Clinical Guideline:
Parenteral Feeding of Infants on the Neonatal Unit.

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Guidance specific to the care of neonatal patients

Used by: Medical Staff, Neonatal Nurse Practitioners, Dietitians, Pharmacists

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Clinical Lead Mark Dyke	**APPROVED**

Ratified by ODN Board:

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I confirm that this guideline has followed due process for guideline development and has been approved on the above date by the Clinical Oversight Group and subsequently ratified at the ODN Board on the date stated. S. Rattigan, Neonatal ODN Director.

Audit Standards:

- 100% infants meeting the absolute indicators within the prescribing criteria commence parenteral nutrition within 24 hours of birth.
- 100% infants meeting prescribing criteria receive a minimum of 1.5g/kg/day amino acid on day 1 of PN.
- 100% infants have PN accurately prescribed using the East of England Standardised PN prescribing proforma.

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Glossary of Terms

PN	Parenteral Nutrition
GOR	Glucose Oxidation Rate
EFA	Essential Fatty Acid
SMOF	Soya, Medium chain, Olive oil, Fish oil intravenous lipid blend
ESPGHAN	European Society of Paediatric Gastroenterology, Hepatology & Nutrition
NEC	Necrotising Enterocolitis
UVC	Umbilical Venous Catheter
AREDF	Absent/ Reduced End Diastolic Flow
VLBW	Very Low Birth Weight Infant
ELBW	Extremely Low Birth Weight Infant
NCEPOD	National Confidential Enquiry into Patient Outcome and Death
PNALD	Parenteral Nutrition Associated Liver Disease
IUGR	Intra-Uterine Growth Retardation
IVC	Inferior Vena Cava
SVC	Superior Vena Cava
PAU	Pharmacy Aseptic Unit

1.0 Introduction

Early postnatal growth failure, with associated longer term neuro-developmental implications is frequently encountered in very premature infants and is most evident in the smallest sickest infants. Although multi-factorial in origin (1) postnatal growth failure can be considered in part due to inadequate nutritional intake in the first four weeks after delivery and is most marked in the first week of life. (2).

Delivery of intravenous nutrients, as parenteral nutrition, dominates the nutritional management processes in this group. In order to minimise the growth failure and neuro-cognitive effects of early nutrient deficit, the development of strategies for effective PN delivery are essential.

A recent case review of neonates receiving parenteral nutrition has highlighted large variations in neonatal PN quality and practice throughout the UK, with the provision of early PN deemed inadequate in a third of infants and PN monitoring inadequate in a fifth. The commencement of PN was delayed in 45% of cases reviewed either because the need went unrecognised or was not acted upon. (3)

In order for PN to be successful, agreed guidelines that are both based on and referenced to published evidence need to be in place (4). Relevant clinical indications, nutrient requirements and mode of delivery also need to be clearly defined.(5) Guidelines developed by the European Society of Paediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN) in 2005 seek to establish a framework for the provision of appropriate PN for preterm infants and children (6). This framework forms the basis of this document and as such is intended to serve as an aid to clinical judgement and not as a replacement.

2.0 Indications for Parenteral Nutrition

Premature infants are born with an immature gut consequently the smallest infants are unable to digest sufficient milk to meet their nutritional requirements. They are also born with low nutritional reserves (7) such that a 1 kg infant will become deficient in essential fatty acids within 2 days of birth and survive only 4 days if not provided with appropriate nutrition (8,9). Virtually all preterm infants <30 weeks gestation will require parenteral nutrition for a period of time, the duration of

which is determined by gestation, birth weight and other concurrent morbidities. Complete dependence on PN (>75% nutritional intake) can be expected for a mean of 15 days in all infants <29 weeks (10) with a further period of partial dependence required before full enteral feeds are established (mean 34 days in infants <600g) (1).
Parenteral nutritional support in the preterm infant should commence within the first day of life and ideally within 6 hours of birth or following confirmation of UVC or long-line placement. (11-13). Table 1 provides some indications for neonatal PN prescribing, however any neonate who is unlikely to meet their nutritional requirements via the enteral route within three to five days of birth should be considered for PN.

Table 1: Indications for PN in Neonates

Absolute Indications	Premature infants < 30 weeks gestation or <1.25kg Intestinal Failure (i.e. short gut, pseudo-obstruction) Gastrointestinal Surgery Necrotising Enterocolitis (NEC) Congenital gastrointestinal defects (i.e.gastroschisis, intestinal atresia)
Relative Indications	Premature infants ≥30 weeks gestation or >1.25kg who are not expected to receive adequate enteral feeds (≥100ml/kg/day feeds) within approximately 3 to 5 days. Severe IUGR with associated absent or reduced end-diastolic flow (AREDF) Promotion of growth Protracted diarrhoea

Recommendation

- Parenteral Nutrition (PN) should be commenced within on the first day of life for any infant unlikely to receive >100ml/kg/day enteral feeds by day 3-5 of life. Ideally this should be within 6 hours of birth or following confirmation of UVC or long-line placement.

3.0 Preterm infants

3.1 Fluid and Electrolyte Requirements

Immediately after birth the adaptation process of water and electrolyte metabolism commences. This process occurs in 3 phases (6)

Phase I – Transitional period: initial oliguria followed by a diuretic phase usually associated with up to 10% weight loss. In the very low birth weight infant (VLBW) sodium (and other electrolytes) may require restriction. Extremely low birth weight (ELBW) infants are liable to early excess water losses and may become dehydrated without meticulous attention to early fluid balance.
Phase II: - Characterised by diminished insensible losses, fall in urine volume and low sodium excretion. During this phase electrolyte losses are generally repleted.
Phase III: - The Stable growth phase with a positive net balance of sodium and water.

Care should be taken in the timely repletion of electrolytes in preterm infant in order to minimise the risk of Chronic Lung Disease development. In practice the addition of maintenance sodium supplementation to parenteral fluids should be deferred in babies <28 weeks gestation until there has been a weight loss of the order of 6% birth weight(14).

Account should be taken of insensible losses and influencing environmental factors when determining fluid requirement for preterm infants, especially in the first week of life (15). The use of

double wall incubators can reduce insensible water losses and subsequent fluid needs in preterm infants whereas the use of radiant warmers or single wall incubators may increase water loss and impair thermoregulation.

Parenteral Fluid Requirements for the Premature Infant (6)

	<1500 g (ml/kg/day)		**>1500g (ml/kg/day)**
Day 1	80 – 90	Day 1	60-80
Day 2	100-110	Day 2	80-100
Day 3	120-130	Day 3	100-120
Day 4	130-150	Day 4	120-150
Day 5	140-160	Day 5	140-160
Day 6	160-180	Day 6	140-160

Parenteral Electrolyte Requirements for premature infants (6)	**Phase I**	**Phase II**	**Phase III**
Sodium			
<1500g infant	0-3 mmol/kg	2-3 mmol/kg	3-5 mmol/kg
>1500g infant	0-3 mmol/kg	3-5 mmol/kg	3-5 mmol/kg
Potassium			
<1500g infant	0-2 mmol/kg	1-2 mmol/kg	2-5 mmol/kg
>1500g infant	0-2 mmol/kg	1-3 mmol/kg	2-5 mmol/kg
Chloride			
<1500g infant	0-5 mmol/kg	2-3 mmol/kg	2-5 mmol/kg
>1500g infant	0-5 mmol/kg	3-5 mmol/kg	2-5 mmol/kg

Recommendations

- The contribution of intravenous medication and enteral nutrition (where present) should be considered when calculating fluid and sodium requirements for PN.
- Maintenance sodium supplementation should be governed by the phased adaptation of fluid and electrolyte metabolism and deferred in babies <28 weeks gestation until there has been a weight loss of the order of 6% birth weight representing contraction of the extracellular fluid volume

3.2 Energy Requirements

Due to the preterm infant's limited nutritional stores the goal is to initiate nutritional support as soon as possible and achieve early energy accretion (16). A number of conditions and treatment (including medication) can affect the energy needs of preterm infants and as such should be considered when assessing energy needs. (see table 2)
Energy intake impacts directly on nitrogen balance. Although the minimal energy needs of preterm infants can be met with 50-60Kcal/kg/day, 100-120Kcal/kg/day is required to facilitate maximal protein accretion (17). This figure is reduced to 90-100Kcal/kg/day in the newborn infant receiving PN rather than enteral nutrition as there is no energy loss in stool and lower thermogenesis.(18). The ESPGHAN suggested total energy requirement for neonatal PN is 110-120 kcal/kg/day (85-105 non nitrogen Kcal/kg/day).(6) As this is a theoretical prediction consideration should be given to the factors in the table below, as well as anthropometric and biochemical monitoring parameters when reviewing and assessing energy needs.

Table 2 Factors that may impact on energy requirements of the neonate. (19-22)

Factor	Comment
Physical activity	Activity is estimated to be 10% of a preterm infant's total energy requirements. This figure is reduced if the baby is ventilated, sedated and on muscle relaxants
Feeding	The thermic effect of food is 10% if bolus feeds are given. The effect is negligible with PN and continuous enteral feeding.
Human milk	Non nutritive factors aid absorption thereby reducing the energy required for digestion
Prematurity	Gestational age is negatively correlated with energy expenditure
Excessive energy intake	Increases thermogenesis and the production of CO_2
Weight gain	Energy requirements require adjustment as the child grows.
Mechanical ventilation	Depending on ventilation mode and pressure support there is either no effect or a reduction in energy expenditure.
Nasal CPAP	Reduces work of breathing thereby reducing energy expenditure.
Thermal environment	Both cold and heat can increase energy requirements.
Chronic Lung Disease	Increases work of breathing which leads to higher O_2 requirements, increased CO_2 production and increased energy expenditure.
Sepsis	No clear evidence.. Some studies have indicated no change in energy expenditure, some a reduction..
Surgery/ NEC	Evidence is equivocal

Recommendations

- Most preterm infants will meet their energy requirements by the total energy provision of 110-120 kcal/kg/day via PN (85-105nnKcal/kg/day).
- Factors that may reduce/increase requirements should be taken into account when estimating an individual infant's requirement.

