LOCAL OPERATING PROCEDURE

NEONATAL SERVICES DIVISION

Approved by Quality & Patient Care Committee
March 2018

PARENTERAL NUTRITION IN NEWBORNS

Summary: **Parenteral nutrition soon after birth should be used for preterm infants <32 weeks and/or <1500 g; infants at high risk of necrotising enterocolitis; and those infants with illness in whom establishment of enteral feeding is thought to be delayed by 3-5 days.**

National Standard: Standard 1: Governance for Safety and Quality in Health Service Organisations

Standard 9: Recognising and Responding to Clinical Deterioration in Acute Health Care

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Observation chart

Compliance with the Guideline is recommended

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1. Introduction

- Parenteral nutrition (PN) is an essential component in the management of many newborn infants, admitted to Newborn Intensive Care Units (NICUs).
- All New South Wales (NSW) NICUs and subsequently other Australian NICUs formed a PN Consensus Group in 2010. Formulations were standardised in July 2011 with further amendments in 2012 and 2013. The consensus group recommendations and the improved nutritional outcomes following the implementation of consensus formulations were published in 2014.[1,2] Although nutritional intakes improved significantly, amino acid targets were not achieved in extremely preterm infants.
- In February 2015, the group reconvened in Sydney, now comprising 49 tertiary and non-tertiary NICUs from Australia, New Zealand, Malaysia, Singapore and India who participated in the consensus meeting in-person or via video link. A survey was conducted to explore the clinical PN practice in each NICU.[3] Outcomes of 2010 consensus formulations were presented, gaps in knowledge identified, topics for updating the formulations prioritised with tasks distributed to participants.
- In September 2017, delegates reconvened, evidence was reviewed and guidelines and formulations were updated. Physicochemical compatibility and stability of updated formulations were checked and confirmed compliant by Compounding pharmaceutical facility (Baxter Pharmaceuticals Pty Ltd). New formulations are due to release in March 2018.
- Updated PN guidelines are based on the majority consensus of the PN consensus group. They are written balancing the potential benefits of PN against associated risks. These practice guidelines do not account for every variation in the clinical circumstance, particularly very sick and unstable. The professional judgement of the health professional in these individual cases must take precedence.

The risks addressed by this policy:

Postnatal growth failure is common in infants born premature and in sick infants.

The aims / expected outcome of this policy

Parenteral nutrition is associated with important risks and benefits and clinical judgement is required to balance these competing outcomes. Optimal parenteral nutrition practices will reduce postnatal growth failure whilst minimising the risks of excessive nutrients intakes and electrolyte abnormalities, and optimising vitamin, trace element and mineral intake.

2. Guideline Statement

Parenteral nutrition soon after birth should be used for:

- preterm infants <32 weeks and/or <1500 g;
- infants at high risk of necrotising enterocolitis; and
- Those infants with illness in whom establishment of enteral feeding is thought to be delayed by 3-5 days.

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3. Principles/Guidelines

3.1 Summary

3.1.1 INDICATIONS

1. PN is associated with important risks and benefits and clinical judgement is required when making a risk benefit assessment.[4]
2. No study has defined definitive gestation or birthweight criteria for initiating PN. Common indications are extreme prematurity (<28 weeks or <1000 g) or birthweight <1500 g as well as infants with gastrointestinal disease and other conditions associated with delayed establishment or cessation of enteral feeds.
3. The survey of Australian and New Zealand NICUs in 2015 demonstrated that 100% of extremely preterm infants weighing <1000 g and 90% of very preterm infants 1000-1500 g are commenced on PN from day 1 of life, and 75% of NICUs administer PN to any infant who fails to establish enteral feeds by day 3-5 of life.[3]

Consensus recommendation for commencement of PN soon after birth include:

(i) Gestational age <32 weeks and/or birthweight <1500 g – PN should be commenced within the first 12 hours of life, and

(ii) high risk of NEC (e.g. absent or reversed foetal umbilical artery flow, perinatal asphyxia) or diagnosis of illness for which establishment of enteral feeding is thought to be delayed for 3-5 days.

3.1.2 ENERGY

- American Academy of Pediatrics (AAP) Committee on Nutrition 2014 recommends a parenteral caloric intake of 90-115 kcal/kg/day in preterm infants. ESPGHAN 2005 recommends parenteral intakes of 90-110 kcal/kg/day for extreme low birth weight infants. Other recommended preterm parenteral caloric intake varies from 89 to 120 kcal/kg/day.[5-7] Minimal energy requirements are met with 50–60 kcal/kg/day, but intakes of 100–120 kcal/kg/day facilitates maximal protein accretion.[8] Glucose and amino acid are estimated to provide 4 kcal/g and lipid emulsion 10 kcal/g.[10,11]
- A newborn infant receiving PN needs fewer calories (90–100 kcal/kg/day) than a newborn fed enterally because there is no faecal energy loss and less thermogenesis.[12] Trials of early and/or higher energy intake (commencing PN up to 60 kcal/kg/day and increasing up to 90-108 kcal/kg/day) report associated positive nitrogen balance, glucose and biochemical tolerance, and growth.[13-15]
- The 2017 updated starter PN solution infused at 60 ml/kg/day (33 kcal/kg/day) and new starter concentrated PN solution at 40 ml/kg/day and lipid emulsion at 1 g/kg/day (10 kcal/kg/day) provides approximately 43 kcal/kg/day. The standardised preterm PN solution infused at 135 ml/kg/day (70.2 kcal/kg/day) and new concentrated preterm PN at 100 ml/kg/day and lipid emulsion at 3 g/kg/day (30 kcal/kg/day) provides approximately 100 kcal/kg/day (LOE I, GOR B).

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3.1.3 FLUIDS

- Systematic review of five studies indicates that restricted fluid intake is significantly associated with postnatal weight loss and reduced risks of patent ductus arteriosus and necrotizing enterocolitis.[16] (LOE 1, GOR B) Restricted water intake was shown to also be associated with trending towards increased risk of dehydration and reduced risk of bronchopulmonary dysplasia, intracranial haemorrhage, and death, but these trends were not statistically significant.[16]

- The 2017 consensus agreement is similar to that in 2012: Standardised PN should be formulated to provide recommended Reasonable Nutrient Intakes (RNI) in a total fluid intake of 150 ml/kg/day. This includes 135 ml/kg/day of AA/Dextrose formulation and 15 ml/kg/day water in the 20% lipid emulsion. The 2012 agreement on starting fluid intake at 60 ml/kg/day with daily increase by 20-30 ml/kg/day to an average maximum of 150 ml/kg/day remains. Alternatively, for those units who opt for a total water intake below 150 ml/kg/day, or unwell babies with multiple non-protein intravenous infusions such as inotropes and opioid analgesics contributing to a significant proportion of fluid volume, the new concentrated PN solutions provide an adequate nutrient and mineral intake on a lower volume.

3.1.4 AMINO ACIDS

- There is no definitive evidence about what dose of parenteral amino acid is appropriate and when to initiate parenteral AA supplementation in neonates. Delay in administering amino acids could result in a protein catabolic state and could impact on growth and development in preterm neonates. However, potential benefits of improved nitrogen balance, growth and infant health may be outweighed by the infant's ability to utilise high intakes of parenteral amino acid, especially in the days after birth, resulting in high concentrations of amino acids, ammonia and urea, and an exacerbation of metabolic acidosis. Three systematic reviews evaluated the efficacy and safety of parenteral AA in preterm neonates.
- Trivedi et al reviewed the effect of early administration of amino acids within the first 24 hours of birth on growth, neurodevelopmental outcome in preterm newborns. They found no benefits of early administration of amino acids on mortality, early and late growth and neurodevelopment. Early administration of amino acids was associated with a positive nitrogen balance but the clinical relevance of this finding is not known. Acid-base status and ammonia levels were normal in infants who received amino acids early.[17]
- Leenders et al performed a systematic review to determine the effects of early parenteral amino acid supplementation (within 24 h of birth) versus later initiation and high dose (>3.0 g/kg/day) versus a lower dose on growth and morbidities. No differences were observed in growth or morbidity after early or high-dose amino-acid supplementation, but for several outcomes, meta-analysis was not possible due to study heterogeneity. Initiation of amino acids within the first 24 h of life appeared to be safe and well tolerated.[18]

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- In the latest Cochrane review, Osborn et al evaluated whether higher versus lower intake of parenteral AA is associated with improved growth and disability free survival in newborn infants. There were 21 studies that reported clinical outcomes in very preterm or low birth weight infants. Overall, higher AA intake had no effect on mortality prior to hospital discharge (typical RR 0.90, 95% CI 0.69 to 1.17; participants =1407; studies = 14; I^2 = 0%; GRADE quality of evidence low). There was insufficient evidence to determine an effect on neurodevelopment with no reported benefit found [quality of evidence: very low]. Similarly, they did not notice any beneficial impact on mortality or neurodevelopmental outcome in the subgroup analyses including high amino acid (>2 g/kg/day) at commencement, high amino acid at maximal infusion rate (>3 to <4 g/kg/day) and high amino acid intake within 24 hours of birth. Higher AA intake was associated with a reduction in postnatal growth failure (< 10th centile) at discharge (typical RR 0.74, 95% CI 0.56 to 0.97; participants = 203; studies = 3; I^2 = 22%; typical RD -0.15, 95% CI -0.27 to -0.02; NNTB 7, 95% CI 4 to 50; quality of evidence: very low). Reduced postnatal growth failure was found in subgroup analyses of studies that commenced on high amino acid intake (> 2 to ≤ 3 g/kg/day); that increased amino acid and non-protein caloric intake; commenced intake < 24 hours age; and provided an early lipid infusion. Higher AA intake was associated with a reduction in days to regain birth weight (MD -1.14, 95% CI -1.73 to -0.56; participants = 950; studies = 13; I^2 = 77%). There were varying effects on growth parameters and no consistent effects on anthropometric z-scores at any time point. Increased growth in head circumference at discharge was found (MD 0.09 cm/week, 95% CI 0.06 to 0.13; participants = 315; studies = 4; I^2 = 90%; quality of evidence: very low). Higher AA intake was not associated with an effect on days to full enteral feeds, late onset sepsis, necrotising enterocolitis, chronic lung disease, any or severe intraventricular haemorrhage or periventricular leukomalacia. There was a reduction in retinopathy of prematurity (typical RR 0.44, 95% CI 0.21 to 0.93; participants = 269; studies = 4; I^2 = 31%; quality of evidence: very low), but no difference in severe retinopathy of prematurity. Higher AA intake was associated with an increase in positive protein balance and nitrogen balance. Potential biochemical intolerances were reported including risk of abnormal blood urea nitrogen levels (typical RR 2.77, 95% CI 2.13 to 3.61; participants = 688; studies = 7; I^2 = 6%; typical RD 0.26, 95% CI 0.20 to 0.32; NNTH 4; 95% CI 3 to 5: quality of evidence: high). Higher amino acid intake in parenteral nutrition was associated with a reduction in hyperglycaemia (> 8.3 mmol/L) (typical RR 0.69, 95% CI 0.49 to 0.96; participants = 505; studies = 5; I^2 = 68%) although the incidence of hyperglycaemia treated with insulin was not different.[19]
- The Consensus Group agreed to (1) commence parenteral AA within the first 24 hours of birth (LOE I, GOR C), (2) commence parenteral AA at 2 g/kg/day (LOE I, GOR C) and (3) incrementally increase amino acid infusions to a maximum 4 g/kg/day by day 3-5 of life in preterm neonates (LOE I, GOR C). The Consensus Group considered the safety of (1) commencement parenteral AA in excess of 3 to 3.5 g/kg/day and (2) maintenance AA intake in excess of 4.5 g/kg/day has not been proven in clinical trials.

