Clinical Practice Guideline
Guideline coverage includes NICU KEMH, NICU PMH and NETS WA

Parenteral Nutrition (PN)

This document should be read in conjunction with the Disclaimer

Parenteral Nutrition (PN) is intravenous nutrition that is administered to assist in meeting the infant's nutritional requirements for growth and development when enteral feeding is withheld or delayed.

Standard PN is used preferentially at WNHS (KEMH and PMH NICU) for preterm and term infants. Standard PN consists of predetermined amounts of glucose and amino acids and standard concentrations of electrolytes, trace elements, vitamins and heparin.

Although discouraged, if clinically indicated, consultants may order Non-Standard PN by making modifications to the concentration of glucose, amino acids, sodium, potassium and/or acid/base balance in the Standard PN.

Keypoints

- In KEMH NICU only, Starter Packs of glucose, amino acids and heparin are given on admission as first fluids on Day 1 of life to preterm infants born < 30 weeks gestation (per 100 mL: **< 27** weeks gestation - 5% glucose; 2.5 g amino acids and 50 units heparin; **≥ 27** weeks gestation - 8% glucose; 3 g amino acids and 50 units heparin).
- STANDARD PN is available and preferred for preterm and term neonates in PMH and KEMH NICUs.
- Preterm STANDARD PN (per 100 mL) contain either 5% glucose (< 27 weeks GA) or 8% glucose (≥ 27 - < 35 weeks GA), 3 g amino acid, 50 units of heparin, standard concentrations of electrolytes and trace elements.
- Near-Term/Term (≥ 35 weeks GA) STANDARD PN (per 100 mL) contains 12% glucose and 2.3 g of amino acid, 50 units of heparin, standard concentrations of electrolytes and trace elements.
- STANDARD PNs meet age-appropriate nutrient guidelines when infused at a maximum of 140 mL/kg/d.
- In KEMH and PMH NICUs, SMOF Lipid 20% with vitamins (Final lipid concentration 17%) is available for preterm and term neonates (6 mL SMOF 17% with vitamins = 1 g fat).
- SMOF Lipid with Vitamins (17%) provides optimal fat and vitamin intake at 18-20 mL/kg/d.
- Prescribing NON-Standard PN is discouraged; Non-Standard PN orders must be authorised by a Consultant; the following components ONLY can be modified: glucose, amino acids, sodium, potassium and acetate/chloride balance.

Indications for PN

- Prematurity < 32 weeks gestation and/or < 1500g.
- Infants < 35 weeks who are unlikely to achieve full enteral feeds by day 5.
- Necrotising enterocolitis (NEC).
- Surgically correctable gastrointestinal tract anomalies (exomphalus, gastroschisis, tracheo-oesophageal fistula etc.).
- Prolonged NBM due to other surgery e.g. CDH.
- Short bowel syndrome.

Types of Formulations

1. Starter PN Bags (KEMH only)

Starter PN is available at KEMH only and prescribed as **first fluids** on **day 1 of life.**

Two Starter PN formulations with differing glucose and amino acid concentrations are available for different gestational age groups; each Starter Bag also contains heparin (50 units per 100 mL), but no other additives.

Indication	**< 27 weeks GA**	**≥ 27 weeks GA**
Glucose (%)	5	8
Amino acid (g/100mL)	2.5	3
Heparin (Units/100 mL)	50	50

2. Standard PN Bags - infused up to a maximum of 140 mL/kg/day

Three Standard PN formulations are available in KEMH and PCH NICUs. The glucose, amino acid, electrolyte and trace element contents of each Standard PN formulation are designed to meet the nutrition requirements of infants of different gestational age groups when infused at a maximum volume of 140 mL/kg/d.

	Preterm <27 weeks GA	**Preterm ≥ 27 to <35 weeks GA**	**Near-Term/Term ≥35 weeks GA**
Glucose (%)	5	8	12
Amino acid (g/100mL)	3	3	2.3
Heparin (Units/100 mL)	50	50	50

3. Modifications to Standard PN (Non-Standard PN)

If clinically indicated, modification to one or more of the following components of Standard PN can be authorised by the consultant: amino acids, glucose, potassium, sodium and/or acetate-chloride balance components; NO other components can be modified.

Clinical situations in which Non-standard PN solutions may be considered include fluid restriction, metabolic disorder, protein restriction, electrolyte abnormalities and renal failure.

Composition of PN

Protein

Crystalline amino acids are the building blocks for protein in PN solutions. Primene 10% contains essential amino acids that mimic amino acids in the umbilical cord in the last trimester of pregnancy.

