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 CAHS (KEMH NICU and PCH NICU) for preterm and term infants. Standard PN consists of pre-determined amounts of glucose and amino acids and standard concentrations of electrolytes, trace elements and heparin.

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.

If clinically indicated, consultants may request that phosphate and calcium is modified in standard amounts by pharmacy.

**Key Points**

- In **KEMH NICU only**, Starter Packs of glucose, amino acids, heparin and electrolytes are given on admission as first fluids to preterm infants born < 30 weeks gestation.
- STANDARD PN is available and preferred for preterm and term infants in PCH and KEMH NICUs.
- Preterm STANDARD PN (per 100 mL) contains either 5% glucose (< 27 weeks GA) or 8% glucose (≥ 27 - < 35 weeks GA), 3 g amino acids, 50 units of heparin and standard amounts 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 PCH 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) and should be commenced at 6-12 ml/kg/d with Starter and Standard PN, increasing to 18-20 mL/kg/d.
• Prescribing NON-Standard (customised) PN is discouraged; NON-standard PN orders must be authorised by a consultant; the following components can be modified:
  o Glucose, amino acids, sodium, potassium and acetate/chloride balance
  o Phosphate and calcium can be modified in standard amounts by pharmacy if hypophosphataemia (and/or hypocalcaemia) is identified (phosphate <1.4 mmol. L\(^{-1}\) which is a common feature of refeeding syndrome). Note that for solubility issues, both calcium and phosphate need to be increased – clinician must contact neonatal pharmacist.

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).
• Surgical 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) infused up to 80 mL/kg/day on day 1 of life.
   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), and standard amounts of electrolytes (Table 1).

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 (Table 1).

3. Modifications to Standard PN (Non-Standard PN)
   (i) If clinically indicated, NON-Standard PN can be ordered under Consultant authorisation and medical order, by modification to one or more of the following components of Standard PN: Amino acids, glucose, potassium, sodium and/or acetate-chloride balance components;
   (ii) If hypophosphataemia (and /or hypocalcaemia) is identified, phosphate and calcium can be modified under consultant authorisation in standard amounts by pharmacy for preterm (from 0.75 mmol.L\(^{-1}\) to 1.5 mmol.L\(^{-1}\)) and term (from 0.75 mmol.L\(^{-1}\) to 1.0 mmol.L\(^{-1}\)) infants – pharmacy must be contacted for changes to be made. Note that for solubility issues, both calcium and phosphate need to be increased in the TPN.

Clinical situations in which Non-standard PN solutions may be considered include fluid restriction, metabolic disorder, protein restriction, electrolyte abnormalities, refeeding syndrome 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 0.1515g Nitrogen, equivalent to approximately 0.94g protein and 15.9 kJ or 3.8 kcal of energy. It is anticipated that infants at KEMH will receive between 1.9–2.3g protein/kg/d within the first 24 hours of life when Starter PN is infused at 80 mL/kg/d.

Infants will receive between 3.0g protein/kg/d (Near Term/Term) to 3.9g protein/kg/day (Preterm) within 3-5 days of commencing Standard PN.

Glucose
Rate of glucose oxidation in appropriate for gestational age preterm infants is 6-8 mg/kg/min (8.6-11.5 g/kg/d). In term infants after surgery, or infants on long term PN, the maximal rate of glucose oxidations is 12 mg/kg/min (17.2 g/kg/d). 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 3.8 kcal, equivalent to 15.9 kJ of energy.

Electrolytes and Paediatric Trace Elements (Biomed®)
Electrolytes are added in standard amounts per 100mL of Preterm Starter PN and in standard amounts to Preterm and Near-Term/Term Standard PN (Table 1).

Trace Elements (Biomed)
Trace elements (Biomed ®) are added in standard amounts to Standard PN (Table 1).

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 with Vitamins 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-tocopherol, 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 18.75 mL of SMOF fat emulsion, 1.25 mL Soluvit N Infant and 5 mL Vitalipid N infant and 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.

Lipid emulsion with vitamins should be started at 6-12 mL/kg/d (1-2 g fat/kg/d) with Starter pack (KEMH only) and with the first order of Standard PN and increased to a maximum of 18-20 mL/kg/day (3.1-3.4g fat/kg/day) with subsequent lipid orders.

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.

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.
Non-Standard PN:
(iii) If clinically indicated, NON-Standard PN can be ordered under Consultant authorisation and medical order, by modification to one or more of the following components of Standard PN: Amino acids, glucose, potassium, sodium and/or acetate-chloride balance components;
(iv) If hypophosphataemia (and/or hypocalcaemia) is identified, phosphate and calcium can be modified under consultant authorisation in standard amounts by pharmacy for preterm (from 0.75 mmol.L\(^{-1}\) to 1.5 mmol.L\(^{-1}\)) and term (from 0.75 mmol.L\(^{-1}\) to 1.0 mmol.L\(^{-1}\)) infants – pharmacy must be contacted for changes to be made. Note that for solubility issues, both calcium and phosphate need to be increased in the TPN.