3.3 Protein Requirements

Early, aggressive amino acid introduction is essential in the preterm infant if the high accretion rates seen in fetal life are to be matched and the large deficits found in the first week of life are to be avoided. (2) Recent evidence suggests it is safe to commence amino acid provision immediately from birth onwards without metabolic complications (11-13, 23-27)

Estimates of amino acid requirements in preterm infants are based on the quantity required to achieve a positive nitrogen balance. The preterm infant excretes between 0.6-1.1 g/kg protein per day. An amino acid intake of 0.9g/kg/day is required to prevent significant loss (28). In the presence of adequate non nitrogen energy (90 kcal/kg/day), a positive nitrogen balance can be achieved with an amino acid intake of 3.2 g/kg/day (29). Levels of 3.5-3.9 g amino acid/kg/day have been shown to be well tolerated and can result in positive nitrogen balance on day one of life (5,30,31). Current recommendations support amino acid intakes of 3.9gAA/kg/day (3.5g protein) up to a maximum of 4.48gAA/kg/day (4.0g protein) (average 4.0gprotein/kg/day), commencing with at least 1.5g/kg/day on the first day of life. (6,32)

Increasing amino acid provision without adequate non nitrogen energy will result in the inefficient utilisation of protein. It is generally accepted that 20-25Kcal/kg/g amino acid is needed to optimise protein uptake (33,34) with a daily provision of 100-120Kcal total energy/kg/day required for optimal protein accretion.(16) These values are supported by recent studies that evaluated the effect of different amino acid doses on the growth and amino acid profiles of preterm infants (35).

The amino acids taurine cysteine and tyrosine are considered semi-essential during the neonatal period. It is therefore important to use amino acid solutions in neonatal PN that have been specifically manufactured to meet the needs of this population.

Recommendation

- Amino acid provision should commence on the first day of life, preferable within 6 hours of birth.
- Amino acid provision should commence at a minimum of 1.5g /kg/day increasing to 4.3g amino acid/kg/day (3.8g protein), maximum 4.48g/kg/day(4.0g protein).
- Amino acid solutions specifically designed for neonates and containing cysteine, tyrosine and taurine should be used for compounding PN for preterm infants.

3.4 Carbohydrate Requirements

Carbohydrate in PN is prescribed as glucose. It serves as the primary source of energy for the brain, renal medulla and erythrocytes and as metabolic fuel for muscle, liver, heart, kidney and the gut. Glucose usually provides between 60-75% of total energy and is the major contributor to the osmolality of a PN solution (5,36).

Glucose supply should be calculated using the glucose oxidation rate (GOR) for preterm infants. The minimum quantity of glucose required is 4-8mg/kg/minute (5.8-11.5g/kg/day) with maximum glucose oxidation at 8.3mg/kg/minute (12g/kg/day) after birth. Term surgical infants or those on long term PN have a maximal glucose oxidation rate of 18g/kg/day. (6) Glucose should be increased gradually as tolerated by approximately 2-3g/kg/day with attention paid to glucose provided by other sources, e.g. other IV infusions.

Care must be given not to provide glucose over and above oxidation rates as excess is directed to lipogenesis, thereby promoting fat deposition. Excessive glucose provision may also impair liver function by inducing steatosis. It has been suggested that high glucose feeding increases total VLDL triglyceride secretion and can also impair protein metabolism.

Hyperglycaemia is a common complication of preterm parenteral nutrition which is frequently managed with insulin infusions. The safety and effects of insulin therapy on clinical outcomes in this population are currently unknown, therefore use should be limited to situations where reasonable adaptation of glucose infusion rate does not control hyperglycaemia (6)

Recommendation

- Glucose should provide 60-75% of total energy.
- Glucose requirements should be calculated using glucose oxidation rates (GOR) to ensure supply is within a safe range.
- Glucose infusion should commence in preterm infants at 4-8mg/kg/minute (6-11.5g/kg/day)
- Maximum glucose infusion for long-term PN should not exceed 18g/kg/day
- Insulin infusions can be used in preterm infants with hyperglycaemia but use should be restricted to situations where reasonable adaptation of glucose infusion rates does not control hyperglycaemia.

3.5 Lipid Requirements

In premature infants, lipid administration is important for ensuring an increased calorie intake within a low volume and for the provision of essential fatty acids (EFA). EFA deficiency can develop within 2-3 days in the preterm infant who does not receive an adequate infusion of lipid.(37,38) Preterm minimum essential fatty acid requirements are 0.25g/kg/day linoleic acid (met by 0.5g[2.5ml]/kg/day Intralipid or 1.5g[7.5ml]/kg/day SMOFLipid). Total lipid requirements are based

on optimal fat oxidation, which is itself linked to the supply of glucose. Maximum fat oxidation occurs when intravenous lipid emulsions provide 25-40% of a preterm infants' non protein energy requirement. The maximum lipid requirement for preterm infants is 3–4g/kg/day. (6)

The evidence base for the gradual introduction of lipid (starting at 1g/kg/day and increasing to 3-4g/kg/day) remains limited (6) though gradual incremental increase allows for the monitoring of hypertriglyceridaemia.

The early administration of lipids (day 1-5) in the first days of life does not increase the incidence of chronic lung disease in premature infants when compared to late administration (day 5-14) (39). There are concerns about the potential adverse effects of early lipid administration in infants <800g (40), although one study found that when lipid infusion rates did not exceed 3.6g/kg/day sick, very low birth weight infants could tolerate intravenous lipids with stepwise dose increases from the first day of life without an increased incidence of possible adverse effects (41).

In the >800g infant the benefits of infusing lipids on the first day are thought to outweigh any potential risks (42).

High doses of lipid could be detrimental in the preterm infant with severe acute respiratory failure with or without pulmonary hypertension.(6) Lipids should generally be continued in such cases, though possibly at a lower dose in order to provide the minimal EFA requirement.(6) Regular monitoring of triglyceride level is recommended in such cases, to avoid hypertriglyceridaemia.

Serum triglyceride (Tg) levels should be closely monitored in these infants and in those receiving high lipid doses (>3.5g/kg/day) or who are septic, catabolic, critically ill, ELBW or have severe unexplained thrombocytopenia[i] or significant acidosis. Serum triglycerides and bilirubin levels should also be closely monitored in infants at risk of hyperbilirubinaemia(6).

Recommendation

- Intravenous lipids should commence as soon as possible on the first day of life.
- Incremental introduction may reduce the risks of hypertriglyceridaemia.
- Preterm infants should receive a minimum 0.25g/kg/day linoleic acid in order to prevent EFA deficiency (met by 0.5g[2.5ml]/kg/day Intralipid or 1.5g[7.5ml]/kg/day SMOFLipid).
- Maximum lipid provision should be 3-4g/kg/day.
- Lipid should provide 25-40% non protein calories.

3.6 Vitamin, mineral and trace element requirements.

3.6.1 Vitamins

The optimal parenteral vitamin requirements for preterm infants have never been determined. Available recommendations are therefore based on expert opinion and best practice (6). Until further research is available, these will remain the recommended intakes for vitamins in neonatal PN. The adequate provision of fat and water soluble vitamins is limited by the availability of commercial preparations and is addressed in section 2 of this guidance.

An adequate supply of vitamins is essential for growth and development. As preterm infants may have low or borderline body stores of fat soluble vitamins secondary to limited cross maternal placental transfer, a sufficient supply from the first day of life is recommended. Water soluble vitamins must be administered regularly as they are not stored in any significant amounts.

Vitamins administered intravenously can adhere to delivery tubing and/or be degraded by light. As a result the actual amount delivered to the infant may be significantly lower than the intended dose.

This is particularly the case with vitamin A if the fat soluble vitamins are administered in the aqueous PN, and when the infusion rate is slow.

Vitamin preparations can protect lipid emulsions from peroxidation, therefore administration of both fat and water soluble vitamin preparations with the lipid emulsion provides a practical way to limit vitamin loss and reduce lipid peroxidation.(43, 44)

3.6.2 Minerals and trace elements.

The individual requirements for minerals and trace elements also remain a matter of debate (6). Trace elements are involved in enzymatic activities and immunological reactions, preterm infants are consequently at risk of trace element deficiency secondary to low body stores at birth and the high demands of rapid growth. (45, 46) Parenteral mineral and trace element recommendations are consequently calculated to prevent the development of deficiency syndromes (47) and match in-utero accretion rates (48).

Preterm infants receiving PN for >3 weeks, with minimal or no enteral feeds, may require additional parenteral iron and zinc supplementation (6). Trace element status, including copper should also be monitored monthly (6).

Iron is not routinely provided in neonatal PN and is often not a component of commercially available trace element preparations. Concerns exist regarding iron overload and the role intravenous iron can play in the impairment of immune function and the increase in infection risk secondary to bacterial overgrowth. (49).

Where a preterm infant receives PN as the sole source of nutrition for >3 weeks, parenteral iron supplementation at a dose of between 100microgram and 200microgram/kg/day as a regular daily dose should be considered and iron status closely monitored using serum ferritin levels(6). Where an infant is receiving some enteral nutrition, the alternative use of enteral iron supplements may be considered.

