertion site as they may promote fungal infection, antimicrobial resistance and damage the surface of the catheters. With tunnelled catheters swimming is possible if the catheter is secured with a water resistant dressing.

4. Ordering and monitoring PN in hospitals

The quality of nutritional care in general and of PN specifically can be improved by establishment of a multi-disciplinary paediatric nutrition support team (e.g. paediatrician, paediatric surgeon, nurse, dietitian/nutritionist, pharmacist, possibly others) which has an important role in coordinating optimum nutritional care, educating staff, developing guidelines, promoting research and reducing inappropriate PN use. A specialist clinical nurse and staff training by a nutrition nurse can reduce the prevalence of catheter sepsis. The implementation of nutrition support teams is strongly recommended (6).

Since the purpose of PN is to correct or prevent nutritional deficiencies when adequate oral or enteral feeding is precluded by impairment or immaturity of gastrointestinal function, the PN order should be part of an overall nutritional care plan. Mandatory steps before the initiation of PN include a thorough nutritional assessment (medical and dietary history, physical examination, laboratory data, etc). Probable duration of PN administration should be estimated, and nutritional goals set. The process is dynamic, and the order should take into account changes in nutritional and clinical status. Nutritional support algorithms should be followed for the ordering and monitoring of parenteral nutrition because this has been demonstrated to improve quality of care. Compliance with the algorithm should be monitored.

Accurate clinical evaluation, assessment of nutritional status, and laboratory measurements should be performed prior to and during PN, where the choice of parameters used and of the frequency of evaluation should be made based on the clinical assessment of the patient (Table 13 and Table 14).

Table 13 Suggested assessment for infants and children prior to ordering PN and for monitoring during PN. The choice of parameters depends on the clinical assessment. These parameters are initially examined 2-3 times per week, and the frequency is then "tapered" based on the patients' clinical status and long term goals. When PN extends beyond three months, trace elements, ferritin, folate, vitamin B_{12}, thyroid function, clotting, and fat soluble vitamins are often measured.

- complete diet history;
- anthropometry (weight, height/length, head circumference; cf. table 14);
- full blood count (including platelets and differential white count);
- electrolytes;
- urea/creatinine;
- glucose;
- calcium/phosphate;
- albumin (or pre-albumin);
- liver function tests;
- cholesterol/triglycerides;
- urinary glucose and ketones.

Table 14 Assessment of nutritional status prior to and during parenteral nutrition

- Weight for height (% expected): 100 x weight, divided by 50th centile weight for observed height;
- Triceps skin fold thickness;
- Mid arm circumference;
- Arm fat area;
- Mid arm circumference: head circumference ratio.

Although individualized PN has traditionally been preferred in paediatric patients, standard PN solutions can be used in the majority of hospital patients with adequate monitoring and the scope for adding deficient electrolytes and nutrients, at least for short periods of PN (7). Computer assisted prescribing of PN should be encouraged, as this can save time and improve the quality of nutritional care.

All PN solutions should be administered with accurate flow control. The infusion system should undergo regular visual inspection. Peripheral infusions should be checked frequently for signs of extravasation. The pump should have free flow prevention if opened during use, and have lockable settings. All PN solutions should be administered through a terminal filter. Lipid emulsion (or all-in-one mixes) should be passed

through a membrane of pore size around 1.2 - 1.5 μm. Aqueous only solutions should be passed through a filter of 0.22 μm.

Whenever PN is used, attempts should be made to initiate and advance oral and enteral feeding as tolerated. Rather than enteral starvation, minimal enteral feeds should be given and small volumes of oral feeds should be maintained whenever possible. An experienced dietician / nutrition support team should be involved where appropriate. When introducing enteral feeding, only one change in treatment at a time should be made to assess tolerance. In severe intestinal failure feed volumes should be increased slowly, according to digestive tolerance. Enteral feeding can be introduced as liquid enteral feed infused as continuous enteral nutrition over 4 to 24 hour periods, using a volumetric pump via an artificial feeding device. If tolerated, liquid enteral nutrition may also be given as bolus or sip feeds either orally or via an artificial feeding device. Children who rapidly recover intestinal function may be weaned straight on to normal food.

