Kent, Surrey and Sussex Neonatal Operational Delivery Network

Principles of Practice

Standardised Parenteral Nutrition (PN)

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Introduction

Parenteral Nutrition (PN) is an essential aspect of neonatal care by which an infant's nutritional requirements can be met intravenously. Using PN allows the provision of optimal nutrition early in life, which minimises growth failure and associated neuro-cognitive defects.[1]

Infants may require PN because of prematurity and the inability of the immature gut to digest sufficient milk, or because they cannot tolerate enteral feeds due to congenital or acquired gut disorders.

Using a standardised approach to the provision of neonatal PN offers several advantages:

- Maximised nutrient delivery in line with national and international guidance (NICE[2], BAPM[3], ESPGHAN[4])
- Availability of ready-made standard PN formulations avoids delays in initiation and administration
- Continuity and consistency of PN provision across multiple neonatal units within a location
- Minimised risk of errors in prescribing and compounding

The standard PN formulation provides concentrated nutrition to conserve nutritional delivery while other infusions (medications or fluids) run concurrently.

The principles outlined in this document aim to guide the timely, consistent and appropriate use of PN for infants admitted to neonatal care in the KSS ODN.

Indications and Cautions

Absolute indications – PN should be initiated for

1. All preterm infants born before 31+0 weeks or with birthweight less than 1500g
2. Failure to establish enteral nutrition by day 5 of life (regardless of gestation or birthweight)
3. Infants who are unlikely to establish sufficient enteral feeding, for example, infants with:
    a. a congenital gut disorder
    b. a critical illness

Relative indications – Consider initiating PN for

1. Preterm infants born at or after 31+0 weeks or with birthweight greater than 1500g are unlikely to achieve ≥100mL/kg/day of enteral feeding by day 3-5 of life.
2. Preterm infants whose enteral feeds are stopped or reduced to <50% of nutritional requirements, and are unlikely to restart again or be advanced for 48 hours
3. Term infants whose enteral feeds are stopped or reduced to <50% of nutritional requirements, and are unlikely to restart again or be advanced for 72 hours

Cautions – Discuss with the responsible consultant and (if possible) a neonatal pharmacist before prescribing

1. *Significant* renal impairment/renal failure (Creatinine >100 micromol/L, urine output <1mL/kg/hour)
2. Suspicion of a metabolic disorder
3. *Significant* septicaemia
4. Hyperbilirubinaemia requiring exchange transfusion

When an infant meets the indications for PN, start it as soon as possible and within 8 hours.

Standard PN Formulations

The standard PN is presented in separate aqueous and lipid phases. The lipid phase is SMOF 20% + Vitamins, and there are 2 options for the Aqueous phase: SEE Neonatal PN ELECTROLYTE FREE or SEE Neonatal PN MAINTENANCE

The nutrient provision for each formulation is detailed below:

	Aqueous PN		**Lipid PN**	**Combined**	
	SEE Neonatal PN ELECTROLYTE FREE at 100mL/kg/day	**SEE Neonatal PN MAINTENANCE at 100mL/kg/day**	**SMOF 20% + Vitamins at 20mL/kg/day**	**Electrolyte-free + Lipid at 120mL/kg/day**	**Maintenance + Lipid at 120mL/kg/day**
Glucose g/kg/day	12	12		12	12
Lipid g/kg/day			3.3	3.3	3.3
Protein gAA/kg/day	3.8	3.8		3.8	3.8
Protein gN/kg/day	0.56	0.56		0.56	0.56
Energy kcal/kg/day	62	62	33	95	95
Non-Nitrogen energy kcal/kg/day	48	48	33	81	81
Sodium mmol/kg/day	0	4		0	4
Potassium mmol/k/day	0	2		0	2
Calcium mmol/kg/day	0	1.76		0	1.76
Phosphate mmol/kg/day	0	2	0.28	0.28	2.28
Magnesium mmol/kg/day	0	0.2		0	0.2
Chloride mmol/kg/day	0.58	0.58		0.58	0.58
Acetate mmol/kg/day	0	2		0	2
Peditrace mL/kg/day	1	1		1	1
Solivito N mL/kg/day			1.1	1.1	1.1
Vitlipid Infant mL/kg/day			4.4	4.4	4.4
Osmolarity mOsm/L	957.2	1083.4	280	844.3	949.5