Vitamin, mineral and trace element requirements for preterm infants (ESPGHAN)

Vitamins	**Fat soluble vitamins** Infants (dose/kg/day) Vit A (microgram RE) 150 – 300 Vit D (microgram) 0.8 Vit E (mg) 2.8-3.5 Vit K (microgram) 10 **Water soluble Vitamins** (dose/kg/day) Ascorbic Acid (mg) 15-25 Thiamine (mg) 0.35-0.5 Riboflavin (mg) 0.15-0.2 Pyridoxine (mg) 0.15-0.2 Niacin (mg) 4-6.8 B12 (microgram) 0.3 Pantothenic acid (mg) 1-2 Biotin (microgram) 5-8 Folic acid (microgram) 56	**Minerals & trace elements**	Molybdenum 1microgram/kg/day Selenium 2-3 microgram/kg/day Zinc 450-500 microgram/kg/day

Recommended vitamin and mineral additives (Kabi Fresenius product data)

Nutrients	Product	Dose
Fat Soluble Vitamins Vit A,D,E &K	Vitlipid N Infant	4ml/kg/day up to 2.5kg. 10ml/day for all infants>2.5kg.
Water soluble Vitamins Vit C & B complex	Solivito N	1ml/kg/day
Trace elements Zn,Cu,Mn,Se,F & I	Peditrace	1ml/kg/day

Recommendations

- Preterm infants receiving PN should receive parenteral vitamins, minerals and trace elements as per table.
- Parenteral lipid soluble and water soluble vitamins should be given with the lipid emulsion wherever possible to increase vitamin stability and reduce lipid peroxidation.
- Preterm infants receiving PN >3 weeks should be considered for additional supplementation of iron and zinc.
  Trace elements and fat soluble vitamin levels should be monitored monthly in infants receiving long term PN

3.7 Calcium and Phosphorus

In preterm infants the retention of calcium and phosphorus is proportional to growth (50). Fetal bone mineral accretion rates of 2mmol Ca and 1.52mmol P per 10g newly grown body weight can be achieved if the infant receives adequate quantities of both minerals. (51) These figures have therefore been used as the reference mark for Ca and P PN requirements for preterm infants (6). However phosphate is also a component of lean tissue and an important substrate for muscle function. A recent study and associated regional experience suggests that higher aminoacid intakes provided by enhanced PN formulations, that donot have adequate phosphate supply might cause a metabolic derangement similar to that seen in “re-feeding” syndrome.(86)

Recommendations

- European recommendations suggest that preterm infants should receive between 1.3 - 3mmol Ca/kg/day and 1 – 2.3mmol P/kg/day with a molar Ca:P ratio of 1.3 -1.7 : 1, however regional experience would suggest a molar Ca:P ratio of 1:1 is required to prevent the metabolic derangement akin to “re-feeding” syndrome seen in infants (particularly those who were IUGR) within the East of England.

4.0 Term or infants born near to term (>35 weeks)

Infants born at or near to term who are normal weight for gestation have nutritional requirements that differ from those of the preterm infant. Parenteral formulations designed for preterm use are therefore not suitable for use in this population.

In recognition of this the East of England Neonatal Standardised Parenteral Formulations include a regimen that meets the nutritional needs of the term neonate.

The nutritional requirements of IUGR infants born at or near to term are unknown. The decision to utilise either the term PN or preterm PN formulation should be made individually by the attending clinician.

Term infant nutritional requirements

Nutrient	Recommended intake Stable growth (ESPGHAN) Per /kg /day	Nutrient	Recommended intake Stable growth (ESPGHAN) Per /kg /day
volume	140-160ml/kg	**Calcium mmol**	0.8
Lipid g/kg	3 -4g/kg	**Phosphate mmol**	0.5
Aminoacid g	1.5 -3g/kg	**Ca:P ratio**	No rec
Carbohydrate g	< 18g/kg	**Magnesium mmol**	0.2
Sodium mmol	2-3mmol/kg	**Chloride mmol**	No recc
Potassium mmol	1.5-3mmol/kg	**Acetate mmol**	No recc

5.0 Standardised versus individualised parenteral nutrition

Individualised PN has always been considered the “gold standard“ for achieving optimal nutrient intake and safety in neonatal PN. However evidence indicates that current practices lead to significant energy and protein deficits by the fifth week of life (52). Despite this few studies have assessed the most effective way to deliver PN in the clinical setting. Of those studies available some identify failings that reflect the limited knowledge of neonatal PN prescribers (53, 54) whilst the 2010 NCEPOD report found good neonatal PN practice in only 23.5% of patients with 37% of neonates received inadequate PN for their nutritional needs.(3) As a result, there has been a move towards standardisation of neonatal PN(55) where with careful attention to local workload, formulations and PN prescribing practices the majority of infants can be managed using standardised regimens (56,57). The Paediatric Chief Pharmacists Group state in their 2011 report that the rationalisation and standardisation of PN formulations, where appropriate, has an important part to play in simplifying both the prescribing and compounding processes in PN production. Through removing the need for multiple additions during the compounding process standardisation may be related to a lower risk of error and could apply to 80% of neonatal prescriptions. It may also enable the improvement of early nutrient supply and allow for the advance preparation of solutions by pharmacies and commercial providers, facilitating end product testing and quality assurance by the provider. (4)

Most difficulties related to standardised practice relate to variations in electrolyte (especially sodium) requirements rather than macronutrient requirements. Providing access to standardised PN formulations that allow for some flexibility in electrolyte prescription can help to overcome these difficulties. (58,59)

Recommendation:

- Standard PN solutions should be used where ever possible in order maximise nutrient delivery and to minimise the risk of errors in prescription and compounding.

6.0 PN associated liver disease

PN associated liver disease (PNALD) is a serious complication of prolonged PN use. Prolonged PN dependence is frequently associated with gastrointestinal conditions that lead to intestinal failure and can be defined as a dependence on PN for some or all nutritional requirements for 28 or more days. Risk factors for PNALD include prematurity, surgical conditions such as gastroschisis, jejunal atresia, NEC which may lead to short gut and/or dysmotility, intestinal failure, intolerance of enteral intake and sepsis.

One factor contributing to the development of PNALD is thought to be the composition of intravenous lipid emulsions. The lipid emulsion most frequently used for neonatal PN in the East of England is based on soya bean oil. Soy based emulsions are rich in omega-6 fatty acids and phytosterols, both of which are known to be inflammatory compounds which may contribute to liver injury. There is increasing evidence that using an alternative lipid preparation containing higher proportions of omega-3 fatty acids as fish oils can improve and/or reverse liver disease over a 4-6 week period (60-63). Infants with significant PN associated liver disease should be discussed with paediatric gastroenterology teams and consideration be given to reduction in lipid dose or cycling of lipid, especially in older infants who are partially enterally fed.(64)

6.1 SMOFLipid

SMOFLipid (Soya bean [30%], Medium chain triglyceride [30%], Olive oil [25%], Fish oil [15%]) is a complex mixed-type emulsion. It has the advantage of containing fish oil but also provides essential fatty acids, in contrast to pure fish-oil based lipids. A number of studies have shown that SMOFLipid is as safe as the traditionally used soy-bean oil-based lipid emulsion (65,66) but further studies are required to establish whether SMOFLipid can prevent or reverse PN associated liver disease (67).

The British Society of Paediatric Gastroenterology, Hepatology and Nutrition recommend that SMOFlipid should be considered in infants and children with intestinal failure associated liver disease (68).

SMOFlipid is now increasingly being used by intestinal failure units and other paediatric centres as the preferred lipid for patients who develop signs of liver dysfunction on Intralipid (69) with some units using it as a first line lipid in high risk infants (70).

Recommendation:

Use SMOF as first line lipid in the following infants :

- Definitive diagnosis of short gut at commencement of PN
- Complex gastroschisis where feeds are unlikely to be established within 28 days.

Consider using SMOFLipid in the following infants :

- Infants at high risk of needing PN for >28 days.
- PN dependent >28 days even if liver function tests are normal.
- Significant liver dysfunction before 28 days on PN conjugated bilirubin >50micromol/litre ultrasound evidence of hepatomegaly, or clinical cholestasis (pale stools, dark urine)

7.0 Enteral Nutrition

The provision of nutritionally insignificant volumes of enteral nutrition as trophic feeds have been found to encourage intestinal adaptation and have been linked to enhanced gut motility, decreased incidence of PN-induced cholestasis and bacterial translocation. Trophic feeds should be considered early in infants receiving PN (where clinically indicated) in order to utilize maternal colostrum and stimulate gut trophic hormones.

The maximum volume classed as a "trophic feed" is 1ml/kg/hour or 24ml/kg/day (71) however there is no recognised consensus on method of delivery (72). Individual infants should be assessed daily for tolerance and decisions made with regard to the provision of enteral feeds in line with the East of England Perinatal Network Standardised Feeding Regimen. (73)

Recommendations:

- Trophic feeds should be commenced as soon as clinically indicated in the infant receiving parenteral nutrition.
- Decisions regarding enteral feeds should be made in line with the East of England Enteral Feeding guideline..

8.0 Monitoring of Parenteral Nutrition

Serious and unexpected biochemical instability as a consequence of PN is rare, but can be potentially fatal. Routine biochemical monitoring against an agreed protocol which takes account of length of time on PN, prematurity, co-morbidities and other administered medicines is therefore crucial(4). It is essential that the individual responsible for reviewing biochemical results and taking appropriate action when abnormal values are observed is clearly identified in each unit. (4). Below is a suggested schedule of monitoring based on European recommendations for practice (6). Requirements may differ for individual infants and situations.