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3.1.5 CARBOHYDRATES

- Carbohydrate is recommended to provide 40-60% of total energy so is the largest source of non-protein energy.[20] ESPGHAN 2005 recommended glucose commencement infusion rates of 4- 8mg/kg/min in preterm neonates, cautioning against exceeding the maximum rate of glucose oxidation and potentiating hyperglycaemia.[20] Maximal glucose oxidation in preterm and term infants is reported to be 8.3 mg/kg per min (12 g/kg per day)[21,22] and 13 mg/kg per min (18 g/kg per day) respectively.[23,24] Elevated neonatal blood glucose concentration has been linked to adverse outcomes including death,[25,26] intraventricular haemorrhage,[25] late onset bacterial sepsis,[27] fungal infection,[28,29] retinopathy of prematurity[30-32] and necrotizing enterocolitis.[27] Attempts to maintain glucose intake using insulin have yielded variable results.[33-34] A systematic review for prevention of hyperglycaemia located two small trials which compared lower versus higher glucose infusion rates.[34] These trials provided some evidence that a lower glucose infusion rate reduced both mean blood glucose concentrations and the risk of hyperglycaemia, but the trials were insufficiently powered to test for significant effects on death or major morbidities.[15,35] The trials had glucose infusion rates up to 8.4 mg/kg/min in the first 7 days in the highest infusion group. In contrast, the multicentre trial of insulin infusion reported that although insulin infusion reduced mean glucose concentrations and reduced hyperglycaemia, but it also resulted in an increase in the risk of death before 28 days and an increase in the proportion of neonates with a hypoglycaemic episode.[36] Glucose infusion rates were higher in the insulin group (median 9.3 mg/kg/min) compared to the standard care group (median 7.6 mg/kg/min). The review concluded that the evidence did not support the routine use of insulin infusions to prevent hyperglycaemia in VLBW neonates. A second systematic review found two trials comparing the use of insulin infusion for treatment of hyperglycaemia in preterm infants receiving intravenous glucose and total parenteral nutrition.[33] Collins et al reported that infants treated with insulin infusion received and tolerated significantly higher glucose infusion rates (20.1 ± 2.5 mg/kg/min) than control infants who did not receive insulin therapy (13.2 ± 3.2 mg/kg/min) and they also demonstrated significant increases in non-protein energy intake and short-term weight gain.[37] Meetze 1998 reported glucose infusion rate averaged approximately 10.0 mg/kg/min in the insulin infusion group and approximately 7.6 mg/kg/min in the glucose reduction group, and significant increase in total energy intake.[38] Neither reported a significant difference in neonatal mortality or morbidity.
- Proposed standard preterm and term PN formulations contain 10% and 12% dextrose respectively, providing 13.5 g/kg/day (9.4 mg/kg/min) and 17 g/kg/day (11.8 mg/kg/min) at 135 ml/kg/day respectively (LOE 1, GOR C).

3.1.6 LIPIDS

- Administration of lipid in premature infants requiring PN provides essential fatty acids and is energy dense increasing caloric intake within a low fluid volume.[6] Two systematic reviews found that although no side effects were reported there was no statistically significant benefit of introducing lipids before two to five days of age, including no measured beneficial effects on growth.[39-40] However, composition of growth was not assessed in these studies, and it is therefore uncertain if increased energy intake derived from early lipid infusion is protective against induced protein catabolism in the preterm neonate. Further, essential fatty acid deficiency occurs rapidly and can be prevented with introduction of as little as 0.5 to 1 g/kg/day of lipid infusion.[39] The Consensus group agreed to commencement of parenteral lipid on day 1 of PN administration, particularly for extremely preterm neonates (LOE 1, GOR C).
- There are variations in terms of starting dose of lipid emulsions, however starting dose 1 g/kg/day was safely tolerated in most clinical trials. The consensus agreed to commence lipids at the dose of 1 g/kg/day. There is no evidence that gradual increments in the infusion rate of lipids improve fat tolerance. If lipid infusion is increased in increments of 0.5 to 1.0 g/kg/day, it may be possible to monitor for hypertriglyceridemia.[6]

Compliance with the Guideline is recommended

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- Several types of intravenous lipid emulsions (IVLE) are available for neonatal use including 100% soybean oil based IVLEs (e.g. Intralipid 20%, Ivelip 20%); mixed 80% olive oil/20% soybean oil IVLE (e.g. Clinoleic 20%); mixed 30% soybean oil/25% olive oil/30% medium-chain triglyceride oil/15% fish oil IVLE (e.g. SMOFlipid); and 100% fish oil based IVLE (e.g. Omegaven). The IVLEs are largely well tolerated. No reproducible clinical benefits have been reported for any specific IVLE in newborn infants.[41-60] Although reduced peroxide formation,[52-53] lower retinopathy of prematurity (early stage 1 or 2)[57] and some biochemical difference in infants have been reported,[50,54-56] recent systematic reviews showed no statistically significant differences in clinically important outcomes including mortality, growth, chronic lung disease, sepsis, severe ROP ≥ stage 3, and cholestasis by using any specific preparation in newborns.[58-60] (LOE 1, GOR C). The 2015 Survey revealed 67% of units in ANZ use both SMOFlipid and clinoleic. All units use water and fat soluble vitamins added to lipid emulsion. The consensus 2017 proposed both SMOFlipid and Clinoleic as suitable lipid preparations and anticipate individual units will take cost and waste minimisation into consideration when choosing the specific type of lipid preparation most suited to their needs.
- All lipid emulsions with added fat and water soluble vitamin discussed above are formulated to provide 1 g of lipid in 6 mL of lipid emulsion with vitamins. Thus, 1 g lipid/kg/d equates to 6 mL lipid emulsion with vitamins/kg/d, which equates to an energy intake of 10 kcal/kg/day. Similarly, 2 g lipid/kg/day equates to 12 ml lipid emulsion with vitamins/kg/day and 3 g lipid/kg/day equates to 18 ml lipid emulsion with vitamins/kg/day. Majority consensus was to commence lipids at 1 g/kg/day and increase by 1 g/kg (6 mL/kg) each day to 3 g/kg/day (18 mL/kg/day). The lipid emulsions contain 80% water (6 mL lipid emulsion with vitamins contains 5 mL water; 12 mL lipid emulsion with vitamins contains 10 mL water; 18 mL lipid emulsion with vitamins contains 15 mL water). In view of benefits associated with restricted fluid intake,[16] the group proposed to include the water content of lipid infusions in the total fluid intake, which equates to 15 ml/kg/d of water when the lipid intake reaches 3 g/kg/day (LOE I, GOR B). [**see appendix 3**]:

SMOFLipid formulations:

Contents	45 mL syringe For ≤1 Kg	145 mL bag For > 1Kg
SMOFlipid	32.5 mL	100 mL
Soluvit N	2.5 mL	8.4 mL
Vitalipid N Infant	10 mL	36.6 mL

ClinOleic formulations:

Contents	45 mL syringe For ≤1 kg	90 mL Bag For >1 to ≤2 Kg	150 mL bag For >2 kg
ClinOleic	32.5 mL	65 mL	108 mL
Soluvit N	2.5 mL	5 mL	8.4 mL
Vitalipid N Infant	10 mL	20 mL	33.6 mL

- Above formulations have been designed in such a way that volumes of preparations per each gram of lipid is the same for all the formulations:
  - 1 g/kg/day equates to 6 ml/kg/day
  - 2 g/kg/day equates to 12 ml/kg/day
  - 3 g/kg/day equates to 18 ml/kg/day
- Majority consensus was to commence lipids at 1 g/kg/day and increase by 1 g each day to 3 g/kg/day.

Compliance with the Guideline is recommended

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- Suggested plasma triglyceride monitoring: Check plasma triglycerides before each step of increase to 3 g/kg/day and then 24 later and then whenever the infant is sick as long as the infant is on lipid emulsions.
- If triglyceride levels >2.8mmol/L, consider reducing the lipid emulsions by 1 g/kg/day increments but continue at least 0.5g/kg/day to prevent essential fatty acid deficiency.[6]

Lipid Emulsions and water content:

The above lipid emulsions contain 80% water. This means:

1. 1 g/kg/day - 6 ml/kg/day – 5 ml is water.
2. 2 g/kg/day - 12 ml/kg/day – 10 ml is water.
3. 3 g/kg/day – 18 ml/kg/day – 15 ml is water.

In view of benefits with restricted fluid intake,[8] the group proposed to include lipids in the total fluid intake. (LOE I, GOR B).