Using the standard PN formulations in the recommended ratio (see Prescription and Administration below) will provide:

- Calcium and Phosphate in a ratio of 0.77:1 mmol.
  Note this is Calcium:Phosphate ratio, not Calcium:Phosphorous ratio) (NICE recommendation 0.75:1)
- Non-Nitrogen calories as 60% Carbohydrate and 40% Lipid
  (NICE recommendation 60-75% Carbohydrate and 25-40% Lipid)
- Non-Nitrogen calories to protein provision in a ratio of 22kcal:1g Amino Acids
  (NICE recommendation 20-30:1)

Prescription and Administration

Prescription

The standard prescription of PN should maintain the proportion of each component as 5/6th Aqueous and 1/6th Lipid unless there are clinical or biochemical reasons to adjust this.

The maximum rate of PN is 120mL/kg/day, with a maximum for aqueous PN at 100mL/kg/day and a maximum for Lipid PN at 20mL/kg/day. Additional fluid requirements, which are not already accounted for by other infusions (i.e. continuous drug infusions), should be provided using an infusion fluid suitable for the infant's clinical condition and biochemical parameters.

Recommended PN prescription volumes based on common total fluid requirements are:

Total IV fluid requirement	60mL/kg/day	90mL/kg/day	120mL/kg/day	135mL/kg/day	150mL/kg/day	165mL/kg/day
Total PN volume	60mL/kg	90mL/kg	120mL/kg	120mL/kg	120mL/kg	120mL/kg
Aqueous PN volume	50mL/kg	75mL/kg	100mL/kg	100mL/kg	100mL/kg	100mL/kg
Lipid PN volume	10mL/kg	15mL/kg	20mL/kg	20mL/kg	20mL/kg	20mL/kg
Additional IV fluids	Nil	Nil	Nil	15mL/kg	30mL/kg	45mL/kg

The fluid volumes given in the table above do not account for any continuous drug infusions or enteral feeds.

- If the infant is receiving continuous drug infusions, these should be accounted for in the total fluid intake (TFI) and the remaining fluid intake provided as PN in the correct proportions of Aqueous and Lipid PN, respectively (5/6th of the total volume as aqueous PN, and 1/6th of the total volume as lipid PN).
- If the infant is receiving a combination of parenteral and enteral nutrition, and the volume of enteral nutrition is sufficient to be included in the TFI, the PN volumes and rates must be adjusted accordingly to maintain the desired TFI with the correct proportions of Aqueous and Lipid PN, respectively (5/6th of the total volume as aqueous PN, and 1/6th of the total volume as lipid PN).

Aqueous and Lipid PN phases are separate infusions and must be prescribed separately. Each prescription for a PN infusion must include:

- The name of the PN formulation to be administered, stated in full.
- The date and time for the PN infusion to be administered
- The volume of PN bag to be used (total volume of the bag being used)
- The rate of PN infusion in mL/hour
- The fluid volume that the PN contributes to the infant's TFI in mL/kg/day
- The prescriber's name, signature and date of prescription in line with the Trust process for prescription writing (the format may vary between Trusts, and between paper and electronic prescribing systems)

Trusts are recommended to develop standard template prescriptions for PN to ensure all PN prescriptions are uniform, complete, and unambiguous.

Administration

1. **Safety & error prevention**

PN infusion set up, attachment of the giving set, and connection to the infant must be performed using full aseptic non-touch technique.

All PN must be checked against the prescription and fluid requirements by two registered nurses, one of whom must be qualified in speciality. Both nurses must remain present until PN infusions are set up in infusion devices and lines are connected to the infant. Safety checks must be undertaken at the point of administration of PN for:

- PN type matches the prescription
- Date of infusion matches the prescription
- Rate of infusion matches the prescription
- The PN is not expired, and will not expire during the planned infusion time
- The appearance of the PN solutions (for discolouration or precipitation)

Upon PN administration, both nurses must record the administration and check against the prescription in a way that clearly identifies the nurses involved and the date and time that the infusion began.

Particular attention must be paid to ensure that the aqueous and lipid phases are being delivered via the correct infusion pump and at the correct rate. Flow rates of aqueous and lipid solutions are controlled by separate infusion pumps; there have been instances where the rates/pumps have been confused, resulting in significant over-infusion of lipids and under-infusion of aqueous PN.