	First week of PN			**Stable PN**			
	daily	**Twice weekly**	**weekly**	**daily**	**Twice weekly**	**weekly**	Monthly Long term PN
Infusion site – assess hourly	✓			✓			
Fluid balance – including weight	✓			✓			
Urine Glucose	6 hrly			✓			
Blood Glucose	6-8 hrly			✓			
Electrolytes (Na, K, Cl)	✓				✓		
Urea, Creatinine	✓				✓		
Calcium	✓				✓		
Phosphate,	✓				✓		
Magnesium		✓			✓		
Triglyceride (see below)							
LFTs, Alk Phos,	✓					✓	
Albumin	✓				✓		
Bilirubin	✓					✓	
Acid Base Balance	✓			✓			
Full Blood Count			✓			✓	
Ferritin – if receiving IV iron						✓	
Trace Elements Zn, Cu, Mn, Se							✓
Vitamin A, D, E							✓
Growth (Head circumference)			✓			✓	

8.1 Long term PN

- Infants receiving PN long-term, i.e. >3 weeks with minimal or no enteral feeds should receive the following additional monitoring on a monthly basis(6):
  - trace element status, including copper, manganese, selenium and zinc.
  - fat soluble vitamin status.

8.2 Trace elements

Trace elements should be monitored in infants on long-term PN, i.e. >3 weeks with minimal or no enteral feeds and in those with pre-existing imbalances or reduced excretion of bile or urine as in cholestasis, renal failure or hepatic disease.

8.3 Triglyceride monitoring (Tg)

Triglycerides should be monitored with each increase of 5ml/kg/d of IV lipids and weekly after the maximum dose is achieved and tolerated (6). More frequent monitoring may be required if the infant is receiving high lipid doses (>20ml[3.5g]/kg/day), or is septic, catabolic, critically ill, ELBW or has severe unexplained thrombocytopenia (6).

Triglycerides and bilirubin levels should be measured and monitored in infants at risk of hyperbilirubinaemia and lipid doses adjusted if necessary (6). In cases where there is marked progressive cholestasis associated with PN which is unrelated to acute infection, possible causes should be explored (see sections 12 & 13) and a decrease or a transient interruption in IV lipid should be considered (6).

Suggested IV Lipid Intake Based on Triglyceride (Tg) Level	
Tg Level	**IV Lipid Intake Prescribed (for infusion)**
<2.0mmol/L	- Advance lipid intake as normal. - Assess Tg every 24-48hrs until satisfactory lipid intake tolerated. When satisfactory lipid intake tolerated, assess Tg weekly.
2.0 – 2.8mmol/L	- If lipid intake ≤15ml[2.7g]/kg/day → continue current lipid intake (do not advance). - If lipid intake >15ml[2.7g]/kg/day → reduce lipid intake to 15ml[2.7g]/kg/day. - Assess Tg 24hrs later.
>2.8mmol/L	- Hold IV lipid infusion for 4-6 hours. - Reduce lipid intake to amount previously tolerated. (i.e. that coincided with Tg ≤2.8mmol/L). - Assess Tg 24hrs later.
Normal lipid plus vit advancement: start at 5ml[0.9g]/kg/day (day 1 of life); Advance by 5ml/kg/day every 24hrs. Aim for a lipid plus Vit intake of 15 – 20ml[2.7-3.6g]/kg/day. Aim to provide minimum lipid intake of 0.5g[2.5ml]/kg/day (1.5g[7.5ml]/kg/day SMOFLipid) to meet essential fatty acid requirement. If lipid infusion is interrupted consideration should be given to the provision of vitamins. Whereas water soluble vitamins can be added to the aqueous PN there will be no fat soluble vitamin provision until infusion recommences.	

Recommendations:

- All infants on PN should receive consistent regular monitoring.
- Infants receiving PN long-term, i.e. >3 weeks with minimal or no enteral feeds should receive additional monthly monitoring of trace elements and fat soluble vitamins.
- Triglycerides should be monitored with each increase of 5ml/kg/d of IV lipids and weekly after the maximum dose is achieved and tolerated.

Prescribing and Administration Guideline

9.0 Prescribing and Compounding

9.1 The decision to initiate PN should be made by a senior clinician(4) following the guidance in Table 1. (pg 6)

9.2 The standardised EOE Perinatal Network Standard/Concentrated bags, either with or without electrolytes, should be used as the first line option as the use of standardised macronutrient formulations reduces the risk of errors in prescription and compounding of PN (4). Electrolytes may be tailored to specific requirements by local Pharmacy Aseptic Units (PAU) using the standardised electrolyte-free bags or by the use of same-day ordering with the PN supplier if there is no local PAU or insufficient local PAU capacity. Fully bespoke or individualised PN should only be used where there is no suitable standardised macronutrient formulation due to unusual nutrient requirements or severe fluid restriction. Care should be taken to ensure the prescription meets published recommended nutrient intakes wherever possible.(3,4) Fully bespoke/individualised PN should be prescribed with the support of a pharmacist/neonatal dietitian.

9.3 Prescription of PN should be performed by the clinical team caring for the patient. Ideally this should involve as a minimum a senior clinician and pharmacist/neonatal dietitian.(4)

9.4 The clinician that decides on the nutrient requirements and the PN formulation should also sign the prescription.(4)

9.5 PN should be prescribed 48 hourly in stable neonates but may be prescribed daily in unstable neonates with frequently changing electrolyte requirements.

9.6 The volume of PN prescribed will depend on overall fluid requirements, other infusions (IV medications) and enteral feed volumes. Priority should be given to maximising PN volumes in order to maximise protein provision. This includes situations where PN is commenced in infants already receiving prescribed volumes greater than the traditional initial PN volume of 60ml/kg. Refer to Appendix 1 for PN nutrient composition tables for standard and concentrated bags related to volume per kg/day to ensure volume prescribed satisfies nutritional requirements.

9.7 Lipid should not provide more than 40% of non-protein energy requirements therefore when prescribing consideration should be given to the balance of lipid:glucose calorie provision.

9.8 Both fat and water soluble vitamins should be given with the lipid emulsion to improve vitamin stability.(42,43) In units where vitamin and mineral additions are to be made locally Solivito N should be reconstituted in 20% Intralipid according to the formula given in the box below:

Reconstitute 1 vial of Solivito N with 10ml of Intralipid 20%
Add 1.75ml of the resultant solution per 35ml syringe of Intralipid 20%.
Add 7ml Vitlipid N infant per 35ml syringe

20ml/kg would then provide: -
Solivito 1ml/kg
Vitlipid N 4ml/kg
Lipid 3.6g/kg

Consideration should be given to other routes of vitamin administration when the lipid emulsion is stopped.(4) Solivito can be added to aqueous PN if necessary but this route should only be used if lipid is not being given.

9.9 PN should be prescribed based on birth weight in the first week of life. Thereafter it should be prescribed on the greatest recent weight (birth weight or current weight) as long as there is no significant oedema.

9.10 Any change in infusion rate from that on the label of the PN solution must be within the maximal rate of infusion on the label and be clearly documented on the patient's prescription chart.(4)

9.11 In chronic or acute severe renal failure Peditrace should be used with caution along with careful monitoring of trace elements.

10.0 Administration

10.1 Prolonged PN should be given via a central line(6); either a properly sited umbilical venous catheter or peripheral percutaneous central venous line (long-line). Where umbilical venous catheters are used they should not be left in place for more than 14 days(6).

10.2 All central lines to be used for PN must be inserted according to local/network guidelines with strict adherence to approved aseptic techniques. The line tip position must be confirmed by x-ray (with radio-opaque contrast for long-lines) (72) prior to the infusion of PN. The preferred position for the central line tip should be either the IVC (level of the diaphragm) or SVC(74) (long-line only). Atrial positioning should be avoided due to the risk of atrial perforation (75-77).

10.3 Catheter-related blood stream infection remains the most common complication related to central venous access therefore meticulous attention to sterility of the line that is used for PN delivery is vital. Lines used for PN should not be used for blood sampling. Access to the line should be minimised and ideally the line should be used solely for PN, although in the Neonatal Intensive Care setting this is often impractical due to difficulties in venous access and the need to preserve peripheral veins. If other infusions do need to run alongside the PN then compatibility must be confirmed (6).

10.4 Peripheral Venous catheters should be avoided for the routine administration of PN. Some units may decide to use this route on an individual patient basis in the short-term (e.g. day 1 in an infant meeting the criteria for PN but with no central line) after an assessment has been made to balance the risks of extravasation injury against potential complications associated with obtaining/maintaining central venous access and nutritional needs of the infant. If PN is administered via a peripheral line then the maximum osmolarity should be limited. There is debate as to the recommended maximum osmolarity. ESPGHAN recommend less than 600mOsm/L(6) but ASPEN recommend less than 900mOsm/L(78). Maximum glucose

concentration is 12.5%(6,79). PN that is not suitable for peripheral line administration must be clearly labelled: 'to be given by central line only'(4).The EOE Concentrated PN bags must never be used for peripheral infusion.

10.5 Additions to PN solutions, either lipid or aqueous, contained in infusion bags and/or syringes, must only be made on a PAU. **Additions to PN (including electrolytes) must never be made at ward level**. (4,80)

10.6 Both lipid and aqueous PN solutions should be protected from light as exposure increases the products of oxidation in PN which may contribute to increased oxidative stress in preterm infants(81). Light protection decreases the accumulation of triglycerides in plasma and may allow for higher rates of lipid infusion and improved nutrition (82). Light protection also helps to prevent light-induced vitamin degradation (43).