3.1.7 SODIUM, POTASSIUM AND CHLORIDE

- Water and sodium balances change over time after birth. Initially after birth, the extracellular fluid space contracts in association with a net negative sodium and water balance with accompanying weight loss. Excess water loss is associated with early hypernatraemia. On the other hand, early hyponatraemia within the first 48 hours of life likely represents maternal sodium status and/or with too much water administration. In addition, higher renal fractional excretion of sodium in extreme preterm infants may ameliorate the tendency to hypernatraemia and may lead to hyponatremia late in the first week of life.
- The timing of the introduction of sodium supplementation in neonates is controversial. Traditional guidelines suggest addition of sodium only after the onset of postnatal diuresis from the second or third day after birth. However salt wasting due to renal immaturity is common in extremely preterm infants and inadequate sodium intakes have been attributed to postnatal growth failure. It is unclear whether early fluid therapy should contain some sodium to facilitate extracellular volume reduction or large amounts of sodium to compensate for renal sodium losses. Higher early sodium intake may be associated with early hypernatraemia and increased oxygen requirements to 28 days.[61-64] There is insufficient evidence to determine an effect on other neonatal outcomes and mortality.[54-5] Subsequent higher sodium intake may reduce the incidence of hyponatraemia.[61-63,65]
- Al-Dahhan et al 1984, in a RCT supplemented 4-5 mmol/kg/day of sodium either parenterally or orally from day 4-14 of life to preterm infants 27-34 weeks and showed significantly less weight loss and increased weight gain that lasted beyond the supplementation period without any adverse clinical adverse outcomes including PDA, NEC and IVH.[66] At 10-13 years of age neurodevelopmental follow-up assessment, children in the sodium supplemented group performed better in all modalities tested than those from the unsupplemented group. The differences were statistically significant for motor function, performance IQ, the general memory index, and behaviour.[67]
- Shaffer et al 1989 randomised 20 VLBW infants to receive IV or oral sodium in doses of either 1 or 3 mmol/kg/day for the first 10 postnatal days. Serum sodium increased in both groups in the first 3 days. After day 5, serum sodium was stable in the group receiving 3 mmol/kg/day but decreased in the group receiving 1 mmol/kg/day and remained lower when measured on days 20 and 30. Five and 2 infants in the higher and lower Na supplementation groups respectively, developed hypernatraemia though this was thought to be due to loss of free water.[63]

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- A RCT conducted by Costarino et al evaluated two regimens of sodium intake in 17 VLBW infants. In the restricted group, there was no sodium supplementation in the first 5 days of life. In the maintenance group, 3-4 mmol/kg/day of sodium was supplemented for 4 days from day 2. The restricted group had a more negative sodium balance, lower serum sodium concentration, and lower incidence of hypernatraemia and hyperosmolality. The incidence of CLD was also significantly less. There were no differences in the incidence of PDA, IVH or survival.[61] Hartnoll et al, conducted a RCT comparing early (from day 2 of life) against delayed (only after 6% of loss of birthweight) sodium supplementation (4 mmol/kg/day) in infants 25-30 weeks gestational age. By the end of the first week, there were significantly fewer infants in the delayed group requiring oxygen, and a trend toward less incidence of CLD at 28 days and 36 weeks corrected age.[62] A Cochrane review assessing the benefits and harms of higher versus lower sodium intakes in preterm infants is currently underway.[68]
- The 2017 consensus reaffirmed the consensus reached in 2013, agreeing to minimal sodium intake of approximately 1 mmol/kg/d on day 1 using a starter PN formulation. Sodium in starter formulation is a component of organic phosphate (sodium glycerophosphate which contains 2 mmol Na per mmol of phosphate) and can only be altered by replacing with other sodium free nutrients. The currently designed starter and standard formulations will increase sodium from 1 mmol/kg/day on day 1 (starter formulation) to a maximum 4.6 mmol/kg/d in preterm infants and 3.4 mmol/kg/day in term infants at 135 ml/kg/day (standard formulations) (LOE II, GOR C). The new starter concentrated PN solutions will gradually increase sodium from 1.2 mmol/kg/day on day 1 in the starter concentrated PN to a maximum 5.0 mmol/kg/day in the concentrated preterm PN in extremely preterm infants.
- Hyperkalaemia is a common complication in the first 48 hours of life in extremely low birth weight and/or extremely preterm infants, but is not affected by early and high administration of protein.[69,70] After 3 days, balance studies reported a potassium intake of 2-3 mmol/L/day resulted in a net retention of 1-2 mmol/day.[71-72] The consensus group agreed on minimal potassium intake using starter PN formulation, with an increase in standard formulations to a maximum 3.0 mmol/kg/d in preterm and 2.7 mmol/kg/day in term infants (LOE III-2, GOR C). These intakes are within the recommended intakes of AAP and ESPGHAN recommendations.[5-6]
- Hyperchloraemia (>115 mmol/L) is common in VLBW infants on PN and is associated with acidosis.73-74 Trial evidence found the incidence of hyperchloraemia and acidosis is reduced by partly replacing chloride with acetate in parenteral nutrition.[73] Supplementation of acetate beyond this level was associated with hypercarbia [73] (LOE II, GOR C). The 2013 consensus was to adopt the trial recommendation such that the first 3 mmol/kg/day of anion is provided as chloride, next 6 mmol/kg/day of anion is provided as acetate and thereafter as chloride again. However, there have been concerns about hypercarbia in some infants using 2013 formulations. Moreover, 2017 consensus formulations contain organic phosphate resulting in an increase of pH of the formulations. Therefore, the 2017 consensus is to reduce the acetate content to a maximum of 3.5 mmol/kg/day in the updated standard formulations.

3.1.8 CALCIUM, PHOSPHORUS AND MAGNESIUM

- One mmol of calcium (Ca) equates to 40 mg calcium and 1 mmol of phosphorus equates to 31 mg phosphorus (P).75 A 1:1 Ca:P molar ratio is equal to 1.3: 1 weight (mg) ratio. Transplacental Ca and P delivery to the fetus occurs actively against a concentration gradient and is greatest after the 24th gestational week. Generally, it is estimated that 80% of mineral accretion occurs in the 3rd trimester of pregnancy.[76] The average accretion rates during the last 3 months of pregnancy are 3 mmol/kg/day of Ca and 1.9 mmol/kg/day of P.[77] From 27 weeks gestation, based on estimated fetal weight gain of approximately 30 g per day, the fetus requires about 310 mg/day of Ca and 170 mg/day of P.[78-79]

Compliance with the Guideline is recommended

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- ELBW infants, particularly those born <27 weeks gestation are at increased risk of developing metabolic bone disease due to the missed period of greatest mineral accretion in the 3rd trimester as well as delayed establishment of enteral feeding. Lower mineral (Ca and P) intake results in hyperparathyroidism resulting in osteopenia, maintenance or increase of serum calcium and hypophosphataemia and hyperphosphaturia. Total body calcium deficiency and hypophosphataemia leads to osteopenia of prematurity. In addition, studies have reported an increased risk of late onset sepsis associated with hypophosphataemia due to phagocytic dysfunction.[82-84]
- There is a wide range in the recommended doses of Ca and P delivered by PN in preterm infants. American Academy of Pediatrics 2014 recommends 1.5-2.0 mmol/kg/day of Ca and 1.5-1.9 mmol/kg/day of phosphorus whereas ESPGHAN 2005 recommends 1.3-3 mmol Ca/kg/day and 1.0-2.3 mmol P/kg/day, with optimal Ca:P ratio between 1.3-1.7.[6, 87] However, these numbers are based on in-utero accretion rates. While a number of clinical studies evaluated the efficacy and safety of various parenteral intakes of Ca and P in preterm infants, none of them tested the ESPGHAN recommended maximum intake levels of 3 mmol/kg/day of Ca and 2.3 mmol/kg/day of P in preterm neonates.[88-92] The one exception is the RCT by Prestridge et al, where inorganic phosphate was used for an estimated maximum P intake 2.6 mmol/kg/day with a maximal Ca intake 2 mmol/kg/day.[86]
- Until recently, only inorganic phosphate has been registered by Therapeutics Goods Administration Australia and higher intakes of calcium and phosphate intravenously were not possible while maintaining compatibility to prevent calcium-phosphate precipitation.[85-86] Recently, organic phosphate in the form of sodium glycerophosphate has been registered. Substitution of inorganic phosphate by organic phosphate improves physicochemical compatibility with trial evidence reported increased mineral intake and mineral retention.[93]
- Consensus 2017: Due to paucity of studies on the safety of maximum parenteral RDIs for Ca and P and the availability of organic phosphate with improved physicochemical stability, the group increased the parenteral Ca and P intakes to a maximum of 2.3 mmol/kg/day and 1.8 mmol/kg/day respectively. Furthermore, there is additional 0.19 mmol/kg/day phosphorus from ClinOleic or SMOFLipid at 3 g/kg/day.
- Balance studies indicate that a magnesium (Mg) intake of 0.375 mmol/kg/day may result in elevated serum magnesium levels without clinical evidence of hypomagnesaemia.[94-95] A minimum Mg intake of 0.2 mmol/kg/day and maximum 0.3 mmol/kg/day is considered appropriate for LBW infants. (LOE 111-3, GOR C).

3.1.9 VITAMINS

• There is no optimal neonatal vitamin formulation available. Water and fat soluble vitamins (Soluvit N® and Vitalipid N Infant® 10%) are added to the lipid emulsion to increase the vitamin stability.[96] Appendix 4 shows the quantity of vitamins supplied to infants through the proposed lipid emulsion when infused at 3 g/kg/day. The doses of vitamin K, pyridoxine, riboflavin and vitamin B12 are slightly above recommended parenteral doses, and ascorbate below.[5,6] Loss of vitamins and formation of peroxides from exposure to light is substantially reduced by adding the preparation to the lipid infusate, covering the tubing and by use of amber/dark syringes and tubing.[97-99] (LOE II, GOR B).

Optimal doses and conditions of infusion for vitamins in infants and children have not been established.[6] The doses of many vitamins (eg Thiamine, Riboflavin, Folate, Vitamin B12, Pyridoxine, and Vitamin C) are largely determined by studies determining vitamin levels during intravenous supply undertaken with commercially available mixtures.[6,100-102]

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Vitamin A: Systematic review found that supplementation of very low birthweight infants with vitamin A is associated with reduction in death or oxygen use at one month of age and oxygen use at 36 weeks' postmenstrual age, but this needs to be balanced against the lack of other proven benefits and the acceptability of treatment.[103] Current dosing recommendations for parenteral vitamin A supplementation for premature infants are based on clinical studies measuring vitamin levels during supplementation.[6] (LOE I GOR C).

Vitamin C: A single randomised trial reported no significant benefits or harmful effects were associated with treatment allocation to higher or lower ascorbic acid supplementation throughout the first 28 days.[104] The lower group received 10 mg parenterally provided in Soluvit and Vitalipid (LOE II, GOR C).

Vitamin D: The consensus formulation delivers vitamin D 160 IU/kg/day, above the minimal required vitamin D intake reported to maintain 25(OH) vitamin D levels [88] and consistent with studies reporting stable vitamin D status in preterm infants on PN.[105] (LOE III-3, GOR C).

Vitamin E: Systematic review found Vitamin E supplementation in preterm infants reduced the risk of intracranial hemorrhage but increased the risk of sepsis. It concluded evidence does not support the routine use of vitamin E supplementation by intravenous route at high doses or aiming at serum tocopherol levels greater than 3.5 mg/dL, supporting the current recommendation for parenteral intake of vitamin E.[106] (LOE I, GOR B).

