



Guideline

Women and Babies: Enteral Nutrition for the Preterm Infant

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Summary:	Guideline for appropriate enteral nutrition of the preterm infant.
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Note: Sydney Local Health District (LHD) and South Western Sydney LHD were established on 1 July 2011, with the dissolution of the former Sydney South West Area Health Service (SSWAHS) in January 2011. The former SSWAHS was established on 1 January 2005 with the amalgamation of the former Central Sydney Area Health Service (CSAHS) and the former South Western Sydney Area Health Service (SWSAHS).

In the interim period between 1 January 2011 and the release of specific LHN policies (dated after 1 January 2011) and SLHD (dated after July 2011), the former SSWAHS, CSAHS and SWSAHS policies are applicable to the LHDs as follows:

Where there is a relevant SSWAHS policy, that policy will apply

Where there is no relevant SSWAHS policy, relevant CSAHS policies will apply to Sydney LHD; and relevant SWSAHS policies will apply to South Western Sydney LHD.

Women and Babies:

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Women and Babies: Title

1. Introduction

The risks addressed by this policy:

Clinical risk of inadequate nutrition of the preterm infant

The aims / expected outcome of this policy

Good nutrition and growth for preterm infants.

2. Policy Statement

That all preterm babies should have enteral nutrition introduced and maintained according to these guideline to achieve as close as possible to expected in-utero growth curves.

3. Summary of Recommendations.

3.1 What Milk?

- **First choice milk:** Maternal expressed breast milk. This should be supplemented with FM85 human milk fortifier to 26calories/30ml when the baby is tolerating 150ml/kg/day and in babies born before 33 weeks or 33 and 34 week infants who are less than the 10th centile (33 weeks <1600g; 34 weeks <1800g). If maternal EBM not available, use donor EBM on an individualised basis in high risk babies.
- **Second choice milk:**
 - Low birth weight formula in babies born before 33 weeks or 33 and 34 week infants who are less than the 10th centile (33w <1600g; 34 weeks <1800g).
 - Normal term formula in babies born after 32 weeks (e.g from 33 weeks onwards) who are over the 10th centile (33w >1600g; 34 weeks >1800g).
- **In special situations (see above):** consider extensively hydrolysed formula such as Neocate but supplement with calcium, phosphate, iron and vitamins in babies born before 32 weeks and those born 33 and 34 weeks who are less than the 10th centile (33w <1600g; 34 weeks <1800g).

3.2 When should milk be started?

- **Babies born after 32 weeks (33 weeks and over) who are normally grown (>10th centile)** can be started immediately on intermittent bolus milk feeds according to usual fluid requirements. In mothers who wish to breast feed, we should discuss with them the transitional use of formula milk while we await sufficient supply of EBM.

- **Babies born between 30 and 32 weeks who are well** (e.g not on respiratory support) should have a peripheral IV inserted to allow slow increase in enteral milk feeds starting at 1ml/hr on day 1 or as maternal breast milk becomes available.
- **Babies born before 30 weeks and babies born from 30 weeks onwards who have respiratory problems or other complications** should start minimal enteric feeds at 1 ml every 4 hours as soon as mother's breast milk is available.

3.3 How quickly should milk feeds be increased?

- **In babies born before 28 weeks**, caution should be applied to increasing feeds above 1ml/hr within the first 5-7 days.
- **In preterm babies born after 27 weeks (e.g. 28 weeks onwards), who commence on IV fluids at birth:** The rate of increase needs to be individualised however the Cochrane review would suggest that in uncomplicated preterm babies, feeds can be advanced up to 30 to 35 ml/kg per day if tolerated without adverse effect.¹⁴ In babies born after 31 weeks who start on IV fluids, it may be reasonable to increase feeds faster than that.
- **How should the rate of increase be individualised?** In terms of the hourly bolus feeds, this can range from an increase of 1ml/hr every 4 hours to 1ml/hr every 24 hours or even longer in some babies and should be titrated against maturity, feed tolerance and other abdominal signs.