10.7 Aqueous PN solutions should be infused over 48 hours in stable neonates. Lipid infusions are to be changed every 24 hours and should be infused over 24 hours as this has been shown to improve lipid tolerance in preterm infants without adversely affecting lipid monitoring.(83-85)

10.8 Each unit must make arrangements for pre-prepared PN (both aqueous solutions and lipid emulsions) to be available 24 hours a day(4) to ensure that all preterm infants meeting the criteria can be commenced on PN as early as possible within the first 24 hours and ideally within 6 hours of birth.(11-13)

10.9 PN should always be infused via in-line filters; 0.22 micron filters for aqueous PN and 1.2-1.5 micron filters for lipid emulsions.(6)

10.10 PN giving set and filters must be changed every 48 hours for aqueous PN and every 24 hours for lipid..

10.11 PN infusion set up, attachment of the giving set and connection to the patient should be performed using full aseptic non-touch technique (ANTT).

10.12 Checking - all TPN should be checked against prescription and fluid requirements by two registered nurses, one of whom must be qualified in speciality. Both nurses to remain present until PN infusions are set up in infusion devices and lines are connected to the patient. A final safety check at the point of administration of PN should be performed including checking the labels of PN solutions (aqueous and lipid) against the prescription for:

- Name of patient and hospital number
- Route of administration (central or peripheral)
- Date of infusion
- Rate of infusion
- Expiry
- Doses of all ingredients prescribed
- Appearance of the parenteral nutrition solutions

10.13 All nurses that put up PN infusions should be trained in ANTT and IV management and receive appropriate updates.

Training records should be kept for all nurses to demonstrate individual competence.

11.0 Weaning of PN

11.1 Enteral feeding should be introduced according to the EOE Enteral Feeding Guideline (72). Once enteral feed volumes start to be increased beyond trophic feeds (24ml/kg/day) and the clinical team consider that they are being tolerated and absorbed then the volume of enteral feed should be considered when prescribing total PN volumes.

11.2 As enteral feeds increase then PN should be reduced by a similar amount (6). Both the aqueous and the lipid components should be reduced proportionately to the increase in enteral feeds. The lipid component should also be reduced in proportion to the reduction in the aqueous volume (6) see table.

Total volume of PN	Reduce lipid (and vitamin) emulsion to the following volumes
Less than 130 ml/kg/day	15 ml/kg/day
Less than 100 ml/kg/day	10 ml/kg/day
Less than 70 ml/kg/day	5 ml/kg/day
Less than 50ml/kg/day	Stop lipid infusion

11.3 PN should be continued until at least 120ml/kg/day of enteral feed is tolerated in order to maximise nutrition provision. Total fluid volume may be increased above 150ml/kg/day if needed as long as there are no clinical contraindications in order to avoid ordering excessively small PN volumes.

East of England Neonatal Parenteral Nutrition Formulations

12.0 STANDARD PRETERM (amended formulation February 2015)

Nutrient	Bag 1 Standard PN Per 100ml	Bag 2 Standard PN electrolyte free per 100ml	Nutritional provision Per/kg body weight	Recommended intake for stable growth (ESPGHAN/TSANG) Per /kg body weight
Volume ml			**130ml/kg aqueous plus 20ml/kg lipid. (total 150ml/kg)**	**150 – 180ml/kg**
Energy Kcal/kg			**93-97nnKcal/kg 60%CHO:40%Lipid 24-25kcal/g AA**	**90-115nnKcal/kg(T) 85-105nnKcal/kg(E) 110-120total Kcal/kg(E) 40% Kcal as lipid(E) 20-25Kcal/gAA (34)**
Lipid mlkg	**20ml/kg**	**20ml/kg**	**20ml/kg [3.6g/kg with Vits] [4g/kg if no Vits]**	***3-4(E) 3(T)***
Aminoacid g	**3.3**	**3.3**	**4.3**	***3.5-4.0(protein)(T) 4.0(E)***
Nitrogen g	**0.47**	**0.47**	**0.62**	***0.51-0.64(T) 0.57(E)***
Carbohydrate g	**11**	**11**	**14.3 (11% dextrose)**	***Max GOR day 1 8.3mg/kg/min (12g/kg/day) Max 18g/kg/day by day 4***
Sodium mmol	**3**		**4**	***3-5(T&E)***
Potassium mmol	**1.9**		**2.5**	***2-5(T&E)***
Chloride mmol			**4**	***3-7(T) 3-5(E)***
Calcium mmol	**1.7**		**2.2**	***1.5-2(T)/3.0(E)***
Phosphate mmol	**1.45 (previously 1.1)**		**1.9 aqueous 0.3 lipid Total 2.2mmol/kg**	***1.5-2(T)/2.3(E)***
Ca:P ratio			**1:1**	***1.3-1.7:1(E) Practice shows this is inadequate. Aim for ratio of 1:1***
Magnesium mmol	**0.19**		**0.25**	***0.18-0.3 (T)0.2 (E)***
Acetate mmol	**1.5**		**2**	***2***

13.0 PRETERM CONCENTRATED (amended formulation February 2015)

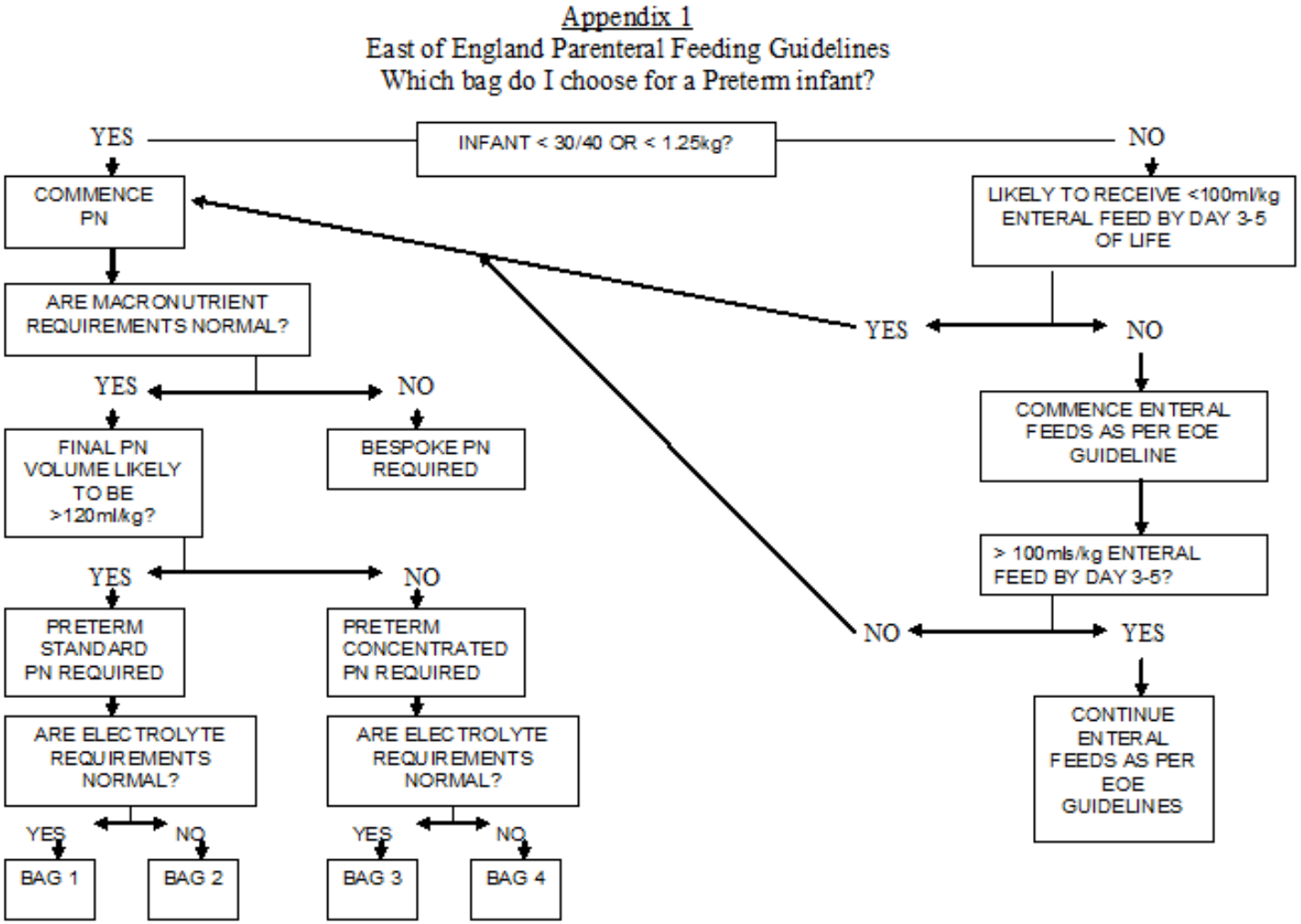
Nutrient	Bag 3 Concentrated PN Per 100ml	Bag 4 Concentrated PN electrolyte free per 100ml	Nutritional provision Per/kg body weight	Recommended intake In full PN (ESPGHAN/TSANG) Per /kg body weight
Volume			**100ml/kg aqueous plus 20ml/kg lipid. (total 120ml/kg)**	
Energy Kcal/kg			**94-98nnKcal/kg 60%CHO:40%Lipid 24-25kcal/g amino acid**	**90-115nnKcal/kg(T) 85-105nnKcal/kg(E) 110-120total Kcal/kg(E) 40% Kcal as lipid(E) 20-25Kcal/gAA(34)**
Lipid m/kg	**20ml/kg**	**20ml/kg**	**20ml/kg [3.6g/kg with Vits] [4g/kg if no Vits]**	***3.0-4.0(E) 3.0(T)***
Aminoacid g/100ml	**4.3**	**4.3**	**4.3**	***3.5-4.0(protein) (T) 4.0(E)***
Nitrogen g/100ml	**0.62**	**0.62**	**0.62**	***0.51-0.64(T) 0.57(E)***
Carbohydrate g/100ml	**14.5**	**14.5**	**14.5 (14.5% dextrose)**	***Max GOR day 1 8.3mg/kg/min (12g/kg/day) Max 18g/kg/day by day 4***
Sodium mmol/100ml	**3.9**		**3.9**	***3-5(T&E)***
Potassium mmol/100ml	**2.4**		**2.4**	***2-5(T&E)***
Chloride mmol/100ml	**3.9**		**3.9**	***3-7(T) 3-5(E)***
Calcium mmol/100ml	**1.98**		**1.98**	***1.5-2(T)/3(E)***
Phosphate mmol/100ml	**1.8**		**1.8 aqueous 0.3 lipid Total 2.1mmol/kg**	***1.5-2(T)/2.3€***
Ca:P ratio			**1:1.06**	***1.3-1.7:1(E) Practice shows this is inadequate. Aim for ratio of 1:1 actual is 1:1.06***
Magnesium mmol/100ml	**0.24**		**0.24**	***0.18-0.3 (T)0.2(E)***
Acetate mmol/100ml	**1.9**		**1.9**	***2***