Vitamin K: Preterm infants who received intramuscular Vitamin K 0.5-1 mg at birth, followed by parenteral intake (60 µg/day for infants <1000 g and 130 µg/day for infants 1000 to 3000g) had much higher vitamin K plasma concentrations at 2 and 6 weeks of age than previously reported in healthy, term, formula-fed infants (4–6 ng/mL).[107] The only formulation available in Australia delivers in excess of current recommendation and is associated with high vitamin K plasma concentrations.[6] (LOE 111-3, GOR C).

3.1.10 TRACE ELEMENTS

Chromium, copper, iodine, manganese, molybdenum, selenium and zinc are essential micronutrients involved in many metabolic processes. **Appendix 4** shows the parenteral RDIs of trace elements (EPSGHAN 2005)[6] and the comparison to the consensus group formulations. Nutritional deficiency in low birth weight infants or preterm infants on PN has been mostly reported for zinc and copper.[108] The risk is substantially increased in surgical infants with increased gastrointestinal losses. There are no reports of clinical manganese deficiency in newborns on PN.[108] Copper and manganese may need to be withheld if the neonate develops PN-associated liver disease. Copper has the potential for hepatotoxicity and biliary excretion is important for manganese which is potentially neurotoxic.[108] Low blood selenium concentrations in preterm infants have been reported as a potential risk factor for chronic neonatal lung disease and retinopathy of prematurity.[109] Iodine deficiency and excess have been reported in preterm infants, with iodine excess associated with transient hypothyroidism.[110-112] There have been few reports of chromium deficiency in humans.[108] PN solutions may be contaminated with chromium, causing serum concentrations to be significantly higher (10%-100%) than recommended.[113] There is a concern excess chromium intake may be associated with renal impairment in preterm infants.[114]

Zinc: Zinc doses are derived from clinical trials reporting zinc levels and zinc balance in preterm and term infants.[115-117] Clinical benefits from different parenteral intake have not been reported in trials. Parenteral zinc is recommended at a dose of 450–500 µg/kg/day for premature infants and 250 µg/kg/day for infants less than 3 months.[6] Zinc is recommended to be added to solutions of patients on short-term PN from commencement.[6,108] (LOE II. GOR C).

Compliance with the Guideline is recommended

PARENTERAL NUTRITION IN NEWBORNS cont'd

Copper: Copper doses are derived from clinical trials reporting copper levels and copper balance in preterm and term infants.[115-117] Clinical benefits from different parenteral intake have not been reported in trials. Parenteral copper intake is recommended at a dose of 20 µg/kg/day,[6] and commenced 2 to 4 weeks after PN commencement.108 Copper should be carefully monitored in patients with cholestatic liver disease.[6,108] (LOE II, GOR C).

Selenium: Systematic review found supplementing very preterm infants with selenium is associated with a reduction in episodes of sepsis, but was not associated with improved survival, a reduction in neonatal chronic lung disease or retinopathy of prematurity. Doses of 3 µg/kg/day may prevent a decline in cord levels and doses up to 7 µg may be required to achieve concentrations above those in cords and close to concentrations found in healthy breast fed infants.109 Selenium supply of 2 to 3 µg/kg/day is currently recommended for parenterally fed LBW infants.[6] (LOE I, GOR C).

Iodine: The recommended parenteral intake is currently 1 µg/kg/day.[6] (LOE III-3, GOR D). Observational data suggest preterm infants receiving PN containing a mean iodine intake of 3 µg/kg/day are in negative iodine balance.[111] However, the relationship to transient thyroid dysfunction in preterm infants is unclear. Enterally fed infants are recommended to receive iodine 11–55 µg/kg/day,[118] although a small trial reported no evidence of an effect of higher enteral iodine intake on thyroid hormone levels in very preterm infants.[119] Iodine intake needs to be appraised in the context of iodine status and iodine exposures of pregnant women and their infants. The recommended parenteral intake is currently

Manganese: A randomised trial comparing PN intake of 1 µmol/kg/day versus 0.0182 µmol/kg/day reported no significant difference between peak manganese levels between groups.[120] However, peak levels in both groups were above normal ranges and there was no significant difference between groups in incidence of cholestasis or morbidity and mortality. Subgroup analysis raised the concern that infants on the higher dose for >14 days had an increased rate of cholestasis. Supplementation should be stopped in infants with cholestasis.[108] In infants receiving long-term PN, a low dose supply of no more than 1 µg/kg/day (0.0182 µmol/kg/day) is recommended.[6] (LOE II, GOR C).

Molybdenum: Deficiency has not been reported in newborns. Observational data led to the speculation that an intravenous intake of 1 µg/kg/day would be adequate for the LBW infant.[121] Intravenous molybdenum supply of 1 µg/kg/day (0.01 µmol/kg/day) is recommended for the LBW infant.[6] (LOE III-3. GOR D).

There are 2 commercial trace element formulas available in Australia and neither of them has the optimal mixture of trace elements for neonatal use. AUSPEN Neonatal Trace elements (Baxter Healthcare Pty Ltd) contains more copper and manganese but less zinc. Peditrace (Fresenius-Kabi Pty Ltd) contains fluorine.

The 2012 Consensus was to add zinc, selenium and iodine as individual trace elements to all AA/Dextrose formulations, with the exception of the starter formulation to which trace elements could not be added due to physicochemical compatibility concerns. The 2018 formulations contain organic phosphate allowing addition of trace elements in all formulations including the starter formulation without any physicochemical instability. For those infants, who are on exclusive PN for more than 2-4 weeks with minimal enteral intake, other trace elements, copper can be added to the formulations.

PARENTERAL NUTRITION IN NEWBORNS cont'd

3.1.11 HEPARIN

Systematic review of prophylactic use of heparin for peripherally placed percutaneous central venous catheters found a reduced risk of catheter occlusion with no statistically significant difference in the duration of catheter patency, risk of thrombosis, catheter related sepsis or extension of intraventricular haemorrhage.[122] Heparin was added at 0.5 to 1 IU/ml to parenteral nutrition solution with no adverse effect reported. Our previous and current consensus is to add heparin 0.5 IU/ml to AA/Dextrose formulations (LOE I, GOR C) and remains the same.

3.1.12 PHYSICOCHEMICAL STABILITY

Physicochemical stability of the latest formulations have been tested by Baxter Pharmaceuticals and confirmed to be stable for up to 61 days at 2-8^{0}C and 5 days at below 25^{0}C.

3.1.13 HANGING TIME

AA/Dextrose solution: In a randomised trial enrolling 166 infants, there was no significant difference in bacterial or fungal colonisation of infusate or neonatal sepsis in infants receiving 24 or 48 hour infusions of parenteral nutrition solution.[123] A before-after intervention study reported extending PN solution hang time from 24 to 48 hours did not alter central line associated blood stream infection rate and was associated with a reduced PN-related cost and perceived nursing workload.[124]

Lipid infusion: In the previously mentioned randomised trial, fungal contamination may be increased in infants receiving lipid infusion for 24 hours compared to 48 hours.[123] In another trial randomising PN set changes (rather than infants), microbial contamination of infusion sets was significantly more frequent with 72-hour than with 24-hour set changes in neonates receiving lipid solutions.[125]

The majority consensus 2017 recommended a hanging time of 48 hours for PN solution and 24-48 hours for lipid (LOE II, GOR C).

3.1.14 ROUTE OF PN ADMINISTRATION

Umbilical catheters: In neonates, umbilical vessels can be used for PN.[6] Umbilical venous catheters compared to peripheral venous catheter reduces insertion attempts with no increase in risk of infection or necrotising enterocolitis.[126] The risk of complication may increase if umbilical venous catheters are being left in place for more than 14 days.[127-128]

Central cannula: Peripherally inserted central catheters (PICC's) should be used preferentially to provide central venous access in neonates receiving prolonged PN as PICC use results in improved nutrient intake and fewer insertion attempts.[6,129]

Peripheral cannula: As phlebitis of peripheral veins were reported when the osmolality of the intravenous solution exceeded 600 mOsm,[130] peripheral veins have been recommended for short term venous access.[6,130] The group has developed a peripheral preterm PN solution (see below) with reduced mineral content that can be used to run through the peripheral cannula for short periods of time, although there is limited evidence for the role of minerals in the development of tissue injury. Although extravasation injury occurs in up to 10% of infants managed only with peripheral infusion of PN,[129] it is unclear if the risk of peripheral TPN is greater than the risk of peripheral crystalloid infusion.

PARENTERAL NUTRITION IN NEWBORNS cont'd

Osmolality: American Society of Parenteral and Enteral Nutrition (ASPEN) recommends the osmolarity of peripheral parenteral nutrition solutions be limited to 900 mOsm/L to lower the risk of phlebitis due to infiltration based on a study that evaluated the feasibility of infusing a 900-mOsm/L solution through peripheral veins in 15 adult participants.[131] A prospective study reported that administration of PN with an osmolarity ≤1000 mOsm/L resulted in an 8% (15 of 181) incidence of extravasation/phlebitis, whereas peripheral administration of PN with osmolarity >1000 mOsm/L resulted in a 30% (40 of 134) incidence of extravasation/phlebitis, suggesting that peripheral administration of PN in neonates should be limited to 1000 mOsm/L.[132] Another retrospective, matched-cohort study that included 151 neonates found that administration of PN with osmolarity >1000 mOsm/L vs ≤1000 mOsm/L significantly increased infiltration (17% vs 7%; odds ratio [OR, 2.47]; 95% confidence interval [CI], 1.24–4.94; P = .01) and the combined composite end point of phlebitis or infiltration (45% vs 34%; OR, 1.65; 95% CI, 1.07–2.54; P = .02). In multivariate analysis, osmolarity >1000 mOsm/L vs ≤1000 mOsm/L was an independent risk factor for developing complications (OR, 1.67; 95% CI, 1.08–2.52; P = .02).[133]

Consensus 2017: PN solutions with osmolality below 1000 mosm/L can be administered peripherally for short term use provided that close monitoring of the IV site for any extravasation/phlebitis is followed. In view of the dearth of evidence, the consensus group agreed to continue the peripheral PN formulation in case of concerns regarding the amount of calcium infused through peripheral veins.