One suggested strategy to prevent this is to set the infusion pumps on the same pole-mount, with the top/higher pump always assigned to deliver aqueous PN at the higher rate and the bottom/lower pump assigned to deliver the lipid PN at the lower rate.

2. **Light protection**

Both aqueous and lipid PN must always be protected from UV light (during storage and administration) to prevent photodegradation and oxidation of PN components.
During PN administration, the PN bag must be covered by a light-protective bag and amber infusion lines must be used to connect the PN bags through the infusion pumps to the IV access device.

3. **Filter**

PN must be administered via a filter to reduce the risk of harmful events that can occur if PN is contaminated with particulate matter, microorganisms or precipitates.

- Aqueous PN must be administered via a 0.2-micron filter
- Lipid PN must be administered via a 1.2 – 1.5-micron filter
- The use of filters integrated into giving sets is preferable to separate filters, where these are available.
- PN filters and administration sets should be changed with each new PN container, based on PN shelf-life, local infection control policies and as per filter shelf-life.

4. IV access

Use a central venous catheter to administer neonatal PN.
The SEE Neonatal PN formulation can be used peripherally; however, due to the high osmolarity, this should only be considered for short-term administration if:

- It would avoid a delay in starting PN
- It would avoid interruption in PN delivery
- Central venous access is impractical

Use of PN via peripheral access must not exceed 5-days of administration

Consider requesting surgical insertion of a central venous catheter if:

- Long-term PN is anticipated
- Non-surgical insertion is not possible

5. Infusion duration

As standard, PN should be delivered by continuous IV infusion. There may be circumstances where the daily PN volume is administered over a shorter time, and gaps in PN administration are created – if this is required for an infant, the direction to do so will be made by a consultant.

The total duration of each PN infusion should be determined by each unit based on the PN shelf-life, filter shelf-life and local infection control policy, but must not exceed 48 hours.

Monitoring

Infants receiving PN require monitoring of various parameters to assess effectiveness and prevent or detect complications. The recommended parameters and frequency of monitoring are summarised in Table 3 (below). For laboratory investigations, use minimum blood volumes and co-ordinate the timing of blood tests to minimise blood samples.

	First week & when PN volume/rate is increasing				Stable PN			
	Hourly	Daily	Twice Weekly	Weekly	Daily	Twice Weekly	Weekly	Monthly
Infusion site	✓				✓			
Fluid balance		✓				✓		
Weight			✓			✓		
Head circumference				✓			✓	
Length				✓			✓	
Blood glucose*	✓	✓			✓			
	Measure 1-2 hours after first starting PN, 1-2 hours after each bag change and every 6-12 hours when PN is increasing				Measure 12-24 hourly when PN is stable			
Sodium Potassium Chloride Urea Creatinine Calcium Phosphate Magnesium		✓				✓		
Triglycerides*			✓				✓	
Liver Function Albumin Bilirubin*		✓					✓	
Conjugated bilirubin				✓			✓	
Acid-Base balance		✓			✓			
Full Blood Count*				✓			✓	
Trace Elements (Copper, Zinc, Selenium, Manganese) Vitamins A, D & E Iron Status**								✓
					For infants on long-term PN, measure on day 28 and then monthly for the duration of PN			

*** These parameters may require more frequent monitoring based on previous abnormal results or the infant's clinical condition. Do not monitor triglyceride levels more frequently than once each day.**

** Blood samples for monitoring of trace element levels should not be taken while the infant has active infection or inflammation, the results will not be a true reflection of trace element status. Some trace elements are acute phase reactants, and the impact of acute phase response on their serum levels is described in the table below.[7]

Trace Element	Effect of acute phase response on serum level
Copper	Increased
Zinc	Decreased
Manganese	No effect
Plasma Selenium (red cell selenium is not affected)	Decreased
Iron	Decreased
Ferritin	Increased

Complications

1. **Central-line associated complications**

Central line-associated bloodstream infections (CLABSI) are a recognised risk and complication of PN administration. Use aseptic non-touch technique when handling central lines and avoid co-infusion of medications to minimise the risk of CLABSI.

If a change in clinical or biochemical status raises concern over a potential CLABSI, take blood cultures before starting antibiotic therapy. Consider paired blood cultures taken simultaneously from the central line and a peripheral vein if this is practically possible (dependent on the central line in situ), and the recommended practice by individual Trusts microbiology departments.