5. Home parenteral nutrition

When a child that depends on long-term PN does not need hospitalization for other reasons, home PN (HPN) is generally the best option for improving the quality of life of these children and their families within the constraints of the disease. HPN is also less costly than hospital care. Therefore, all children who depend on long-term PN should be discharged on HPN, if familial and other criteria are fulfilled. The age when PN can be safely commenced at home depends on the circumstances of the patient and his or her caregivers. Given the right circumstances even infants under the age of 6 months can be cared for with HPN. Patients eligible for HPN should be in a stable condition with respect to the underlying disease, fluid and electrolyte balance, and reliable central venous access (8).

Parents or other caregivers have to be informed and motivated, and should be able to cope with all medical, emotional and technical problems related to HPN. Family suitability for HPN must be carefully assessed by a health care team member. Parents should undergo a structured teaching and training programme, conducted by a nurse from the HPN centre's nutrition support team, and parents' skills and knowledge should be checked prior to home discharge (Table 15). Community health professionals and staff from the local hospital should be involved in all aspects of discharge planning and subsequent shared care.

Table 15 Parents' knowledge required before discharge of children to home parenteral nutrition

Parents' knowledge	Handling	Catheter and line	Pump	Child
Current care	Hand washing technique Preparation of sterile field Drawing up solutions into syringe	Flushing or heparinisation Initiation and termination of infusion	Operation Maintenance	Catheter exit site Temperature
Emergency What to do? Who to contact?	Materials missing	Blockage of line Breakage/split catheter Air in the line	Alarms	Exit site infection Fever Digestive problem

HPN delivery should generally be cyclic. A progressive increase and decrease in infusion rate should be considered to avoid hypo-/hyperglycaemia. Single lumen catheters should not routinely be used for blood sampling, but to reduce stress and trauma to the child, blood sampling from single lumen catheters when connecting or disconnecting PN may be considered on an individual basis. Flow control should be provided by a pump with free flow prevention, air alarm, occlusion alarm and lockable settings. Filters should be used to avoid the risk of precipitates / particulates entering the circulation. In infants and children, standard PN

mixtures are not usually suitable for long-term PN. Therefore, PN solutions providing macro- and micronutrients for paediatric HPN should be compounded according to the individual patient's needs.

Centres caring for infants and children on HPN must have adequate expertise and resources, including multidisciplinary nutrition support teams, trained and qualified to be responsible for use and prescription of HPN in children, and a 24 hour telephone hotline. The nutrition support team should provide nursing and psychological assistance for children on HPN and their families. Paediatric HPN patients must be followed-up by an experienced team on a regular basis. Suggestions for a possible monitoring concept are provided in Table 16, but these may have to be adapted according to the patient's situation.

Table 16 Suggestions for possible monitoring of children on long-term home PN

Intervals	Clinical assessment	Other investigations
1 to 3 months	• Weight • Height • Clinical examination • Dietetic assessment	ALT, bilirubin, GGT, alkaline phosphatase, Blood chemistry, including Ca, P, Mg, urea, creatinine Blood count Clotting tests Urinary electrolytes (Ca, Na, K) Ferritin Zinc Thyroid function parameters
6 months to 1 year		Plasma vitamins A, E and D Liver and biliary tract ultrasonography Bone densitometry

6. Complications and their prevention and management

PN associated complications can be categorized in four major groups:

1. Central venous catheter (CVC) related, e.g. infection, occlusion, central venous thrombosis, pulmonary embolism and accidental removal or damage,
2. Instability of the PN solutions, and interactions with added drugs,
3. Metabolic or nutritional complications, e.g. deficiency or excess of individual PN components including electrolytes, minerals, glucose, essential fatty acids, vitamins, trace elements, and the presence of contaminants,
4. Effects on the underlying disease process, other organ systems, or both, e.g. hepatobiliary disease, metabolic bone disease and growth impairment.