3.1.15 PN IN LATER PRETERM (34+0 TO 36+6 WEEKS) AND TERM NEONATES

There is paucity of data on the efficacy and safety of PN in this age group. Two small studies enrolled late preterm and term neonates, but neither reported on any major clinical outcomes. Hata 2002 et al randomised 30 neonatal surgical patients into three groups according to the dose of amino acids given: group H (n = 12, 3.45 +/- 0.07 g/kg per day), group M (n = 8, 2.59 +/- 0.07 g/kg per day), and group L (n = 10, 1.72 +/- 0.06 g/kg per day). All patients received the same amount of dextrose (average 21.5 g/kg per day) and no lipid was administered. The primary outcome was cholestasis. There were no significant differences in liver function tests including direct bilirubin, glutamic oxaloacetic transaminase, glutamic pyruvic transaminase, alkaline phosphatase, gamma-glutamyl transpeptidase, and total bile acids, among the three groups on the tenth day of TPN. No other clinical outcomes were reported.[134]

Makay 2007 et al enrolled newborns with a gestational age ≥ 35 weeks whose clinical condition precluded oral feeding for 3 days. The higher group, early parenteral nutrition group received 1.0 g/kg/day amino acids started within the first 8 hours and 1.0 g/kg/day lipid on day 2. In the lower group, the fluid regimen started with glucose 10% in the first day followed by glucose and electrolyte solution and added amino acids (0.5 g/kg/d) and lipid (0.5 g/kg/d) on day 3 and 4, respectively. In all infants, amino acids and lipid were each increased by 0.5 g/kg/day to a maximum of 3.0 g/kg/day in both groups. Primary outcome was serum bilirubin levels. Serum bilirubin level did not significantly differ between groups. There were no significant differences in the requirement, initiation time, and duration of phototherapy. A higher energy intake was achieved after the first day in early PN group.[135]

2017 Consensus: PN is widely used in Australian facilities in late preterm and term neonates who are not enterally fed. The consensus group followed the human milk approach to develop the PN formulations for this group and nutrient intake estimates are based on the average composition and intake of human milk.[136]

PARENTERAL NUTRITION IN NEWBORNS cont'd

3.1.15 CESSATION OF PN

Amino acid/Dextrose infusion: There is no clear evidence to guide the practice. The risk of late onset sepsis with intravenous access and the cost of PN are to be considered. The 2015 consensus survey revealed that majority of the NICUs in ANZ cease AA/Dextrose formulation once the infant tolerates 120-140 ml/kg/day of enteral feeds.
Lipids: Mature human milk contains 3.5 g of fat per 100 mL. 2015 consensus survey reported majority of NICUs cease IV lipids once the infant tolerates 100 -120 mL/kg/day of enteral feeds.

3.1.16 BIOCHEMICAL MONITORING ON PN

PN administration requires careful clinical and laboratory monitoring. High blood urea nitrogen, hyperglycaemia, metabolic acidosis, hypertriglyceridemia and conjugated hyperbilirubinemia are frequently encountered biochemical abnormalities on PN. In addition to routine observations, periodic measurements of the following biochemical parameters are suggested during PN therapy.

No data are available to determine the effect of higher versus lower amino acid and lipid intake in PN in 'sick' infants (e.g., infants with moderate-severe respiratory distress, receiving cardiovascular support, possible sepsis, acidosis); and 'surgical' or postoperative infants or infants post-cardiopulmonary bypass.

Blood Urea Nitrogen [Conversion blood urea nitrogen = blood urea divided by 2.14]: Six studies reported BUN levels.[19] The criteria for abnormal blood urea nitrogen differed between the studies and varied from >10 mmol/L to 21.4 mmol/L. There was a significant increase in abnormal blood urea nitrogen level from higher amino acid intake in all these studies although a threshold level was not clear. Given the data supporting the importance of early amino-acid administration in premature infants, limiting amino acid intake based on serum BUN alone is not warranted. BUN levels up to 14.3 mmol/L may be considered acceptable in VLBW infants on PN provided there are no other parameters to suggest protein intolerance (eg hyperammonaemia >122 µmol/L).[19]

Hyperglycaemia: It is not uncommon to see mild hyperglycaemia (>8.3 mmol/L).[137] If blood glucose >10 mmol/L (moderate hyperglycaemia),[33,34] further management to control hyperglycaemia needs to be considered including reducing the glucose infusion rate (e.g. changing over to 7.5% Dextrose PN) or insulin infusion. Hypoglycaemia (BGL < 2.6mmol/L)[138,139] can occur particularly with sudden cessation of PN or undetected extravasation of solutions.

Cholestasis: Defined as serum level of direct bilirubin > 20% of total serum bilirubin or serum level of direct bilirubin > 34 mmol/L [mg/dL x 17.10].[140]

Hypoalbuminemia: Defined as serum albumin, preterm < 18 g/L in preterm [141,142] and < 25 g/L in term neonates.[142]

Hypertriglyceridemia (HT) (Plasma triglyceride >2.8 mmol/L): ESPGHAN 2005 Guidelines recommend monitoring of triglycerides in preterm and term infants and suggest a triglyceride level of 2.8mmol/L as the upper limit.[6] 2015 Consensus survey revealed 62% of respondents monitor plasma triglyceride levels either routinely or in specific circumstances.[3] A retrospective review from an Australian NICU in which routine triglyceride monitoring is in place showed HT incidence of 32.5% in 23-25 weeks and 16.1% in 26-28 weeks. Severe HT (>4.5 mmol/L) was noted in 10% in 23-25 weeks and 4.5% in 26-28 weeks. HT was associated with a significant increase in mortality (unadjusted OR 3.5; 95% CI 1.13-10.76; 0.033) and severe retinopathy of prematurity (unadjusted OR 4.06; 95% CI 1.73-9.59; 0.002) on univariate analysis. Further multivariate analysis with adjustment for gestation and birthweight showed no significant association with HT.[143]

Compliance with the Guideline is recommended

PARENTERAL NUTRITION IN NEWBORNS cont'd

3.1.17 SUGGESTED ROUTINE PN BIOCHEMISTRY ORDERS

Test	First 3-7 days	Thereafter
Electrolytes, BUN, HCO_3, Creatinine	Daily or as needed	Once or twice a week
Ca, PO_4, Mg, bilirubin, albumin	As needed	Once a week
Triglyceride	24 hours after each increase	Once a week or when sick
Blood glucose	4-6 hourly	Once or twice a day
Liver function test including alkaline phosphatase	As needed	Once weekly or fortnightly

3.1.18 PROLONGED PN USAGE

- Current solutions have zinc, selenium and iodine in them.
- Infants (e.g. post-surgical infants) who are exclusively on PN for long periods (>4 weeks) may be at risk of other trace element deficiency such as copper and manganese. These can be added to the current formulations for those infants on exclusive PN for greater than 4 weeks.

3.1.19 PARENTERAL NUTRITION IN NON-TERTIARY NEONATAL FACILITIES

- Many non-tertiary nurseries manage moderate to late preterm and growth restricted term neonates often requiring partial parenteral nutrition while establishing enteral feeds.
- No clear cut guidelines can be drawn from the literature for this setting.
- The benefits of parenteral nutrition in this group need to BE balanced against the potential risks of therapy, skill mix and the resource availability.
- Short term PN using peripheral preterm PN via peripheral cannula can be given for these infants if enteral feeding cannot be established by day 3-5 of life.

4.1 PN FORMULATIONS [see appendixes 1-5]

STARTER PN

1. For all preterm and term infants in the first 24-48 hours after birth.
2. Do not use at > 80ml/kg/day in the first 24 hours.
3. Do not use at rates >100 ml/kg/day.

STARTER CONCENTRATED PN

1. For preterm infants on restricted PN and water intake in the first 24-48 hours.
2. Do not use at rates > 60 ml/kg/day.

STANDARD PRETERM PN

1. Standard solution for preterm infants after 24-48 h.
2. Do not use at rates >135ml/kg/day.

CONCENTRATED PRETERM PN

1. For preterm infants with restricted PN and water intake after 24-48 hours.
2. Do not use at the rates >100 ml/kg/day.

Compliance with the Guideline is recommended

PARENTERAL NUTRITION IN NEWBORNS cont'd

HIGH SODIUM PN

1. For preterm infants with hyponatraemia.
2. Provides Na at 8 mmol/kg/day at 135 ml/kg/day.
3. Do not use at rates >135 ml/kg/day.

7.5% GLUCOSE PRETERM PN

1. For hyperglycaemic preterm infants.
2. Do not use at rates >135 ml/kg/day.

PERIPHERAL PRETERM PN

1. For preterm infants without long lines.
2. Do not use at rates >135 ml/kg/day.

34 WEEKS TO TERM PN

Do not use at rates >135ml/kg/day

5. KEY POINTS

Key points	**Level of evidence; Grade of recommendation**
Indication: Preterm Infants <32 weeks and/or <1500 g – PN should be commenced within the first 12 hours of life (on admission).	Consensus
Indication: Infants at high risk of NEC (e.g. absent or reversed foetal umbilical artery flow, perinatal asphyxia) or with illness in whom establishment of enteral feeding is thought to be delayed by 3-5 days.	Consensus
Fluids: Starting parenteral fluid intake at 60 ml/kg/day with daily increase by 20-30 ml/kg/day to an average maximum of 150 ml/kg/day. Titrate to clinical need (urine output and specific gravity, weight, serum sodium).	LOE I GOR B
Energy: Minimal energy requirements are met with 50–60 kcal/kg/day, but 100–120 kcal/kg/day facilitate maximal protein accretion. A newborn infant receiving PN needs fewer calories (90–100 kcal/kg/day) than a newborn fed enterally because there is no energy lost in the stools and there is less thermogenesis.	Consensus
Dextrose: Maximal glucose oxidation has been reported in preterm infants to be 8.3 mg/kg per min (12 g/kg per day) and in term infants 13 mg/kg per min (18 g/kg per day). Carbohydrate provides 40-60% of total energy.	Consensus