When CLABSI is suspected, follow local unit guidance for the choice of empiric antibiotic therapy and duration of treatment.

Additional complications related to the prolonged use of central venous catheters can occur in infants who require prolonged PN. These include thrombosis and extravasation injury.

Newly sited central lines should have their position confirmed by radiological means

Indwelling central lines should have their insertion site monitored daily for signs of swelling, redness or pain.

2. **Liver Disease**

PN-associated liver disease (PNALD) is a serious complication of prolonged PN use. Infants who depend on PN to meet some or all their nutritional requirements for a prolonged period ($\geq$ 28 days) often have gastrointestinal conditions that lead to intestinal failure. Additional risk factors for PNALD include prematurity, jejunal atresia, necrotising enterocolitis (which may lead to short gut and/or dysmotility), intestinal failure, intolerance of enteral intake, sepsis and surgical conditions such as gastroschisis.[6]

Infants on the neonatal unit with PNALD should ideally be discussed with paediatric gastroenterology, who will advise on management strategies.

3. Glucose Control

Hyperglycaemia and (less commonly) hypoglycaemia may occur while an infant is receiving PN. Follow local unit guidelines for the management of either, but also consider the following:

- For infants with hyperglycaemia while receiving PN, it may be beneficial for growth to use insulin to control the blood glucose levels rather than reducing the PN delivery.
- For infants with hypoglycaemia, confirm no mechanical problems are impeding the delivery of the aqueous PN. If hypoglycaemia persists, requiring additional high-concentration glucose infusions alongside PN, additional investigations may be warranted to identify or rule out underlying causes.

4. Metabolic Bone Disease

Prolonged PN use is a risk factor for the development of metabolic bone disease of prematurity, due to the inability to provide calcium and phosphate in sufficient quantities through PN. Refer to the KSS Metabolic Bone Disease guideline for advice on screening, monitoring and management of metabolic bone disease.

5. Metabolic Disturbance

Triglyceride and electrolyte disturbances can occur in infants receiving PN. It is important to consider the clinical condition of the infant alongside the PN administration when identifying causes/contributory factors and forming a management plan.

Triglycerides

Triglyceride levels are monitored to assess the tolerance of the lipid PN phase. The optimal triglyceride level and the levels above which adverse effects may occur are not clearly defined in the neonatal population. It is important to remember that hypertriglyceridaemia may occur due to excess lipid intake, inability to tolerate the lipid, or because of lipogenesis secondary to the provision of excess glucose. Both the lipid and glucose intake must be reviewed before any amendments are made to the PN provision.

If a decision to adjust the lipid intake is made, this should be done by reducing the lipid infusion. Lipids should not be stopped; the lipid phase provides the essential fatty acids and vitamins.

If a triglyceride level is above the upper threshold for the unit (thresholds may vary based on individual lab assays, but a level of 4.5mmol/L should not be exceeded), consider the following:

- Review glucose intake, and reduce if it is excessive
- If glucose intake is not excessive, reduce SMOFLipid + vitamins infusion by 6mL/kg/day = 1g/kg/day. *(If temporarily using plain SMOF lipid without vitamins this would be 5mL/kg/day = 1g/kg/day)*
- The minimum lipid intake using SMOFLipid + vitamins is 9mL/kg/day =1.5g/kg/day to provide the essential fatty acid requirement. *(If temporarily using plain SMOF lipid without vitamins this would be 7.5mL/kg/day = 1.5g/kg/day)*
- After any change, re-check the triglyceride level after 48 hours

If the lipid infusion rate is decreased, give additional fluid to maintain the TFI. Take care that the maximum rate of aqueous PN is not exceeded.

Electrolyte disturbances

In the event of any electrolyte disturbance while on PN, it is important to assess fluid balance and hydration, and all sources of electrolyte intake, alongside the infant's clinical condition, when formulating a management plan.

Weaning PN

As enteral feeds increase, the PN rates should be weaned to maintain the same TFI. When PN is weaned, ensure the infusion rates maintain the correct proportion of aqueous and lipid PN, respectively (5/6th of the total volume as aqueous PN, and 1/6th of the total volume as lipid PN).