14.0 TERM STANDARD

Nutrient	Bag 5 Standard Term PN Per 100ml	Bag 6 Standard Term PN electrolyte free per 100ml	Nutritional provision Per/kg body weight	Recommended intake Stable growth (ESPGHAN) Per /kg body weight
volume			135ml/kg plus 15ml/kg lipid. (total 150ml/kg)	140-160ml/kg
Energy Kcal/kg			87-90kcal/kg/day	90-100kcal/kg/day (total)
Lipid ml/kg	15	15	15ml/kg [3g/kg if no Vits] [2.7g/kg with Vits]	Maximum of 3 - 4g/kg
Aminoacid g	2.1	2.1	2.8	1.5 -3g/kg
Nitrogen g	0.3	0.3	0.4	
Carbohydrate g	11	11	15	< 18g/kg (13mg/kg/min)
Sodium mmol	2.2		3	2-3mmol/kg
Potassium mmol	1.9		2.6	1.5-3mmol/kg
Chloride mmol	1.9		2.6	No recc
Calcium mmol	0.6		0.8	0.8
Phosphate mmol	0.2*		0.5*	0.5
Ca:P ratio			1.6:1	No rec
Magnesium mmol	0.15		0.2	0.2
Acetate mmol				No rec

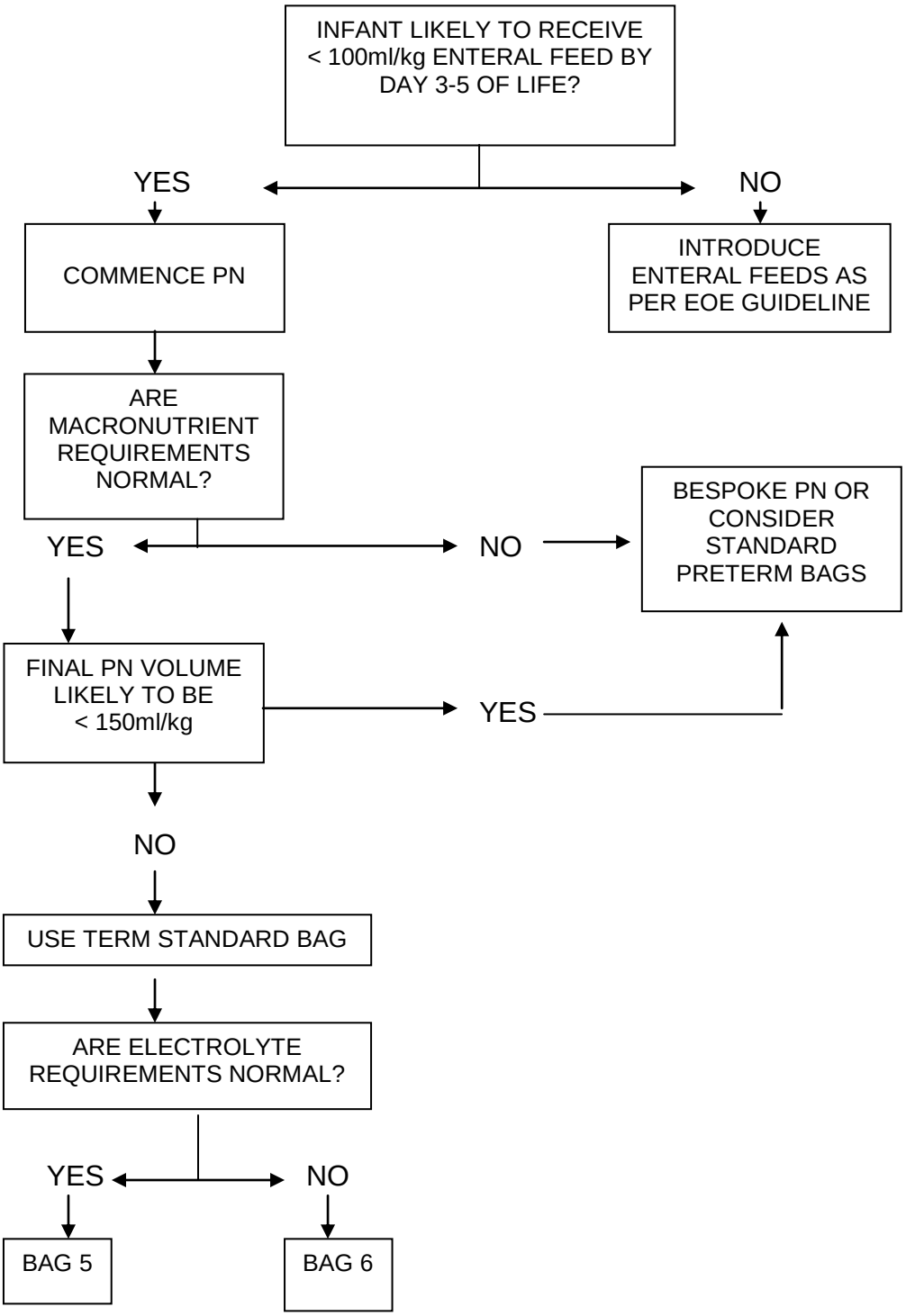
Standard bags - 500ml and 1000ml
Concentrated bags – 400ml and 800ml
Lipid – Intralipid or SMOFLipid prescribed against East of England criteria.
*phosphate to be total of lipid and aqueous provision. (3g = 0.23mmol , 3.5g =0.3mmol)
Vitlipid /Solivito/Peditrace as per recommended prescription doses (see Prescribing Guidelines)

Appendix 1 East of England Neonatal Parenteral Nutrition Algorithms.



Where an electrolyte free bag is indicated [bag 2 or 4] patient specific electrolytes should be prescribed in the "non standard" column of the proforma and ordered either from the local PAU or directly from the supplier for same day delivery.

East of England Parenteral Nutrition Guideline
Which bag do I use for term and near term infants?



Where an electrolyte free bag is indicated [bag 6] patient specific electrolytes should be prescribed in the “non standard” column of the proforma and ordered either from the local PAU or directly from the supplier for same day delivery.

Appendix 2 Nutrient provision by prescribed volume.

Standard Preterm PN (Lipid with vitamins)

													Recommended intake for stable growth (ESPGHAN/TSANG) per/kg body weight
Total PN Volume ml/kg/day	**50**	**55**	**60**	**70**	**80**	**90**	**100**	**110**	**120**	**130**	**140**	**150**	150-180ml
Lipid g/kg/day	0.9	0.9	0.9	0.9	1.8	1.8	1.8	2.7	2.7	2.7	2.7	3.6	3-4g (E) 3g (T)
Lipid volume ml/kg/day	5	5	5	5	10	10	10	15	15	15	15	20	
Aqueous PN volume ml/kg/day	**45**	**50**	**55**	**65**	**70**	**80**	**90**	**95**	**105**	**115**	**125**	**130**	
Amino acid g/kg/day	1.5	1.7	1.8	2.1	2.3	2.6	3.0	3.1	3.5	3.8	4.1	4.3	4g (E) 3.5 – 4.0g(protein) (T)
Nitrogen g/kg/day	0.21	0.24	0.26	0.31	0.33	0.38	0.42	0.45	0.49	0.54	0.59	0.61	0.57g (E) 0.51-0.64g (T)
Carbohydrate g/kg/day	5.0	5.5	6.1	7.2	7.7	8.8	9.9	10.5	11.6	12.7	13.8	14.3	Max 18g/kg/day by day 4
Non Nitrogen Energy kcal/kg/day	29	31	33.4	37.8	48.8	53.2	57.6	69	73.4	77.8	82.2	93.2	85-105nnkcal(E)90-115nnkcal(T)
Energy: nitrogen ratio kcal/g	137	132	129	124	148	141	136	155	149	144	140	153	
Energy:amino acid ratio kcal/g	20	19	18	18	21	20	19	22	21	21	20	22	20-25kcal/g amino acid (33)
Lipid calories kcal/kg/day	9	9	9	9	18	18	18	27	27	27	27	36	
Lipid/ Non Nitrogen Energy %	31%	29%	27%	24%	37%	34%	31%	39%	37%	35%	33%	39%	40% kcal as lipid (E)
Sodium mmol/kg/day	1.4	1.5	1.7	2.0	2.1	2.4	2.7	2.9	3.2	3.5	3.8	3.9	3-5 mmol (T&E)
Potassium mmol/kg/day	0.9	1.0	1.0	1.2	1.3	1.5	1.7	1.8	2.0	2.2	2.4	2.5	2-5 mmol (T&E)
Chloride mmol/kg/day	1.4	1.5	1.7	2.0	2.1	2.4	2.7	2.9	3.2	3.5	3.8	3.9	3-5mmol(E) 3-7mmol(T)
Calcium mmol/kg/day	0.8	0.9	0.9	1.1	1.2	1.4	1.5	1.6	1.8	2.0	2.1	2.2	3mmol(E) 1.5-2mmol(T)
Phosphate mmol/kg/day	0.65	0.73	0.80	0.94	1.02	1.16	1.30	1.38	1.52	1.68	1.81	1.89	
Phosphate from lipd mmol/kg/day	0.08	0.08	0.08	0.08	0.15	0.15	0.15	0.23	0.23	0.23	0.23	0.30	
Total phosphate mmol/kg/day	0.73	0.81	0.88	1.02	1.17	1.31	1.45	1.61	1.75	1.91	2.04	2.18	2.3mmol(E) 1.5-2mmol(T)
Ca:P ratio	1.09:1	1.1:1	1.02:1	1.07:1	1.02:1	1.07:1	1.03:1	1.06:1	1.03:1	1.05:1	1.02:1	1:1	1.3-1.7:1 (E) 1:1 network
Magnesium mmol/kg/day	0.09	0.10	0.10	0.12	0.13	0.15	0.17	0.18	0.20	0.22	0.24	0.25	0.2mmol(E) 0.18-0.3mmol(T)
Acetate mmol/kg/day	0.7	0.8	0.8	1.0	1.1	1.2	1.4	1.4	1.6	1.7	1.9	2.0	2mmol