In the absence of exogenous protein, a preterm infant will catabolise 1g/kg/day of their own body protein to meet their metabolic needs. Therefore the prompt introduction of glucose and amino-acids via PN achieves an early positive nitrogen balance for the infant.

Each 1g of amino acid provides 4 kcal, equivalent to approximately 17 kJ of energy. It is anticipated that infants at KEMH will receive between 2.0-2.5 g protein/kg/d within the first 24 hours of life when Starter PN is infused at 80 mL/kg/d.

Infants will receive between 3.2 g protein/kg/d (Near Term/Term) to 4.2 g protein/kg/day (Preterm) within 3-5 days of commencing Standard PN.

Glucose

Maximum glucose oxidation in preterm infants is 8.3 mg/kg/min (range 7-12 mg/kg/min) or 12 g/kg/day (ESPGHAN 2005). The upper rate of glucose administration is determined by glucose oxidative capacity for energy production and glycogen deposition and is influenced by gestational age and clinical presentation.

Each 1 g of glucose provides 3.4 kcal, equivalent to approximately 14 kJ of energy.

Electrolytes and Paediatric Trace Elements (Biomed®)

Electrolytes and trace elements (Biomed ®) are added in standard amounts per 100mL of Preterm and Near-Term/Term Standard PN.

	PRETERM	**NEAR-TERM/TERM**
Electrolytes	**mmol/100 mL**	
Sodium	4	4
Potassium	2	2
Magnesium	0.25	0.25
Calcium	0.75	0.75
Phosphate	0.75	0.75
Acetate	4	4
Chloride	3.82	3.69
Paediatric Trace Elements	**µg/100 mL**	
Zinc	296	296
Manganese	0.74	0.74
Copper	14.8	14.8
Chromium	0.15	0.15
Iodine	0.74	0.74
Selenium	5.2	5.2

Heparin

All PN formulations contain heparin (50 units /100 mL) to reduce risk of catheter occlusion with no significant difference in the duration of catheter patency, risk of thrombosis, catheter related sepsis or extension of intraventricular haemorrhage.

Lipid Emulsion plus Vitamins

20% SMOF is an isotonic fat emulsion containing refined soya oil (30%), medium chain triglycerides (30%), refined olive oil (25%), and fish oil (15%), rich in omega-3 acids, glycerol, purified egg phospholipids, all-rac-α-tocolpherol, sodium hydroxide, sodium oleate and water.

Water and fat soluble vitamins (Soluvit N Infant and Vitalipid N Infant) are added to the SMOF 20% lipid emulsion.

One pre-filled 25 mL syringe of SMOF 20% fat emulsion with vitamins contains the following:

20% Fat Emulsion	Soluvit N Infant	Vitalipid N infant
18.75 mL	1.25 mL	5 mL
The Final fat content of SMOF emulsion with vitamins is 17%; 6 mL of SMOF emulsion with vitamins contains 1 g fat and provides 10 kcal of energy, equivalent to ~42 kJ.		

Administration of 20mL/kg/d of SMOF lipid emulsion with vitamins in infants requiring PN provides essential fatty acids and	
• Vitamin A (276μg, 920 IU)	• Riboflavin (0.36μg)
• Vitamin D (4μg, 160 IU)	• Pyridoxine (0.4μg)
• Vitamin E (2.56mg, 3.8 IU)	• Biotin (6μg)
• Vitamin K (80μg)	• Nicotinamide (4mg)
• Ascorbate (10mg)	• Pantothenate (1.5mg)
• Thiamine (0.3μg)	• Folate (40μg)
• Vitamin B12 ((0.5μg) and is an excellent source of energy, therefore nitrogen-sparing.	

Lipid emulsion with vitamins should be started at 6 mL/kg/d (1 g fat/kg/d) with Starter pack at KEMH only.

Lipid emulsion with vitamins should be given at 12 mL/kg/day (2 g fat/kg/day) with the First Standard PN order at KEMH and PMH, then increased with the Second Standard PN order to a maximum of 18-20mL /kg/day (3.1-3.4 g fat/kg/day).

Lipid volume is NOT included in the total fluid intake.

Infusion rates of lipid should not exceed 1 mL/kg/hour (0.15 g/kg/d/hour).

- < 34 weeks: 0-5-1 mL/hour
- ≥ 34 weeks gestation: 0.5-3 mL/hour.

In sepsis, consider reducing lipid to 1 g/kg/d.

Prescribing TPN

Starter PN orders (KEMH only) are written on the Fluids Chart (MR725).