3.4 What should be the final feed volume?

- **In babies born before 33 weeks or 33 and 34 weeks and less than 10th centile** (33w <1600g; 34 weeks <1800g), the target total feed volume should be 180 ml/kg/day. This should be achieved by:
 - Increasing hourly bolus feeds with unfortified EBM, DBM or preterm formula to 150 ml/kg/day as described above.
 - After 24-48 hours of tolerance with unfortified EBM or DBM at 150 ml/kg/day, add FM85 to 26 cal/30ml.
 - After 48-72 hours of tolerance of fortified EBM, DBM or preterm formula, increase to 180 ml/kg/day in three daily steps of 10 ml/kg. Consider going faster than this in more mature babies.
- **In babies born after 32 weeks and birth weight above than 10th centile** (33w >1600g; 34 weeks >1800g), the target total feed volume should be 150 ml/kg/day.

3.5 What babies need further supplementation of milk?

- **In babies born before 33 weeks or 33 and 34 weeks and birth weight <10th centile** (33w <1600g; 34 weeks <1800g)
 - **If tolerating 180ml/kg/day of FM85 fortified EBM or LBW formula:** Nutritional and vitamin requirements are met with the possible exception of

Vitamin D. Our view is that the evidence is not strong enough to support routine supplementation of Vitamin D above that provided by FM85.

- **If baby not tolerating FM85 in EBM or has been changed to Neocate:**
 - Add 1.5 mmol/kg/day of calcium and 1.0 mmol/kg day of phosphate
 - Add Pentavite 0.45ml/day when baby is tolerating 150 ml/kg/day.
 - Add Iron as Ferrous Sulphate (6mg elemental iron per ml) from 28 days of age at 1.2mg elemental iron/kg/day (0.2ml/kg/day) in one dose.

3.6 When to stop HMF or LBW formula and post-discharge nutrition?

- Once a baby is feeding at the breast there are practical limitations to providing nutritional supplementation and not enough evidence to support routine supplementation. This will need individualising in babies not growing adequately.
- Prior to establishment of sucking feeds at breast or bottle, we will stop breast milk fortification or change low birth weight formula to normal term formula when:
 - Weight is more than 2.2kg **or**:
 - Has taken at least three suck feeds a day on two consecutive days **and**:
 - Is appropriately grown (>10th centile) and is gaining weight adequately (>15g/kg/day).

3.7 Which babies should get post-discharge iron and vitamin supplement?

- Post-discharge iron and vitamin supplementation should be recommended for all babies who are born before 35 weeks (e.g 34 weeks and less) with birth weight less than 2.5 kg. Supplementation can be considered on an individual basis for babies born after 34 weeks if they are very growth restricted.
 - **Regimen:** Pentavite 0.45ml/day and Ferrous Sulphate (6mg elemental iron per ml) at 1.0ml/day both as a once daily dose to be started when stopping breast milk fortification or changing from LBW to term formula in the smaller babies.
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4. Main Guideline

4.1 Introduction

The goal of nutrition for the preterm infants is to achieve as near to normal weight gain and growth as possible. It is difficult to deliver adequate calories with parenteral nutrition so the aim should be to introduce enteral milk feeds as early as a baby can safely tolerate them.

Nutritional Needs of Preterm Babies: The enteral calorie requirement of a preterm baby will range between 110 and 135 kcal/kg/day and this would usually be administered in milk volumes ranging between 135 and 200 ml/kg/day with most babies' routine feed volumes between 150 and 180 ml/kg/day.¹

Overall adequacy of nutritional intake in any baby is measured by growth, particularly weight gain. In a preterm baby, the target weight gain when a baby is on full enteral feeds is between 10 and 25 grams/kg/day with an average of around 15g/kg/day.² Weight gains in excess of 25g/kg/day should raise concerns about fluid retention.

[Table 1](#) shows the range of nutrient intakes as recommended by ESPGHAN in 2010 comparing

breast milk and different strengths of fortified breast milk.