Amino acids: (1) commence parenteral AA within the first 24 hours of birth (LOE I, GOR C), (2) commence parenteral AA at 2 g/kg/day (LOE I, GOR C), and (3) incrementally increase amino acid infusions to a maximum 4 g/kg/day by day 3-5 of life in preterm neonates (LOE I, GOR C). The safety of (1) commencement parenteral AA in excess of 3 to 3.5 g/kg/day and (2) maintenance AA intake in excess of 4.5 g/kg/day has not been proven in clinical trials.	LOE I
Lipids: Commence lipids at 1 g/kg/day and increase by 1 g each day to 3 g/kg/day. If lipid infusion is increased in increments of 0.5 to 1 g/kg per day, it may be possible to monitor for hypertriglyceridaemia [triglycerides >2.8 mmol/L]. Essential fatty acid deficiency occurs rapidly and can be prevented with introduction of as little as 0.5 to 1 g/kg/day of lipid infusion [reduce but do not stop lipid infusion if event of hypertriglyceridaemia.	Consensus
Sodium: Minimal sodium intake of approximately 1 mmol/kg/d on day 1 using a starter PN formulation. Standard formulations will gradually increase sodium to a maximum 4.6 mmol/kg/d in preterm and 3.4 mmol/kg/day in term infants at 135 ml/kg/day of PN.	LOE II, GOR C
Potassium: Minimal potassium intake using starter PN formulation, with an increase in standard formulations to a maximum 3.0 mmol/kg/day in preterm and 2.7 mmol/kg/day in term infants.	LOE III-2, GOR C
Acetate and chloride: First 3 mmol/kg/day of anion to be provided as chloride, next 3.5 mmol/kg/day of anion [reduced from 6 mmol/kg/day] to be provided as acetate and thereafter as chloride again.	Consensus
Calcium, phosphorus and magnesium: Parenteral Ca and P intakes to a maximum of 2.3 mmol/kg/day and 1.8 mmol/kg/day respectively. LOE II For Mg intake a minimum of 0.2 mmol/kg/day and maximum of 0.3 mmol/kg/day would be appropriate for LBW infants. LOE 111-3	GOR C
Trace elements: Add zinc, selenium and iodine as individual trace elements to all AA/Dextrose formulations. For those infants, who are on exclusive PN for more than 2-4 weeks with minimal enteral intake, other trace elements (copper, manganese and molybdenum) can be added to the formulations.	LOE IV, GOR C
Heparin: heparin for peripherally placed percutaneous central venous catheters found a reduced risk of catheter occlusion.	LOE I, GOR B
Hanging time: 48 hours for PN solution and lipid.	LOE II, GOR C
Route of administration: Peripherally inserted central catheters (PICC's) should be used preferentially to provide central venous access in neonates receiving prolonged PN as PICC use results in improved nutrient intake and fewer insertion attempts. Umbilical vessels can be used for PN. UVC compared to peripheral venous catheter reduces insertion attempts with no increase in risk of infection or necrotising enterocolitis.	LOE I GOR B
Cessation of PN: Amino acid/dextrose infusion: cease when infant tolerating 120 (to 140) mL/kg/day of enteral feeds. Lipid: halve infusion when infant tolerating 100 mL/kg/day enteral feeds and cease when tolerating 120 mL/kg/day enteral feeds.	Consensus

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PARENTERAL NUTRITION IN NEWBORNS cont'd

6. performance measures

1. Postnatal growth failure: weight < 10th centile at 36 weeks postmenstrual age.
2. Postnatal growth failure: weight < 10th centile at 28 days age; weight < 10th centile at discharge from hospital.
3. CLABSI/1000 Central line days.
4. Late-onset sepsis.
    a. Babies with late-onset sepsis born at <28 weeks gestational age;
    b. Babies with late-onset sepsis born at 28-31 weeks gestational age;
    c. Babies with late-onset sepsis born at ≥32weeks gestational age.
5. Biochemical abnormality whilst on PN.

7. Definitions:

1. CLABSI/1000 Central line days derived by the temporal association with a central line up to 48 hours post removal unless manually coded as not central line associated for babies <= 28 weeks gestation and during day 3 - 35 (congenital sepsis is NOT included). [NICUS Spring data]
2. CLABSI = Central line associated blood stream infection = Positive Bacterial Blood Cultures are used for the numerator if they are CODED as Definite Infection.
3. Late-onset sepsis: Positive Bacterial Blood Cultures are used for the numerator if they are CODED as Definite Infection after 48 hours age. [ANZNN data]
4. Hypernatraemia Na >150 mmol/L.
5. Hyponatraemia Na <130 mmol/L.
6. Hyperkalaemia K+ ≥6.5 mmol/L.
7. Hyperchloraemia Cl >110 mmol/L.
8. Metabolic acidosis where pH < 7.25 or base excess (BE) > -5, or both.
9. Abnormal serum ammonia > 122 µmol/L.
10. Abnormal urea levels > 14.3 mmol/L.
11. Hyperglycaemia, plasma glucose > 8.3 mmol/L; any hyperglycaemia treated with insulin therapy.
12. Hypoglycaemia <2.6mmol/L.
13. Cholestasis, serum level of direct bilirubin > 20% of total serum bilirubin or serum level of direct bilirubin > 34 mmol/L.
14. Metabolic bone disease [serum alkaline phosphatase >800 iU/L; PTH >50 pg/mL; radiological; fractures].

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Compliance with the Guideline is recommended

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Compliance with the Guideline is recommended

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Compliance with the Guideline is recommended

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Compliance with the Guideline is recommended

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…./Appendices 1 - 5

Appendix 1: Amino acid-dextrose Formulations

1. For all preterm and term infants in the first 24-48 hours after birth.
2. Do not use at > 80ml/kg/day in the first 24 hours.
3. Do not use at rates >100 ml/kg/day.

	STARTER								
	per 1000mL	**mL/kg/day**							
		40	50	60	70	80	90	100	110
Amino acids, g	37.5	1.5	1.9	2.3	2.6	3.0	3.4	3.8	4.1
Glucose, g	100	4.0	5.0	6.0	7.0	8.0	9.0	10.0	11.0
Sodium, mmol	20	0.8	1.0	1.2	1.4	1.6	1.8	2.0	2.2
Potassium, mmol	0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Calcium, mmol	17	0.7	0.9	1.0	1.2	1.4	1.5	1.7	1.9
Magnesium, mmol	1.5	0.1	0.1	0.1	0.1	0.1	0.1	0.2	0.2
Phosphate, mmol	10	0.4	0.5	0.6	0.7	0.8	0.9	1.0	1.1
Chloride, mmol	10.1	0.4	0.5	0.6	0.7	0.8	0.9	1.0	1.1
Acetate, mmol	0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Zinc, µg	3270	131	164	196	229	262	294	327	360
Selenium, µg	20	0.8	1.0	1.2	1.4	1.6	1.8	2.0	2.2
Iodine, µg	8.16	0.3	0.4	0.5	0.6	0.7	0.7	0.8	0.9
Heparin, units	500	20	25	30	35	40	45	50	55
Osmolarity, mosm/L	933								
Kcal - AA & Glucose	550	Alert - below minimal recommended amino acid if no enteral intake							
Solution pH	5.65	Alert - above maximal starter amino acid intake							
Bag volume, mL	500	Stability: up to 61 days @ 2-8^{O}C and 5 days at below 25^{O}C.							

Compliance with the Guideline is recommended

1. For preterm infants on restricted PN and water intake in the first 24-48 hours.
2. Do not use at rates > 60 ml/kg/day.

	STARTER CONCENTRATED PN					
	per 1000 mL	**mL/kg/day**				
		40	50	60	70	80
Amino acids, g	50	2.0	2.5	3.0	3.5	4.0
Glucose, g	100	4.0	5.0	6.0	7.0	8.0
Sodium, mmol	30	1.2	1.5	1.8	2.1	2.4
Potassium, mmol	0	0.0	0.0	0.0	0.0	0.0
Calcium, mmol	25	1.0	1.3	1.5	1.8	2.0
Magnesium, mmol	1.5	0.1	0.1	0.1	0.1	0.1
Phosphate, mmol	15	0.6	0.8	0.9	1.1	1.2
Chloride, mmol	12.5	0.5	0.6	0.8	0.9	1.0
Acetate, mmol	0	0.0	0.0	0.0	0.0	0.0
Zinc, µg	3270	131	164	196	229	262
Selenium, µg	20	0.8	1.0	1.2	1.4	1.6
Iodine, µg	8.16	0.3	0.4	0.5	0.6	0.7
Heparin, units	500	20	25	30	35	40
Osmolarity, mosm/L	1069					
Kcal – AA & Glucose	600	Alert - above maximal starter amino acid intake				
Solution pH	5.69	Stability: up to 61 days @ 2-8^{O}C and 5 days at below 25^{O}C.				
Bag volume, mL	500					

Compliance with the Guideline is recommended

1. Standard solution for preterm infants after 24-48 h.
2. Do not use at rates >135ml/kg/day.

	STANDARD PRETERM												
	per 1000 mL	mL/kg/day											
		40	50	60	70	80	90	100	110	120	130	135	140	150
Amino acids, g	30	1.2	1.5	1.8	2.1	2.4	2.7	3.0	3.3	3.6	3.9	4.1	4.2	4.5
Glucose, g	100	4.0	5.0	6.0	7.0	8.0	9.0	10.0	11.0	12.0	13.0	13.5	14.0	15.0
Sodium, mmol	34	1.4	1.7	2.0	2.4	2.7	3.1	3.4	3.7	4.1	4.4	4.6	4.8	5.1
Potassium, mmol	22	0.9	1.1	1.3	1.5	1.8	2.0	2.2	2.4	2.6	2.9	3.0	3.1	3.3
Calcium, mmol	17	0.7	0.9	1.0	1.2	1.4	1.5	1.7	1.9	2.0	2.2	2.3	2.4	2.6
Magnesium, mmol	1.5	0.1	0.1	0.1	0.1	0.1	0.1	0.2	0.2	0.2	0.2	0.2	0.2	0.2
Phosphate, mmol	13	0.5	0.7	0.8	0.9	1.0	1.2	1.3	1.4	1.6	1.7	1.8	1.8	2.0
Chloride, mmol	12.7	0.5	0.6	0.8	0.9	1.0	1.1	1.3	1.4	1.5	1.7	1.7	1.8	1.9
Acetate, mmol	26	1.0	1.3	1.6	1.8	2.1	2.3	2.6	2.9	3.1	3.4	3.5	3.6	3.9
Zinc, µg	3270	131	164	196	229	262	294	327	360	392	425	441	458	491
Selenium, µg	20	0.8	1.0	1.2	1.4	1.6	1.8	2.0	2.2	2.4	2.6	2.7	2.8	3.0
Iodine, µg	8.16	0.3	0.4	0.5	0.6	0.7	0.7	0.8	0.9	1.0	1.1	1.1	1.1	1.2
Heparin, units	500	20	25	30	35	40	45	50	55	60	65	68	70	75
Osmolarity, mOsm/L	944													
Kcal	520	Alert - below minimal recommended maintenance AA intake if no enteral intake												
Solution pH	5.98	Alert - above safety limit for calcium and above maximal recommended AA intake												
Bag volume, mL	750	Stability: up to 61 days @ 2-8^{O}C and 5 days at below 25^{O}C.												