Standard and **Non-Standard** PN orders are written on the neonatal parenteral nutrition orders form MR800 (KEMH) or MR827 (PCH), which also incorporates a Quick Reference Guide to assist with correct prescribing of PN.

Standard PN must be prescribed whenever possible. If modifications to Standard PN are required for an individual patient, Non-Standard PN may be ordered under consultant authorisation. Non-Standard PN prescriptions must be reviewed daily.

At KEMH only, pre-made PN is available as replacement PN while awaiting a new pharmacy-supplied PN order. Pre-made PN is prescribed on Neonatal Parenteral Fluid Chart (MR725).

Administration

PN can be administered through peripheral or central lines. If glucose concentration exceeds 12.5%, administer via a central vein catheter.

If a prolonged period of PN is anticipated, insertion of a percutaneous central venous catheter may be considered. The position of the tip of the catheter needs to be in a large vessel, preferably the superior or inferior vena cava outside the heart, with position confirmed by x-ray prior to use. An aseptic technique in preparation and administration of the TPN is essential.

Precautions

- Hyperkalaemia. **Use caution when prescribing potassium in renal impairment or persisting hypotension with poor urine output.**
- Toxicity due to accumulation of certain amino acids should be considered in an infant becoming unwell and acidotic on PN. Serum and urinary amino acids should be measured.
- Fatty acids. Due to fatty acids being precursors of prostaglandin synthesis, potential adverse effects on pro/anti-coagulation homeostasis and pulmonary vascular tone are theoretically possible.

Complications of PN

The line delivering the PN may be compromised by:

- **Malposition**: potentially leading to a fatal complication of pericardial tamponade from a line in the right atrium and a subsequent pericardial effusion of TPN. Measurement of the estimated distance of insertion of central lines is essential as is an X-ray before the infusion commences. Lines should also aspirate blood freely at the length at which they are to be inserted. This is to ensure the line is sitting in a large vessel (see central line insertion procedure guideline).
- **Sepsis**: Minimised by maintaining strict sterility of the line during and after insertion. In adults sepsis induces profound changes in both energy and protein metabolism. Several neonatal studies have documented glucose and lipid intolerance in neonates with sepsis but the single study of protein metabolism in neonates with sepsis did not demonstrate either increased protein requirements or significant protein intolerance. PN may be reduced during the acute phase of an episode of sepsis. Optimal infusions of glucose,

amino acids and lipids should be reinstated as soon as the infant improves and parameters are stable.

- **Catheter** tip thrombi.
- **Thrombophlebitis**, with peripheral lines, requiring close observation of infusion sites.
- **Extravasation** into the soft tissue, with resulting tissue necrosis.

Metabolic Complications

- Hyperglycaemia - Maximum glucose oxidation in preterm infants is 8.3mg/kg/min or 12g/kg/d (ESPGHAN 2005). The upper rate of glucose administration is determined by glucose oxidative capacity for energy production and glycogen deposition and is influenced by gestational age and clinical condition. Glucose administration may range from 7-12 mg/kg/min. Hyperglycaemia is common after preterm birth possibly related to surges in catecholamines, decrease in insulin production and insulin resistance. Hyperglycaemia is associated with death, IVH and sepsis. Excessive glucose intakes may increase carbon dioxide production and exacerbate chronic lung disease. Insulin is not recommended as offers no clinical benefit and infusion is associated with risk of hypoglycaemia and associated morbidity (Beardsall 2008).
- Adverse effects of excess protein include a rise in urea and ammonia, as well as a metabolic acidosis. The addition of a buffer (base), acetate, can reduce metabolic acidosis. In one RCT the partial replacement of chloride by acetate in the amino acid solution resulted in an improved pH, a reduction in both bicarbonate and colloid use, with no adverse effect on ventilation requirements compared to the group receiving standard PN (Peters et al 1997). There are 3 mmol of acetate and 3.82 mmol of chloride in a standard PN. If sodium is ordered as acetate, then the acetate chloride balance can be altered. More acetate can be used if more sodium is prescribed.
- Cholestasis is associated with administration of TPN for >2 weeks. The exact cause of this is unknown. It is thought to be due to either hepatotoxicity of the infusiate or to the lack of hepatic stimulation in the absence of enteral feeds. From studies in older children, it has also been shown that the infusion of fish oil may reverse the cholestasis associated with parenteral nutrition (Gura KM et al Pediatrics 2008).