Infection is one of the commonest complications of CVC's and is potentially fatal. Prevention by using aseptic techniques is essential. PN fluids should be prepared in a suitable environment for aseptic compounding according to Good Pharmaceutical Manufacturing Practice. Amino acid/glucose infusion sets & extensions should be changed after $\leq$72 hours and lipid sets after $\leq$24 hours, respectively, or as recommended by manufacturer. Carers should be taught about the signs of catheter related sepsis (CRS). CVC blood cultures should be taken for any unexplained fever or other signs of CRS. Simultaneous peripheral blood cultures are generally only useful if a semi-quantitative or quantitative culture technique is used. For suspected CRS broad-spectrum IV antibiotics should be commenced promptly after taking CVC blood cultures, the choice of agents being based on local resistance patterns. Change to narrower-spectrum therapy should be practiced once the infecting micro-organism(s) has/have been identified. The duration of therapy should be guided by the organism identified. CVC complication rates should be audited continually, and any change should be investigated and appropriate action taken.

Occlusion of the CVC can originate within the CVC lumen (blood, drug or PN fluid precipitate), in the vein (clot or fibrin sheath), external to the CVC due to the tip resting against a vein wall or due to external compression (e.g. clavicle), or patient positioning. Sodium chloride 0.9 % should be used to flush the CVC between all infusions and heparin should be instilled at least weekly when the CVC is not in use. Terminal in-line filters should be used for all PN fluids. Occlusion of in-line filters should be investigated. Using the CVC for blood sampling should be avoided if possible. Leakage from the exit site, stiffness of the CVC or increased infusion pressures should be reported immediately to an experienced practitioner and appropriate investigations performed. CVC occlusion can be treated with urokinase or alteplase for suspected blood deposits and ethyl alcohol or hydrochloric acid for suspected lipid or drug deposits. Syringes with a volume of less than 10ml should not be routinely used on CVC's to avoid excessive pressure. Unblocking the CVC with a guide-wire is not recommended.

Central venous thrombosis (CVT) and pulmonary embolism (PE) are potentially fatal complications in children receiving prolonged PN. CVT tends to develop after several weeks of PN. It may result in facial swelling, prominent superficial veins or pain on commencing PN. CVT is confirmed by echocardiography, Doppler ultrasound, CT scan and/or venography. PE may present with chest pain, dyspnoea, haemoptysis, syncope, tachypnoea, tachycardia, sweating and fever. Small thrombi may be asymptomatic or have vague symptoms such as tiredness. Symptoms or signs of thromboembolism should be reported immediately to an experienced practitioner and appropriate investigations performed. Acute symptomatic thrombosis can be treated with thrombolytic agents or anticoagulation. Vitamin K antagonists or low molecular weight heparins may be given prophylactically to patients on long-term PN at risk of or with previous thrombo-embolism.

Accidental catheter removal or damage can occur accidentally or deliberately by traction to the CVC. CVC's should be kept securely taped to the body to prevent accidental removal, traction or damage, especially when not in use. Postoperative dressings should be secure but allow observation of the exit site and be easily removable. Any damage to the CVC should be reported immediately to an experienced practitioner and appropriate repairs performed promptly. Luer lock connectors should be used to reduce the risk of accidental leakage and haemorrhage. Clamps should be available at all times to prevent bleeding from a damaged CVC. Children (as soon as they are aware) and all carers should be educated about the safety of the CVC.

Drug interactions with PN components occur in three main ways; physiological interactions that occur at all times, altered behaviour of medications owing to the complications of the presenting condition or sub-optimal nutritional support, and direct chemical interaction in the tubing during administration. PN should be administered wherever possible using an admixture formulation validated by a licensed manufacturer or suitably qualified institution. A matrix table should be sought from the supplier of the formulation detailing permissible limits for additions of electrolytes and other additives. Alternative ingredients should not be substituted without expert advice or repeat validation. Phosphate should be added in an organic-bound form to prevent the risk of calcium-phosphate precipitation. If inorganic phosphate is used, stability matrices and order of mixing must be strictly adhered to and occasional precipitates may still occur. Use of "2 in 1 admixtures" with Y-site addition of lipids should be fully validated by the manufacturer or an accredited laboratory, or the lipid should be infused through an alternative line. PN admixtures should be administered through a terminal filter. Mixing of medications with PN in administration lines should be avoided unless validated by the manufacturer or an accredited laboratory. Medications known to affect plasma protein binding of bilirubin should be avoided in parenterally fed newborn patients with severe hyperbilirubinaemia.