Compliance with the Guideline is recommended

1. For preterm infants with restricted PN or water intake after 24-48 hours.
2. Do not use at the rates >100 ml/kg/day.

	CONCENTRATED PRETERM								
	per 1000 mL	**mL/kg/day**							
		40	50	60	70	80	90	100	110
Amino acids, g	40	1.6	2.0	2.4	2.8	3.2	3.6	4.0	4.4
Glucose, g	100	4.0	5.0	6.0	7.0	8.0	9.0	10.0	11.0
Sodium, mmol	50	2.0	2.5	3.0	3.5	4.0	4.5	5.0	5.5
Potassium, mmol	35	1.4	1.8	2.1	2.5	2.8	3.2	3.5	3.9
Calcium, mmol	22	0.9	1.1	1.3	1.5	1.8	2.0	2.2	2.4
Magnesium, mmol	1.5	0.1	0.1	0.1	0.1	0.1	0.1	0.2	0.2
Phosphate, mmol	15	0.6	0.8	0.9	1.1	1.2	1.4	1.5	1.7
Chloride, mmol	39.6	1.6	2.0	2.4	2.8	3.2	3.6	4.0	4.4
Acetate, mmol	26	1.0	1.3	1.6	1.8	2.1	2.3	2.6	2.9
Zinc, µg	4900	196	245	294	343	392	441	490	539
Selenium, µg	30	1.2	1.5	1.8	2.1	2.4	2.7	3.0	3.3
Iodine, µg	12	0.5	0.6	0.7	0.8	1.0	1.1	1.2	1.3
Heparin, units	500	20	25	30	35	40	45	50	55
Osmolarity, mOsm/L	1092								
Kcal - AA & Glucose	560	Alert - below minimal recommended maintenance AA if no enteral intake							
Solution pH	5.75	Alert - above maximal recommended calcium and amino acid intake							
Bag volume, mL	750	Stability: up to 61 days @ 2-8^{O}C and 5 days at below 25^{O}C.							

Compliance with the Guideline is recommended

HIGH SODIUM PRETERM

CC50328

1. For preterm infants. With hyponatraemia
2. Provides Na at 8 mmol/kg/day at 135 ml/kg/day.
3. Do not use at rates >135 ml/kg/day.

	HIGH SODIUM PRETERM												
	per 1000 mL	**mL/kg/day**											
		40	50	60	70	80	90	100	110	120	130	135	140	150
Amino acids, g	30	1.2	1.5	1.8	2.1	2.4	2.7	3.0	3.3	3.6	3.9	4.1	4.2	4.5
Glucose, g	100	4.0	5.0	6.0	7.0	8.0	9.0	10	11	12	13	13.5	14	15.0
Sodium, mmol	60	2.4	3.0	3.6	4.2	4.8	5.4	6.0	6.6	7.2	7.8	8.1	8.4	9.0
Potassium, mmol	22	0.9	1.1	1.3	1.5	1.8	2.0	2.2	2.4	2.6	2.9	3.0	3.1	3.3
Calcium, mmol	17	0.7	0.9	1.0	1.2	1.4	1.5	1.7	1.9	2.0	2.2	2.3	2.4	2.6
Magnesium, mmol	1.5	0.1	0.1	0.1	0.1	0.1	0.1	0.2	0.2	0.2	0.2	0.2	0.2	0.2
Phosphate, mmol	13	0.5	0.7	0.8	0.9	1.0	1.2	1.3	1.4	1.6	1.7	1.8	1.8	2.0
Chloride, mmol	30.7	1.2	1.5	1.8	2.1	2.5	2.8	3.1	3.4	3.7	4.0	4.1	4.3	4.6
Acetate, mmol	34	1.4	1.7	2.0	2.4	2.7	3.1	3.4	3.7	4.1	4.4	4.6	4.8	5.1
Zinc, µg	3270	131	164	196	229	262	294	327	360	392	425	441	458	491
Selenium, µg	20	0.8	1.0	1.2	1.4	1.6	1.8	2.0	2.2	2.4	2.6	2.7	2.8	3.0
Iodine, µg	8.16	0.3	0.4	0.5	0.6	0.7	0.7	0.8	0.9	1.0	1.1	1.1	1.1	1.2
Heparin, units	500	20	25	30	35	40	45	50	55	60	65	68	70	75
Osmolarity, mOsm/L	996													
Kcal	520	Alert - below minimal recommended maintenance AA intake if no enteral intake												
Solution pH	5.95	Alert - bove safety limit for calcium and above maximal recommended AA intake.												
Bag volume, mL	750	Stability: up to 61 days @ 2-8^{O}C and 5 days at below 25^{O}C.												

Compliance with the Guideline is recommended

7.5% GLUCOSE PRETERM

CC50329

1. For hyperglycaemic preterm infants.
2. Do not use at rates >135 ml/kg/day.

	7.5% GLUCOSE PRETERM													
	per 1000 mL	mL/kg/day												
		40	50	60	70	80	90	100	110	120	130	135	140	150
Amino acids, g	30	1.2	1.5	1.8	2.1	2.4	2.7	3.0	3.3	3.6	3.9	4.1	4.2	4.5
Glucose, g	75	3.0	3.8	4.5	5.3	6.0	6.8	7.5	8.3	9.0	9.8	10.1	10.5	11.3
Sodium, mmol	34	1.4	1.7	2.0	2.4	2.7	3.1	3.4	3.7	4.1	4.4	4.6	4.8	5.1
Potassium, mmol	22	0.9	1.1	1.3	1.5	1.8	2.0	2.2	2.4	2.6	2.9	3.0	3.1	3.3
Calcium, mmol	17	0.7	0.9	1.0	1.2	1.4	1.5	1.7	1.9	2.0	2.2	2.3	2.4	2.6
Magnesium, mmol	1.5	0.1	0.1	0.1	0.1	0.1	0.1	0.2	0.2	0.2	0.2	0.2	0.2	0.2
Phosphate, mmol	13	0.5	0.7	0.8	0.9	1.0	1.2	1.3	1.4	1.6	1.7	1.8	1.8	2.0
Chloride, mmol	12.7	0.5	0.6	0.8	0.9	1.0	1.1	1.3	1.4	1.5	1.7	1.7	1.8	1.9
Acetate, mmol	26	1.0	1.3	1.6	1.8	2.1	2.3	2.6	2.9	3.1	3.4	3.5	3.6	3.9
Zinc, µg	3270	131	164	196	229	262	294	327	360	392	425	441	458	491
Selenium, µg	20	0.8	1.0	1.2	1.4	1.6	1.8	2.0	2.2	2.4	2.6	2.7	2.8	3.0
Iodine, µg	8.16	0.3	0.4	0.5	0.6	0.7	0.7	0.8	0.9	1.0	1.1	1.1	1.1	1.2
Heparin, units	500	20	25	30	35	40	45	50	55	60	65	68	70	75
Osmolarity, mOsm/L	805													
Kcal - AA & Glucose	425	Alert - below minimal recommended maintenance AA intake if no enteral intake												
Solution pH	5.9	Alert - above safety limit for calcium and above maximal recommended AA intake												
Bag volume, mL	750	Stability: up to 61 days @ 2-8^{O}C and 5 days at below 25^{O}C.												

Compliance with the Guideline is recommended

PERIPHERAL PRETERM

CC50326

1. For preterm infants without long lines.
2. Do not use at rates >135 ml/kg/day.

	Peripheral Preterm													
	per 1000 mL	**mL/kg/day**												
		40	50	60	70	80	90	100	110	120	130	135	140	150
Amino acids, g	30	1.2	1.5	1.8	2.1	2.4	2.7	3.0	3.3	3.6	3.9	4.1	4.2	4.5
Glucose, g	100	4.0	5.0	6.0	7.0	8.0	9.0	10.0	11.0	12.0	13.0	13.5	14.0	15.0
Sodium, mmol	34	1.4	1.7	2.0	2.4	2.7	3.1	3.4	3.7	4.1	4.4	4.6	4.8	5.1
Potassium, mmol	22	0.9	1.1	1.3	1.5	1.8	2.0	2.2	2.4	2.6	2.9	3.0	3.1	3.3
Calcium, mmol	3.5	0.1	0.2	0.2	0.2	0.3	0.3	0.4	0.4	0.4	0.5	0.5	0.5	0.5
Magnesium, mmol	1.5	0.1	0.1	0.1	0.1	0.1	0.1	0.2	0.2	0.2	0.2	0.2	0.2	0.2
Phosphate, mmol	3	0.1	0.2	0.2	0.2	0.2	0.3	0.3	0.3	0.4	0.4	0.4	0.4	0.5
Chloride, mmol	18.7	0.7	0.9	1.1	1.3	1.5	1.7	1.9	2.1	2.2	2.4	2.5	2.6	2.8
Acetate, mmol	40	1.6	2.0	2.4	2.8	3.2	3.6	4.0	4.4	4.8	5.2	5.4	5.6	6.0
Zinc, µg	3270	131	164	196	229	262	294	327	360	392	425	441	458	491
Selenium, µg	20	0.8	1.0	1.2	1.4	1.6	1.8	2.0	2.2	2.4	2.6	2.7	2.8	3.0
Iodine, µg	8.16	0.3	0.4	0.5	0.6	0.7	0.7	0.8	0.9	1.0	1.1	1.1	1.1	1.2
Heparin, units	500	20	25	30	35	40	45	50	55	60	65	68	70	75
Osmolarity, mOsm/L	913													
Kcal - AA & Glucose	520	Alert - above maximal recommended amino acid intake												
Solution pH value	5.55	Alert - below minimal recommended maintenance AA intake if no enteral intake												
Bag volume, mL	750	Stability: up to 61 days @ 2-8^{O}C and 5 days at below 25^{O}C.												