The total volume of PN being infused should be kept at 5/6th aqueous and 1/6th lipid (unless there has been a reduction in lipid intake due to intolerance).

Once enteral feeds are providing 120- 150mL/kg/day of the TFI, PN may be stopped. The decision to stop PN when enteral feeds reach 120 - 150mL/kg should be based on assessment of the individual infant's degree of prematurity, nutritional status, nutrient provision, fluid balance, feed tolerance and growth parameters.

PN Multi-Disciplinary Team

Each neonatal unit should consider developing a multidisciplinary team with an interest in PN to monitor ongoing use, compliance and complications. This team could include:

- A neonatal pharmacist
- A neonatologist or paediatrician with an interest in nutrition
- A neonatal or paediatric dietitian
- A neonatal nurse with an interest in nutrition

Appendices

Appendix 1: Composition of SEE Neonatal PN

1. **SE Neonatal PN ELECTROLYTE FREE**

Constituent	**Volume**
Glucose 50%	120mL
Water for Injection	193.33mL
Primene 10%	186.67mL
Total Volume	**500mL**

2. **SE Neonatal PN MAINTENANCE**

Constituent	**Volume**
Glucose 50%	120mL
Water for Injection	135.83mL
Primene 10%	186.67mL
Calcium Gluconate 10%	40mL
Magnesium Sulfate 50%	0.5mL
Potassium Acetate 49%	2mL
Sodium Glycerophosphate 21.6%	10mL
Peditrace	5mL
Total Volume	**500mL**

3. **SMOF Lipid 20% + Vitamins**

	Manufactured by Fresenius Kabi	Manufactured by ITH Pharma
SMOFLipid 20%	78mL	76.5mL
Vitlipid N Infant	24mL	23.5mL
Solivito N (dissolved in WFI)	6mL	6mL
Total Volume	108mL	106mL
Shelf Life	60 days	7 days

Appendix 2: Nutritional requirements for preterm infants[16,17]

Nutrient	Enteral Requirement	Parenteral requirement	Key difference
Energy	105 – 135 kcal/kg/day	90 – 110 kcal/kg/day	PN requires *less* energy (no digestive/absorptive losses)
Protein (Amino Acids)	3.5 – 4.5 g/kg/day	3.0 – 4.0 g/kg/day	PN protein slightly *lower* (better utilisation efficiency)
Carbohydrate	10 – 14 g/kg/day	6 – 9 g/kg/day initially, increasing to 11 – 15 g/kg/day (as glucose infusion: 4 – 6mg/kg/minute initially, increasing to 7 - 11 mg/kg/minute)	Similar needs, but PN / IV is expressed more commonly in infusion rate terms
Lipid	4.8 – 6.6 g/kg/day (40 – 50% of energy)	1.0 – 2.0 g/kg/day initially, advancing to 3.0 – 4.0 g/kg/day	PN lipids are advanced more cautiously.
Fluid	135 – 200 mL/kg/day	100 – 150 mL/kg/day	PN is usually more concentrated, less volume needed
Micronutrients	Provided by fortified milk/formula; absorption varies	Supplied in PN solution; requires careful tailoring	PN formulations differ in composition

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Scope of Guideline Framework

The guideline applies to all Neonatal Units covered by Kent Surrey and Sussex Neonatal ODN. This includes the following hospitals:

Kent, Surrey and Sussex	
Medway Hospital NHS Foundation Trust	Medway Maritime Hospital, Gillingham
East Kent Hospitals University NHS Foundation Trust	William Harvey Hospital, Ashford Queen Elizabeth the Queen Mother, Margate
Ashford and St Peter's NHS Foundation Trust	St Peter's Hospital, Chertsey
University Hospitals Sussex NHS Foundation Trust	Royal Sussex County Hospital, Brighton Princess Royal Hospital, Haywards Heath Worthing Hospital
Frimley Health NHS Foundation Trust	Frimley Park Hospital
Surrey and Sussex Healthcare NHS Trust	East Surrey Hospital, Redhill
Maidstone and Tunbridge Wells NHS Trust	Tunbridge Wells Hospital, Pembury
Dartford and Gravesham NHS Trust	Darent Valley Hospital, Dartford
East Sussex Healthcare NHS Trust	Conquest Hospital, Hastings
Royal Surrey NHS Foundation Trust	Royal Surrey County Hospital,

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