4.2 Which Milk?

Breast Milk

Expressed Breast Milk (EBM): Breast milk expressed by the baby's own mother remains the first choice of feed for the preterm infant. Numerous short and long term benefits have been demonstrated including better feed tolerance, reduced risk of NEC and late onset sepsis and, possibly, better neurodevelopmental outcome.³

Donor Breast Milk (DBM): In babies at high risk of NEC where the mother is not able to express adequate breast milk, donor breast milk collected in accordance with the RPA donor breast milk policy can be considered. Although pasteurisation modifies some of the anti-infective constituents of breast milk there is evidence from systematic review, that DBM still confers a protective effect against NEC when compared to formula milk.⁴

The decision to use DBM should be made by senior medical staff on an individual case basis but babies in whom it should be considered include the very premature (born before 30 weeks), or born after 30 weeks and with severe intrauterine growth restriction and absent or reversed end-diastolic umbilical artery flow on fetal Doppler.

Nutritional limitations of Breast Milk for Preterm Babies: In light of the long-term health outcome advantages of expressed maternal breast milk together with probable short-term immunological advantages, this has to be the milk of choice. However breast milk does have limitations in addressing the nutritional needs of the very preterm infant, see [table 1](#).

- It does not have enough calories to ensure optimal early growth at 20 kcal/30ml, particularly it does not have enough protein.³
- It does not have enough sodium to compensate for the high renal sodium losses of the very preterm infant.³
- It does not have enough calcium or phosphate. Historically, osteopenia of prematurity was a problem in breast milk fed babies and those on prolonged parenteral nutrition.⁵
- Breast milk has low concentrations of vitamins and iron relative to the needs of a preterm infant who will have missed out on the last trimester placental vitamin transfer.(see vitamins and minerals below).¹

The Cochrane review concludes that multicomponent human milk fortification results in better short term weight gain and linear and head circumference growth. There is no evidence of longer term growth advantage.⁶

At RPAH, we routinely supplement EBM with FM 85 human milk fortifier up to 26kcal/30ml in babies born before 33 weeks (e.g. 32 weeks and less) and in babies born at 33 and 34 weeks with birth below the approximate 10th centile (see table below).

Gestation	Add FM85 if less than:
33 weeks	1600g
34 weeks	1800g

FM85 provides adequate extra calories, vitamins, sodium, calcium, phosphate and iron but is still deficient in some vitamins particularly D and A. See [table 1](#)

When to start FM85? There are no standards or evidence around when breast milk fortifier should be started. Within the clinical trials of breast milk fortifiers, there was considerable variation as to when it was added with some trials waiting for enteral tolerance of full total fluid requirement with unfortified breast milk and other trials adding it earlier, e.g. from when 100 ml/kg/day is tolerated. More research is needed to confirm the safety of early addition of human milk fortifiers.

At RPAH, we add FM85 to expressed maternal or donor breast milk in babies born before 33 weeks and in babies born at 33 and 34 weeks with birth weight below the approximate 10th centile (see table), once they've been tolerating 150 ml/kg/day for 48 hours.

Babies who do not tolerate FM85 fortification of EBM/DBM should be supplemented with mineral, vitamins and iron as detailed below for Neocate.

Formula Milks

Low Birth Weight Formula: Sometimes it will be necessary to use formula milk in preterm babies whose mothers cannot (or do not wish) to express adequate quantities of breast milk.

There are low birth weight formulas adapted to the nutritional needs of very preterm babies and the randomised study of Lucas et al⁷ showed that babies less than 1750g at birth fed preterm compared to normal formula thrived significantly better. The main difference between the commercial low birth weight formulas is whether the protein is partially hydrolysed. Comparative trials have shown little difference between partially hydrolysed and non-hydrolysed in terms of feed tolerance or growth.^{8,9}

The current LBW formula at RPAH is S26 LBW, see [table 2](#) for nutrient content.

Extensively Hydrolysed Elemental Formula: Elemental formulae have proven efficacy for treatment of feed intolerance and allergy in infants. However, there is a lack of clear evidence for the efficacy and safety in very preterm infants with feed intolerance. An extensively hydrolysed elemental formula, such as Neocate may be trialed in infants with recurrent feed intolerance, colitis or lactose malabsorption where there is recurrent intolerance to a standard LBW formula or breast milk. As well as including extensively hydrolysed protein, Neocate is lactose free and has added medium chain triglycerides. Note that Neocate has several important nutritional shortcomings in relation to the preterm baby's requirements (see [table 2](#)), particularly in terms of protein, sodium and calcium.