Compliance with the Guideline is recommended

Do not use at rates >135ml/kg/day

	34 WEEKS TO TERM PN													
	per 1000 mL	mL/kg/day												
		40	50	60	70	80	90	100	110	120	130	135	140	150
Amino acids, g	23	0.9	1.2	1.4	1.6	1.8	2.1	2.3	2.5	2.8	3.0	3.1	3.2	3.5
Glucose, g	120	4.8	6.0	7.2	8.4	9.6	10.8	12.0	13.2	14.4	15.6	16.2	16.8	18
Sodium, mmol	25	1.0	1.3	1.5	1.8	2.0	2.3	2.5	2.8	3.0	3.3	3.4	3.5	3.8
Potassium, mmol	20	0.8	1.0	1.2	1.4	1.6	1.8	2.0	2.2	2.4	2.6	2.7	2.8	3.0
Calcium, mmol	7	0.3	0.4	0.4	0.5	0.6	0.6	0.7	0.8	0.8	0.9	0.9	1.0	1.1
Magnesium, mmol	1.5	0.1	0.1	0.1	0.1	0.1	0.1	0.2	0.2	0.2	0.2	0.2	0.2	0.2
Phosphate, mmol	4	0.2	0.2	0.2	0.3	0.3	0.4	0.4	0.4	0.5	0.5	0.5	0.6	0.6
Chloride, mmol	28.2	1.1	1.4	1.7	2.0	2.3	2.5	2.8	3.1	3.4	3.7	3.8	3.9	4.2
Acetate, mmol	16.2	0.6	0.8	1.0	1.1	1.3	1.5	1.6	1.8	1.9	2.1	2.2	2.3	2.4
Zinc, ug	1900	76	95	114	133	152	171	190	209	228	247	257	266	285
Selenium, ug	20	0.8	1.0	1.2	1.4	1.6	1.8	2.0	2.2	2.4	2.6	2.7	2.8	3.0
Iodine, ug	8.16	0.3	0.4	0.5	0.6	0.7	0.7	0.8	0.9	1.0	1.1	1.1	1.1	1.2
Heparin, units	500	20	25	30	35	40	45	50	55	60	65	68	70	75
Osmolarity, mOsm/L	957													
Kcal - AA & Glucose	548	Alert - below minimal recommended amino acid if no enteral intake												
Solution pH	5.61	Alert - above recommended maximal calcium and amino acid intake												
Bag volume, mL	1200	Stability: up to 61 days @ 2-8^{O}C and 5 days at below 25^{O}C.												

Compliance with the Guideline is recommended

Appendix 2: Amino acid-dextrose formulations summary table

PN	Starter	Standard Preterm	High Sodium	7.5% Glucose Preterm	Peripheral preterm	34 weeks to Term
Indication	Birth to 24-48 hours	After 24-48 hours	Hyponatremic Preterm	Hyperglycaemic Preterm	No central line	After 24-48 hours
Concentration per litre						
Amino acids, g	37.5	30	30	30	30	23
Glucose, g	100	100	100	75	100	120
Sodium, mmol	20	34	60	34	34	25
Potassium, mmol	0	22	22	22	22	20
Calcium, mmol	17	17	17	17	3.5	7
Magnesium, mmol	1.5	1.5	1.5	1.5	1.5	1.5
Phosphate, mmol	10	13	13	13	3	4
Chloride, mmol	10.1	12.7	30.7	12.7	18.7	28.2
Acetate, mmol	0	26	34	26	40	16.2
Zinc, µg	3270	3270	3270	3270	3270	1900
Selenium, µg	20	20	20	20	20	20
Iodine, µg	8.16	8.16	8.16	8.16	8.16	8.16
Heparin, units	500	500	500	500	500	500
Osmolarity, mosm	933	944	996	805	913	957
At 135 ml/kg/day						
Amino acids, g		4.1	4.1	3.1	4.1	3.1
Glucose, g		13.5	13.5	10.1	13.5	16.2
Sodium, mmol		4.6	8.1	4.6	4.6	3.4
Potassium, mmol		3.0	3.0	3.0	3.0	2.7
Calcium, mmol		2.3	2.3	2.3	0.5	0.9
Magnesium, mmol		0.2	0.2	0.2	0.2	0.2
Phosphate, mmol		1.8	1.8	1.8	0.4	0.5
Chloride, mmol		1.7	4.1	1.7	2.5	3.8
Acetate, mmol		3.5	4.6	3.5	5.4	2.2
Zinc, µg		441	441	441	441	257
Selenium, µg		2.7	2.7	2.7	2.7	2.7
Iodine, µg		1.1	1.1	1.1	1.1	1.1

Compliance with the Guideline is recommended

Appendix 3: Lipid Formulations

SMOFLipid formulations

Contents	45 mL syringe For ≤1 Kg	145 mL bag For >1 Kg
SMOFlipid	32.5 mL	100 mL
Soluvit N	2.5 mL	8.4 mL
Vitalipid N Infant	10 mL	36.6 mL

ClinOleic formulations

Contents	45 mL syringe For ≤1 kg	90 mL bag For >1 to ≤2 Kg	150 mL bag For >2 kg
ClinOleic	32.5 mL	65 mL	108 mL
Soluvit N	2.5 mL	5 mL	8.4 mL
Vitalipid N Infant	10 mL	20 mL	33.6 mL

Appendix 4: 2017 consensus formulations and comparison to recommended parenteral nutrient intakes in preterm neonates

Recommended parenteral nutrient intakes for preterm neonates. Values are per kg per day, unless otherwise indicated.						
Nutrient	ESPGHAN 2005[6]			AAP 2014 consensus[5]		Australasian 2018 consensus®
	Preterm			Weight <1000 gm	Weight 1000-1500 g	
	Day 0	Transition	Growing			
Energy, Kcal				105-115	90-100	100
Protein, g	≥1.5	≤4.0	≤4.0	3.5-4 g	3.2-3.8 g	4.05 g
Carbohydrate, g	5.8-11.5	≤12.0	≤12.0	13-17 g	9.7-15 g	13.5 g
Fat, g	1	1.0-3.0*	≤3.0*	3.0 - 4.0	3.0 - 4.0	3
Linoleic acid, mg	≥250			340-800	340-800	-
Sodium, mmol	0-3.0 (0-7d)	2.0-3.0	3.0-5.0	3.0-5.0	3.0-5.0	4.59
Potassium, mmol	0-2.0 (0-7d)	1.0-2.0	2.0-5.0	2.0 - 3.0	2.0 - 3.0	2.97
Chloride, mmol	0-5.0 (0-7d)	2.0-3.0		3.0 - 7.0	3.0 - 7.0	1.7
Calcium, mmol			1.3-3.0	1.5-2.0	1.5-2.0	2.3
Phosphate, mmol			1.0-2.3	1.5-1.9	1.5-1.9	1.8
Mg, mmol	0.2	0.2	0.2	0.17-0.29	0.17-0.29	0.2
Iron, µg	0	0 (<3 wks)	50-200	100-200	100-200	-
Zinc, µg	450-500	450-500	450-500	400	400	441
Copper, µg	20	20	20	20	20	-
Selenium, µg	2.0-3.0	2.0-3.0	2.0-3.0	1.5-4.5	1.5-4.5	2.7 µg
Chromium, µg	0	0	0	0.05-0.3	0.05-0.3	-
Molybdenum, µg	1	1	1	0.25	0.25	-
Manganese, µg	<1	<1	<1	1	1	-
Iodine, µg/day	1	1	1	1	1	1.1 µg
Vitamin A, IU	495-990	495-990	495-990	700-1500	700-1500	920
Vitamin D, IU	32	32	32	40-160	40-160	160
Vitamin E, IU	2.8-3.5	2.8-3.5	2.8-3.5	2.8-3.5	2.8-3.5	2.8
Vitamin K, µg	10	10	10	10	10	80#
Thiamin, µg	350-500	350-500	350-500	200-350	200-350	310
Riboflavin, µg	150-200	150-200	150-200	150-200	150-200	360#
Niacin, mg	4.0-6.8	4.0-6.8	4.0-6.8	4.0-6.8	4.0-6.8	4
Pyridoxine, µg	150-200	150-200	150-200	150-200	150-200	400#
Folate, µg	56	56	56	56	56	40*
Vitamin B12, µg	0.3	0.3	0.3	0.3	0.3	0.5#
Pantothenate, mg	1.0-2.0	1.0-2.0	1.0-2.0	1.0-2.0	1.0-2.0	1.5
Biotin, µg	5.0-8.0	5.0-8.0	5.0-8.0	5.0-8.0	5.0-8.0	6
Vitamin C, mg	15-25	15-25	15-25	15-25	15-25	10*
Acetate, mmol						3.51

®At135ml/kg/d of standard Preterm PN plus 3 g/kg/d of Lipid: *Below RDI, #Above RDI

Compliance with the Guideline is recommended

Appendix 5: 2017 consensus formulations and comparison to recommended parenteral nutrient intakes in term neonates

Reasonable parenteral nutrient intakes in term neonates					
Nutrient, per/kg/day	**ESPGHAN 2005**			**Australasian 2018 consensus 34wk-Term PN @ 135ml/kg/day**	**Australasian 2018 consensus Lipid @ 3g/kg/day**
	Day 0	**≤30 days**	**1-12 months**		
Energy, Kcal		90-100	90-100	74	30
Protein, g	1.5-3.0	1.5-3.0	1.0-2.5	3.1	
Carbohydrate, g	5.8-11.5	≤18.0	5.0-12	16.2	
Fat, g	1	3.0-4.0	3.0-4.0		3
Sodium, mmol	0-3.0 (0-7days)	2.0-5.0	2.0-3.0	3.4	
Potassium, mmol	0-2.0 (0-7days)	1.0-3.0	1.0-3.0	2.7	
Chloride, mmol	0-5.0 (0-7days)			2.7	
Calcium, mmol	0.8	0.8		2	
Phosphate, mmol	0.5	0.5		1.6	
Magnesium, mmol	0.2	0.2	0.2-0.3	0.2	
Iron, µmol	0	0(<3 weeks)	1.8-3.6		
Zinc, µg	250	250	100 (>3 months)	257	
Copper, µg	20	20	20		
Selenium, µg	2.0-3.0	2.0-3.0	2.0-3.0	2.7	
Chromium, µg	0	0	0		
Molybdenum, µg	0.25	0.25	0.25		
Manganese, µg	<1	<1	<1		
Iodine, (µg/day)	1	1	1	1.1	
Vitamin A, IU	495-990	495-990	495-990		920
Vitamin D, IU	32	32	32		160
Vitamin E, IU	2.8-3.5	2.8-3.5	2.8-3.5		2.8
Vitamin K, µg	10	10	10		80[#]
Thiamin, µg	350-500	350-500	350-500		310
Riboflavin, µg	150-200	150-200	150-200		360[#]
Niacin, mg	4.0-6.8	4.0-6.8	4.0-6.8		4
Pyridoxine, µg	150-200	150-200	150-200		400[#]
Folate, µg	56	56	56		40[*]
Vitamin B12, µg	0.3	0.3	0.3		0.5[#]
Pantothenate, mg	1.0-2.0	1.0-2.0	1.0-2.0		1.5
Biotin, µg	5.0-8.0	5.0-8.0	5.0-8.0		6
Vitamin C, mg	15-25	15-25	15-25		10[*]

[*]Below RDI; [#]Above RDI.

Compliance with the Guideline is recommended