Monitoring

Monitoring PN in preterm infants includes:

- Na, K, Cl, HCO3 and glucose daily in the first week, alternate days thereafter.
- Urea daily to twice weekly and consider phosphate level weekly.
- Plasma TG aiming at 150-250mg/dl (2.8mmol/l) optional and when lipaemic serum noted.
- Liver function tests fortnightly.
- Bone bloods monthly (Alk Phos, Ca, Phosphate, Vitamin D).
- Weight daily or alternate days; and head circumference weekly. Length at admission and discharge.
- If CVL, consider twice weekly CRP for catheter-related sepsis.

References

1. Beardsall K, Vanhaesebrouck S, Ogilvy-Stuart AL et al. Early insulin therapy in very low birthweight infants. NEJM 2008: 359: 1873-84.
2. Blanco CL, Falck A, Green BK, Cornell JE, Gong AK. Metabolic responses to early and high protein supplementation in a randomized trial evaluating the prevention of hyperkalemia in extremely low birth weight infants. J Pediatr. 2008; 153(4): 535-40.
3. Bolisetty S, Osborn D, Sinn J et al. Standardised neonatal parenteral nutrition formulations – an Australasian group consensus 2012. BMC. 2014; 14:48; doi: 10.1186/1471-2431-14-48.
4. Clark R, Thomas P, Peabody J. Extrauterine growth restriction remains a serious problem in prematurely born neonates. Pediatrics. 2003; 111: 986-90.
5. Clark RH, Chace DH, Spitzer AR. Effects of two different doses of amino acid supplementation on growth and blood amino acid levels in premature neonates admitted to the neonatal intensive care unit: a randomized, controlled trial. Pediatrics. 2007; 120(6): 1286-96.
6. Dusick AM, Poindexter BB, Ehrenkranz RA, Lemons JA. Growth failure in the preterm infant: can we catch up? Seminars in Perinatology. 2003; 27(4): 302-10.
7. ESPGHAN Guidelines on Paediatric Parenteral Nutrition. J Pediatr Gastroenterol Nutr 2005; 45: Suppl 2: S5-18.
8. Gobel Y, Koletzko B, Bohles HJ, Engelsberger I, Forget D, Le Brun A, et al. Parenteral fat emulsions based on olive and soybean oils: a randomized clinical trial in preterm infants. J Pediatr Gastroenterol Nutr. 2003; 37: 161-7.
9. Gura KM, Lee S, Valim C, Zhou J, Kim S, Modi BP, Arsenault DA, Strijbosch RA, Lopes S, Duggan C, Puder M. Safety and efficacy of a fish-oil-based fat emulsion in the treatment of parenteral nutrition-associated liver disease. Pediatrics. 2008 Mar;121(3):e678-86.
10. Ibrahim HM, Jeroudi MA, Baier RJ, Dhanireddy R, Krouskop RW. Aggressive early total parental nutrition in low-birth-weight infants. J Perinatol. 2004; 24(8): 482-6.
11. Peters O, Ryan S, Matthew L, Cheng K, Lunn J. Randomised controlled trail of acetate in preterm neonates receiving parenteral nutrition. Arch Dis Child Fetal Neonatal Ed 1996; 77: F12-15.
12. Simmer K, Rao SC. Early introduction of lipids to parenterally-fed preterm infants. Cochrane Database Syst Rev. 2005; (2): CD005256.
13. Simmer K. Aggressive nutrition for preterm infants--benefits and risks. Early Hum Dev. 2007; 83(10): 631-4.
14. Shouman B, Abdel-Hady H, Badr RI, Hammad E, Salama MF. Dose of intravenous lipids and rate of bacterial clearance in preterm infants with blood stream infections. Eur J Pediatr. 2012 May;171(5):811-6.
15. te Braake FW, van den Akker CH, Wattimena DJ, Huijmans JG, van Goudoever JB. Amino acid administration to premature infants directly after birth. J Pediatr. 2005; 147(4): 457-61.
16. Thureen PJ, Melara D, Fennessey PV, Hay WW, Jr. Effect of low versus high intravenous amino acid intake on very low birth weight infants in the early neonatal period. Pediatr Res. 2003; 53(1): 24-32.
17. Tsang RC, Uauy R, Koletzko B, Zlotkin SH, editors. Nutrition of the preterm infant. Scientific basis and practical guidelines. 2nd Edition ed. Cincinnati, Ohio: Digital Educational Publishing, Inc.; 2005.

Related WNHS policies, procedures and guidelines

Neonatal Medication Protocols: SMOF Fat Emulsion 20% with Soluvit N and Vitalipid N Infant

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