Neocate should not be used routinely in preterm babies but can be considered after senior medical consultation in the following situations:

- Preterm babies with unusually prolonged intolerance to standard feeding. This needs to be determined by the attending neonatologist on an individual basis.
- Term and preterm babies with clinical evidence of unexplained colitis which might be due to protein intolerance.

With long term use of Neocate in babies born before 33 weeks and in less than 10th centile babies of 33 and 34 weeks (33w<1600g; 34w<1800g) supplementation should include:

- **Sodium:** Add extra sodium chloride by titrating against serum sodium levels. Most babies born before 32 weeks will need at least an extra 2 mmol/kg/day.
- **Calcium, Phosphate:** To achieve the ESPGHAN recommended intake of calcium and

phosphate, add an extra 1.5 mmol/kg/day of calcium and 1.0 mmol/kg day of phosphate.

- **Vitamins and Iron:**
 - Add Pentavite 0.45ml/day when baby is tolerating 150 ml/kg/day.
 - Add Iron as Ferrous Sulphate (6mg elemental iron per ml) from 28 days of age at 1.2mg elemental iron/kg/day (0.2ml/kg/day) in one dose.
- **Nutritional Supplementation:** Neocate at 180ml/kg/day provides nutrition within the ESPGHAN recommendations although the protein is on the lower end of the range. Extra calorie supplementation can be individualised if babies have unsatisfactory weight gain.

Summary of recommendations on which milk:

First choice milk: Maternal expressed breast milk. This should be supplemented with FM85 breast milk fortifier to 26 calories/30ml when the baby is tolerating 150ml/kg/day in babies born before 33 weeks and 33 and 34 week infants who are less than the 10th centile (33w <1600g; 34 weeks <1800g) . If maternal EBM not available, use donor EBM on an individualised basis in high risk babies.

Second choice milk: Low birth weight formula in babies born before 33 weeks and 33 and 34 week infants who are less than the 10th centile (33w <1600g; 34 weeks <1800g).

Normal term formula in babies born after 32 weeks (e.g from 33 weeks onwards) who are over the 10th centile (33w >1600g; 34 weeks >1800g). Use Nan-HA in babies whose mothers plan to breast feed but need temporary complimentary formula.

In special situations (see above): consider extensively hydrolysed formula such as Neocate but supplement with calcium, phosphate, iron and vitamins in babies born before 33 weeks and those born at 33 and 34 weeks who are less than the 10th centile (33w <1600g; 34 weeks <1800g).

4.3 How should the milk be given?

As preferential nose breathers, a nasogastric tube has a significant space occupying effect on the airway of a preterm baby.¹⁰ Nasogastric tubes are also not possible when babies are receiving nasal CPAP. In view of this, gastric tubes at RPAH are passed via the oro-gastric route.

The controversy remains as to whether feeds should be given by continuous infusion or intermittent bolus. Continuous infusion was hypothesised to reduce respiratory effects of a bolus of milk in the stomach, although there is not much evidence to support this hypothesis. The Cochrane systematic review of trials comparing these two approaches concluded that the evidence did not show any clear advantage of one approach over the other.¹¹

At RPAH, routine feeding is administered by intermittent bolus with the feed interval individualised according to the baby's age and feed tolerance.

4.4 When should milk be started?

This controversy centres on the potential increase risk of NEC with early enteral feeds. The evidence in this area is not strong. In the very preterm infant much of the recent focus has been on minimal enteric (trophic) feeding (MEF). The principle behind this is to commence very low volume enteral feeds on day 1 to 3 of life. The term "trophic" refers to the animal data that suggested this approach augments the maturity of the gut both in terms of structure and function. The most recent systematic review shows neither advantage nor disadvantage from using MEF, though there are non-significant trends to shorter time to feed tolerance without any difference in risk of NEC. The trials are small and inconclusive.¹² We have used MEF at RPAH for some years and there seems no evidence at present to change this practice.