Standard Preterm PN (Lipid without vitamins)

													Recommended intake for stable growth (ESPGHAN/TSANG) per/kg body weight
Total PN Volume ml/kg/day	**50**	**55**	**60**	**70**	**80**	**90**	**100**	**110**	**120**	**130**	**140**	**150**	150-180ml
Lipid g/kg/day	1	1	1	1	2	2	2	2	3	3	3	4	3-4g (E) 3g (T)
Lipid volume ml/kg/day	5	5	5	5	10	10	10	10	15	15	15	20	
Aqueous PN volume ml/kg/day	**45**	**50**	**55**	**65**	**70**	**80**	**90**	**100**	**105**	**115**	**125**	**130**	
Amino acid g/kg/day	1.5	1.7	1.8	2.1	2.3	2.6	3.0	3.3	3.5	3.8	4.1	4.3	4g (E) 3.5 – 4.0g(protein) (T)
Nitrogen g/kg/day	0.21	0.24	0.26	0.31	0.33	0.38	0.42	0.47	0.49	0.54	0.59	0.61	0.57g (E) 0.51-0.64g (T)
Carbohydrate g/kg/day	5.0	5.5	6.1	7.2	7.7	8.8	9.9	11.0	11.6	12.7	13.8	14.3	Max 18g/kg/day by day 4
Non Nitrogen Energy kcal/kg/day	30	32	34.4	38.8	50.8	55.2	59.6	64	76.4	80.8	85.2	97.2	85-105nnkcal(E)90-115nnkcal(T)
Energy: nitrogen ratio kcal/g	142	136	133	127	154	147	141	136	155	149	145	159	
Energy:amino acid ratio kcal/g	20	19	19	18	22	21	20	19	22	21	21	23	20-25kcal/g amino acid (33)
Lipid calories kcal/kg/day	10	10	10	10	20	20	20	20	30	30	30	40	
Lipid/ Non Nitrogen Energy %	33%	31%	29%	26%	39%	36%	34%	31%	39%	37%	35%	41%	40% kcal as lipid (E)
Sodium mmol/kg/day	1.4	1.5	1.7	2.0	2.1	2.4	2.7	3.0	3.2	3.5	3.8	3.9	3-5 mmol (T&E)
Potassium mmol/kg/day	0.9	1.0	1.0	1.2	1.3	1.5	1.7	1.9	2.0	2.2	2.4	2.5	2-5 mmol (T&E)
Chloride mmol/kg/day	1.4	1.5	1.7	2.0	2.1	2.4	2.7	3.0	3.2	3.5	3.8	3.9	3-5mmol(E) 3-7mmol(T)
Calcium mmol/kg/day	0.8	0.9	0.9	1.1	1.2	1.4	1.5	1.7	1.8	2.0	2.1	2.2	3mmol(E) 1.5-2mmol(T)
Phosphate mmol/kg/day	0.65	0.73	0.80	0.94	1.02	1.16	1.30	1.45	1.52	1.68	1.81	1.89	
Phospahte from lipid mmol/kg/day	0.08	0.08	0.08	0.08	0.15	0.15	0.15	0.15	0.23	0.23	0.23	0.30	
Total phosphate mmol/kg/day	0.73	0.81	0.88	1.02	1.17	1.31	1.45	1.6	1.75	1.91	2.04	2.18	2.3mmol(E) 1.5-2mmol(T)
Ca:P ratio	1.09:1	1.1:1	1.02:1	1.07:1	1.02:1	1.07:1	1.03:1	1.06:1	1.03:1	1.05:1	1.02:1	1:1	1.3-1.7:1 (E) 1:1 network
Magnesium mmol/kg/day	0.09	0.10	0.10	0.12	0.13	0.15	0.17	0.19	0.20	0.22	0.24	0.25	0.2mmol(E) 0.18-0.3mmol(T)
Acetate mmol/kg/day	0.7	0.8	0.8	1.0	1.1	1.2	1.4	1.5	1.6	1.7	1.9	2.0	2mmol

Preterm Concentrated PN (Lipid with vitamins)

										Recommended intake for stable growth (ESPGHAN/TSANG) per/kg body weight
Total PN Volume ml/kg/day	**50**	**55**	**60**	**70**	**80**	**90**	**100**	**110**	**120**	150-180ml
Lipid g/kg/day	0.9	0.9	1.8	1.8	1.8	1.8	2.7	2.7	3.6	3-4g (E) 3g (T)
Lipid volume ml/kg/day	5	5	10	10	10	10	15	15	20	
Aqueous PN volume ml/kg/day	**45**	**50**	**50**	**60**	**70**	**80**	**85**	**95**	**100**	
Amino acid g/kg/day	1.9	2.2	2.2	2.6	3.0	3.4	3.7	4.1	4.3	4g (E) 3.5 – 4.0g(protein) (T)
Nitrogen g/kg/day	0.27	0.31	0.31	0.37	0.43	0.49	0.52	0.58	0.61	0.57g (E) 0.51-0.64g (T)
Carbohydrate g/kg/day	6.5	7.3	7.3	8.7	10.2	11.6	12.3	13.8	14.5	Max 18g/kg/day by day 4
Non Nitrogen Energy kcal/kg/day	35	38.2	47.2	52.8	58.8	64.4	76.2	82.2	94	85-105nnkcal(E)9 0-115nnkcal(T)
Energy: nitrogen ratio kcal/g	128	125	155	144	138	132	147	142	154	
Energy:amino acid ratio kcal/g	18	18	22	20	20	19	21	20	22	20-25kcal/g amino acid (33)
Lipid calories kcal/kg/day	9	9	18	18	18	18	27	27	36	
Lipid/ Non Nitrogen Energy %	26%	24%	38%	34%	31%	28%	35%	33%	38%	40% kcal as lipid (E)
Sodium mmol/kg/day	1.8	2.0	2.0	2.4	2.8	3.2	3.4	3.8	4.0	3-5 mmol (T&E)
Potassium mmol/kg/day	1.1	1.3	1.3	1.5	1.8	2.0	2.1	2.4	2.5	2-5 mmol (T&E)
Chloride mmol/kg/day	1.8	2.0	2.0	2.4	2.8	3.2	3.4	3.8	4.0	3-5mmol(E) 3-7mmol(T)
Calcium mmol/kg/day	0.89	0.99	0.99	1.19	1.39	1.58	1.68	1.88	1.98	3mmol(E) 1.5-2mmol(T)
Phosphate mmol/kg/day	0.81	0.9	0.9	1.08	1.26	1.44	1.53	1.71	1.8	
Phospahte from lipd mmol/kg/day	0.08	0.08	0.15	0.15	0.15	0.15	0.23	0.23	0.30	
Total phosphate mmol/kg/day	0.89	0.98	1.05	1.23	1.41	1.59	1.76	1.94	2.1	2.3mmol(E) 1.5-2mmol(T)
Ca:P ratio	1:1	1:1	1:1.06	1:1.03	1.01	1:1	1:1.05	1:1.03	1:1.06	1.3-1.7:1 (E) 1:1 network
Magnesium mmol/kg/day	0.11	0.13	0.13	0.15	0.18	0.20	0.21	0.24	0.25	0.2mmol(E) 0.18-0.3mmol(T)
Acetate mmol/kg/day	0.9	1.0	1.0	1.2	1.4	1.6	1.7	1.9	2	2mmol

Preterm concentrated PN (Lipid without vitamins)