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).

- **Refeeding (RF)** is a potentially serious cluster of electrolyte disturbances (particularly low phosphate <1.4 mmol.L⁻¹) precipitated by the sudden supply of IV amino acids and glucose, following a period of poor nutrition, such as occurs with
placental insufficiency or inadequate intravenous energy and protein intake for several days after birth.

**Monitoring**

Biochemical and anthropometric monitoring for infants commenced on PN includes:
- Daily blood gas in the first week, and as clinically indicated thereafter.
- UEC, phosphate and calcium on days 3, 7 and 14 after commencing PN.
- Bone bloods (Calcium, Phosphate, ALP and Vitamin D) on day 28. Consideration should be given to performing bone bloods earlier, in cases of prolonged TPN use.
- If prolonged TPN, fortnightly liver function tests.
- If CVL, consider twice weekly CRP for catheter-related sepsis.
- Weight daily or alternate days; and head circumference weekly. Length at admission and discharge
### Table 1 Composition of PN Solutions

<table>
<thead>
<tr>
<th></th>
<th>STARTER PN KEMH NICU ONLY</th>
<th>STANDARD PN KEMH/PCH NICUs</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Starter A</td>
<td>Starter B</td>
</tr>
<tr>
<td>Gestational age (week)</td>
<td>&lt;26⁻⁶</td>
<td>≤30</td>
</tr>
<tr>
<td>mL/kg</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Maximum target volume</td>
<td>80</td>
<td>80</td>
</tr>
<tr>
<td>Per 100 mL PN bag</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Glucose %</td>
<td>5</td>
<td>8</td>
</tr>
<tr>
<td>Amino acid g</td>
<td>2.5</td>
<td>3</td>
</tr>
<tr>
<td>Heparin Units</td>
<td>50</td>
<td>50</td>
</tr>
<tr>
<td>Sodium mmol</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Potassium mmol</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Magnesium mmol</td>
<td>0.25</td>
<td>0.25</td>
</tr>
<tr>
<td>Calcium mmol</td>
<td>0.75</td>
<td>0.75</td>
</tr>
<tr>
<td>Phosphate mmol</td>
<td>0.75</td>
<td>0.75</td>
</tr>
<tr>
<td>Acetate mmol</td>
<td>2.6</td>
<td>2.6</td>
</tr>
<tr>
<td>Chloride mmol</td>
<td>2.1</td>
<td>2.2</td>
</tr>
<tr>
<td>Zinc µg</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Manganese µg</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Copper µg</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Molybdenum µg</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Iodine µg</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Selenium µg</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

#### SMOF LIPID EMULSION

<table>
<thead>
<tr>
<th>SMOF Lipid</th>
<th>Per kg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vitamin A IU (µg)</td>
<td>271 (81) - 541 (162)</td>
</tr>
<tr>
<td>Vitamin D IU (µg)</td>
<td>47 (1.2) - 94 (2.4)</td>
</tr>
<tr>
<td>Vitamin E IU (µg)</td>
<td>0.8 (0.8) - 1.5 (1.5)</td>
</tr>
<tr>
<td>Vitamin K µg</td>
<td>24 - 47</td>
</tr>
<tr>
<td>Ascorbate mg</td>
<td>3.3 - 6.6</td>
</tr>
<tr>
<td>Thiamine mg</td>
<td>0.09 - 0.18</td>
</tr>
<tr>
<td>Riboflavin mg</td>
<td>0.14 - 0.29</td>
</tr>
<tr>
<td>Nicotinamide mg</td>
<td>1.18 - 2.35</td>
</tr>
<tr>
<td>Pyridoxine mg</td>
<td>0.14 - 0.29</td>
</tr>
<tr>
<td>Biotin µg</td>
<td>1.76 - 3.53</td>
</tr>
<tr>
<td>Pantothenate mg</td>
<td>0.49 - 0.97</td>
</tr>
<tr>
<td>Folate µg</td>
<td>11.76 - 23.53</td>
</tr>
<tr>
<td>Vitamin B12 µg</td>
<td>0.15 - 0.29</td>
</tr>
</tbody>
</table>
Related CAHS internal policies, procedures and guidelines

Neonatology Medication Protocols

- Fat Emulsion 20% (SMOF) with Vitamins (Solvit and Vitalipid N® KEMH)
- Fat Emulsion 20% (SMOF)

References