Metabolic complications can be prevented in part by appropriate management and monitoring. It is important to assess regularly not only weight changes but also longitudinal growth, since excessive weight gain with growth retardation has been described. In children receiving long-term PN, regular measurements of urinary calcium, plasma calcium, phosphorus, parathyroid hormone and vitamin D concentrations and serum alkaline phosphatase activity and regular assessment of bone mineralisation should be performed. Aluminium contamination of parenteral nutrition solutions provided to patients receiving long-term PN should be kept to a minimum.

PN associated liver disease is found more frequently in preterm infants, with catheter infections occurring in the first weeks and months of life, and with unbalanced and excessive parenteral nutrient intake. Prevention of liver disease requires dedicated and professional PN management, and strictly aseptic techniques to reduce the risk of infection. Maximal tolerated enteral nutrition should be provided, even if residual gut function is minimal. Cyclical PN should be introduced as soon as possible. Intraluminal bacterial overgrowth should be

considered and treated. If conjugated bilirubin steadily increases with no other explanation, the reduction or temporary interruption of i.v. lipid supply should be considered. If the transaminases, alkaline phosphatase or conjugated bilirubin continue to increase, the use of ursodeoxycholic acid should be considered. Early referral to an experienced paediatric liver and intestinal transplant centre for further assessment is recommended in infants/children with poor prognosis or if on PN for >3months and serum bilirubin >50 µmol/l, platelet count <100, PT > 15 sec, PTT > 40 sec or hepatic fibrosis.

7. Summary

- PN is an essential and often life-saving treatment for infants, children and adolescents that cannot be adequately fed orally or enterally.
- PN should only be used when all alternative options have been explored, including adequate care, specialised enteral nutrition, and artificial feeding devices.
- PN can induce severe adverse effects. The risk is reduced by a meticulous approach, establishment of a multidisciplinary nutrition support team, avoidance of unbalanced or excessive substrate supplies, strict hygiene measures to reduce catheter infections, concomitant minimal enteral feeding and aggressive enhancement of enteral feeding where possible to limit the amount and duration of PN.
- Evidence based guidelines on PN in paediatric patients provide guidance on appropriate substrate supply and PN practice.

References

1. Koletzko B, Goulet O, Hunt J, Krohn K, Shamir R; for the Parenteral Nutrition Guidelines Working Group. 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-S87.
2. Koletzko B. Nutritional needs of children and adolescents. In: Sobotka L (ed). Basics in Clinical Nutrition. Prague, Galén, 3rd ed, 2004:45-55
3. Goulet O, Koletzko B. Nutritional support in children and adolescents. In: Sobotka L (ed). Basics in clinical nutrition, 3rd ed. Prague: Galen; 2004, p.439-454.
4. Koletzko B, Akerblom H, Dodds PF, Ashwell M (eds.) Early nutrition and its later consequences: New opportunities. New York, Springer Publishers, Adv Exp Med Biol 2005;569:1-237
5. Demmelmair H, von Rosen J, Koletzko B. Long-term consequences of early nutrition. Early Hum Dev. 2006 Aug;82(8):567-74.
6. ESPGHAN Committee on Nutrition. The need for Nutrition Support Teams in pediatric units: A Commentary by the ESPGHAN Committee on Nutrition. J Pediatr Gastroenterol Nutr 2005;41:8-11.
7. Krohn K, Babl J, Reiter K, Koletzko B. Parenteral Nutrition with Standard Solutions in Paediatric Intensive Care Patients. Clin Nutr 2005;24:274-80
8. Colomb V, Goulet O, Ricour C. Home enteral and parenteral nutrition in children. Baillieres Clin Gastroenterol 1998;12:877-94.

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