										Recommended intake for stable growth (ESPGHAN/TSANG) per/kg body weight
Total PN Volume ml/kg/day	**50**	**55**	**60**	**70**	**80**	**90**	**100**	**110**	**120**	150-180ml
Lipid g/kg/day	1	1	2	2	2	2	3	3	4	3-4g (E) 3g (T)
Lipid volume ml/kg/day	5	5	10	10	10	10	15	15	20	
Aqueous PN volume ml/kg/day	**45**	**50**	**50**	**60**	**70**	**80**	**85**	**95**	**100**	
Amino acid g/kg/day	1.9	2.2	2.2	2.6	3.0	3.4	3.7	4.1	4.3	4g (E) 3.5 – 4.0g(protein) (T)
Nitrogen g/kg/day	0.27	0.31	0.31	0.37	0.43	0.49	0.52	0.58	0.61	0.57g (E) 0.51-0.64g (T)
Carbohydrate g/kg/day	6.5	7.3	7.3	8.7	10.2	11.6	12.3	13.8	14.5	Max 18g/kg/day by day 4
Non Nitrogen Energy kcal/kg/day	36	39.2	49.2	54.8	60.8	66.4	79.2	85.2	98	85-105nnkcal(E)90-115nnkcal(T)
Energy: nitrogen ratio kcal/g	131	129	161	150	142	136	153	147	161	
Energy:amino acid ratio kcal/g	19	18	23	21	20	19	22	21	23	20-25kcal/g amino acid (33)
Lipid calories kcal/kg/day	10	10	20	20	20	20	30	30	40	
Lipid/ Non Nitrogen Energy %	28%	26%	41%	36%	33%	30%	38%	35%	41%	40% kcal as lipid (E)
Sodium mmol/kg/day	1.8	2.0	2.0	2.4	2.8	3.2	3.4	3.8	4.0	3-5 mmol (T&E)
Potassium mmol/kg/day	1.1	1.3	1.3	1.5	1.8	2.0	2.1	2.4	2.5	2-5 mmol (T&E)
Chloride mmol/kg/day	1.8	2.0	2.0	2.4	2.8	3.2	3.4	3.8	4.0	3-5mmol(E) 3-7mmol(T)
Calcium mmol/kg/day	0.89	0.99	0.99	1.19	1.39	1.58	1.68	1.88	1.98	3mmol(E) 1.5-2mmol(T)
Phosphate mmol/kg/day	0.81	0.9	0.9	1.08	1.26	1.44	1.53	1.71	1.8	
Phospahte from lipd mmol/kg/day	0.08	0.08	0.15	0.15	0.15	0.15	0.23	0.23	0.30	
Total phosphate mmol/kg/day	0.89	0.98	1.05	1.23	1.41	1.59	1.76	1.94	2.1	2.3mmol(E) 1.5-2mmol(T)
Ca:P ratio	1:1	1:1	1:1.06	1:1.03	1.01	1:1	1:1.05	1:1.03	1:1.06	1.3-1.7:1 (E) 1:1 network
Magnesium mmol/kg/day	0.11	0.13	0.13	0.15	0.18	0.20	0.21	0.24	0.25	0.2mmol(E) 0.18-0.3mmol(T)
Acetate mmol/kg/day	0.9	1.0	1.0	1.2	1.4	1.6	1.7	1.9	2	2mmol

Standard Term PN (Lipid with vitamins)

													Recommended intake for stable growth (ESPGHAN/TSANG) per/kg body weight
Total PN Volume ml/kg/day	**50**	**55**	**60**	**70**	**80**	**90**	**100**	**110**	**120**	**130**	**140**	**150**	140-160ml
Lipid g/kg/day	0.9	0.9	0.9	0.9	1.8	1.8	1.8	1.8	2.7	2.7	2.7	2.7	Maximum 3-4g
Lipid volume ml/kg/day	5	5	5	5	10	10	10	10	15	15	15	15	
Aqueous PN volume ml/kg/day	**45**	**50**	**55**	**65**	**70**	**80**	**90**	**100**	**105**	**115**	**125**	**135**	
Amino acid g/kg/day	0.9	1.1	1.2	1.4	1.5	1.7	1.9	2.1	2.2	2.4	2.6	2.8	1.5-3g
Nitrogen g/kg/day	0.14	0.15	0.17	0.20	0.21	0.24	0.27	0.30	0.32	0.35	0.38	0.41	
Carbohydrate g/kg/day	5.0	5.5	6.1	7.2	7.7	8.8	9.9	11.0	11.6	12.7	13.8	14.9	Maximum 18g/kg/day
NNEnergy kcal/kg/day	29	31	33.4	37.8	48.8	53.2	57.6	62	73.4	77.8	82.2	86.6	90-100kcal (total)
Energy: nitrogen ratio kcal/g	215	207	202	194	232	222	213	207	233	226	219	214	
Energy:amino acid ratio kcal/g	31	30	29	28	33	32	30	30	33	32	31	31	
Lipid calories kcal/kg/day	9	9	9	9	18	18	18	18	27	27	27	27	
Lipid/ Non Protein Energy %	31%	29%	27%	24%	37%	34%	31%	29%	37%	35%	33%	31%	
Sodium mmol/kg/day	1.0	1.1	1.2	1.4	1.5	1.8	2.0	2.2	2.3	2.5	2.8	3.0	2-3 mmol
Potassium mmol/kg/day	0.9	1.0	1.0	1.2	1.3	1.5	1.7	1.9	2.0	2.2	2.4	2.6	1.5-3 mmol
Chloride mmol/kg/day	0.9	1.0	1.0	1.2	1.3	1.5	1.7	1.9	2.0	2.2	2.4	2.6	No recommendation
Calcium mmol/kg/day	0.3	0.3	0.3	0.4	0.4	0.5	0.5	0.6	0.6	0.7	0.8	0.8	0.8mmol
Phosphate mmol/kg/day	0.09	0.1	0.11	0.13	0.14	0.16	0.18	0.2	0.21	0.23	0.25	0.27	
Phospahte from lipd mmol/kg/day	0.08	0.08	0.08	0.08	0.15	0.15	0.15	0.15	0.23	0.23	0.23	0.23	
Total phosphate mmol/kg/day	0.2	0.2	0.2	0.2	0.3	0.3	0.3	0.4	0.4	0.5	0.5	0.5	0.5mmol
Ca:P ratio	1.6	1.7	1.8	1.9	1.4	1.5	1.6	1.7	1.4	1.5	1.6	1.6	No recommendation
Magnesium mmol/kg/day	0.07	0.08	0.08	0.10	0.11	0.12	0.14	0.15	0.16	0.17	0.19	0.20	0.2mmol
Acetate mmol/kg/day													No recommendation

Standard Term PN (Lipid without vitamins)

													Recommended intake for stable growth (ESPGHAN/TSANG) per/kg body weight
Total PN Volume ml/kg/day	**50**	**55**	**60**	**70**	**80**	**90**	**100**	**110**	**120**	**130**	**140**	**150**	140-160ml
Lipid g/kg/day	1	1	1	1	2	2	2	2	3	3	3	3	Maximum 3-4g
Lipid volume ml/kg/day	5	5	5	5	10	10	10	10	15	15	15	15	
Aqueous PN volume ml/kg/day	**45**	**50**	**55**	**65**	**70**	**80**	**90**	**100**	**105**	**115**	**125**	**135**	
Amino acid g/kg/day	0.9	1.1	1.2	1.4	1.5	1.7	1.9	2.1	2.2	2.4	2.6	2.8	1.5-3g
Nitrogen g/kg/day	0.14	0.15	0.17	0.20	0.21	0.24	0.27	0.30	0.32	0.35	0.38	0.41	
Carbohydrate g/kg/day	5.0	5.5	6.1	7.2	7.7	8.8	9.9	11.0	11.6	12.7	13.8	14.9	Maximum 18g/kg/day
NNEnergy kcal/kg/day	30	32	34.4	38.8	50.8	55.2	59.6	64	76.4	80.8	85.2	89.6	90-100kcal (total)
Energy: nitrogen ratio kcal/g	222	213	208	199	242	230	221	213	243	234	227	221	
Energy:amino acid ratio kcal/g	32	30	30	28	35	33	32	30	35	33	32	32	
Lipid calories kcal/kg/day	10	10	10	10	20	20	20	20	30	30	30	30	
Lipid/ Non Protein Energy %	33%	31%	29%	26%	39%	36%	34%	31%	39%	37%	35%	33%	
Sodium mmol/kg/day	1.0	1.1	1.2	1.4	1.5	1.8	2.0	2.2	2.3	2.5	2.8	3.0	2-3 mmol
Potassium mmol/kg/day	0.9	1.0	1.0	1.2	1.3	1.5	1.7	1.9	2.0	2.2	2.4	2.6	1.5-3 mmol
Chloride mmol/kg/day	0.9	1.0	1.0	1.2	1.3	1.5	1.7	1.9	2.0	2.2	2.4	2.6	No recommendation
Calcium mmol/kg/day	0.3	0.3	0.3	0.4	0.4	0.5	0.5	0.6	0.6	0.7	0.8	0.8	0.8mmol
Phosphate mmol/kg/day	0.09	0.1	0.11	0.13	0.14	0.16	0.18	0.2	0.21	0.23	0.25	0.27	
Phospahte from lipd mmol/kg/day	0.08	0.08	0.08	0.08	0.15	0.15	0.15	0.15	0.23	0.23	0.23	0.23	
Total phosphate mmol/kg/day	0.2	0.2	0.2	0.2	0.3	0.3	0.3	0.4	0.4	0.5	0.5	0.5	0.5mmol
Ca:P ratio	1.6	1.7	1.8	1.9	1.4	1.5	1.6	1.7	1.4	1.5	1.6	1.6	No recommendation
Magnesium mmol/kg/day	0.07	0.08	0.08	0.10	0.11	0.12	0.14	0.15	0.16	0.17	0.19	0.20	0.2mmol
Acetate mmol/kg/day													No recommendation

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