There is no evidence that delayed commencement of feeds protects against NEC in high risk infants (eg growth restricted babies with abnormal antenatal umbilical artery Doppler flows).¹³ However there is good empiric reason in such babies to use breast milk and avoid any early use of formula milk.

Summary of recommendations on when to start:

- **Babies born after 32 weeks (33 weeks and over) who are normally grown (>10th centile)** can be started immediately on intermittent bolus milk feeds according to usual fluid requirements. In mothers who wish to breast feed, we should discuss with them about the transitional use of formula milk (NAN-HA) while we await sufficient supply of EBM.
- **Babies born between 30 and 32 weeks who are well** (e.g not on respiratory support) should have a peripheral IV inserted to allow slow increase in enteral milk feeds starting at 1ml/hr on day 1.
- **Babies born before 30 weeks and babies born from 30 weeks onwards who have respiratory problems or other complications** should start minimal enteric feeds at 1 ml every 4 hours as soon as mother's breast milk is available.
- **In all babies:**
 - Mother's lactation should be supported from birth.
 - Where breast milk is not available by 72 hours, consideration of alternative feeding regimens should be considered in consultation with the mother.
 - Delayed commencement of enteral feeds may need to be considered in unusually sick or complicated babies on an individualised basis.

4.4 How quickly should feeds be increased?

Whether rapid advancement of enteral feeds is a risk factor for NEC remains unresolved. The current Cochrane review amalgamated results from trials which compared daily advancement rates of 15 to 20 ml vs 30 to 35 ml/kg showed no differences in outcomes though slower advancement, predictably, resulted in later achievement of full feeds, median difference 2 to 5 days.¹⁴ The studies were limited by small size and not containing many extremely low birth weight babies.

In a clinical trial not included in the Cochrane review because it was primarily focused on delayed grading up of feeds, Berseth et al¹⁵ randomised babies born before 32 weeks to starting and remaining on 20 ml/kg/day until day 10 versus increasing by 20ml/kg/day up to 140 ml/kg/day. The

trial was stopped early due to an excess of cases of NEC in the rapid advancement arm. Consistent with this, a recent multicentre case control study of babies with NEC showed no difference in day of starting MEF but that babies who developed NEC were advanced from MEF significantly earlier than controls (3.3 vs 6.2 days).¹⁶ These data suggests it may be prudent not to advance from MEF too quickly in the baby at high risk of NEC e.g the extremely preterm baby or the IUGR baby with antenatal Doppler changes.

Summary of recommendations on how quickly to increase:

- **In babies born before 28 weeks**, caution should be applied to increasing feeds above 1ml/hr within the first 5-7 days.
- **In preterm babies born after 27 weeks (e.g 28 weeks onwards), who commence on IV fluids at birth:** The rate of increase needs to be individualised however the Cochrane review would suggest that in uncomplicated preterm babies, feeds can be advanced up to 30 to 35 ml/kg per day if tolerated without adverse effect.¹⁴ In babies born after 31 weeks who start on IV fluids, it may be reasonable to increase feeds faster than that.
- **How should the rate of increase be individualised?** In terms of the hourly bolus feeds, this can range from an increase of 1ml/hr every 4 hours to 1ml/hr every 24 hours or even longer in some babies. The following factors should be considered in individualising the rate of feed increase:
 - Gestation and weight of the baby.
 - How sick the baby is or has been.
 - How well the milk is being tolerated (vomits or large residuals)
 - Any abdominal signs e.g. distension.
 - Bile stained aspirates, though these are common and it may be reasonable to continue to increase if aspirates are small and only lightly bile stained.
 - Special situations (see below).
- **In babies fed with milk from birth:** Feeds should be increased as shown:
 - Day 1- 60 ml/kg
 - Day 2- 90 ml/kg
 - Day 3- 90 ml/kg
 - Day 4- 120 ml/kg
 - Day 5- 120 ml/kg
 - Day 6- 120 ml/kg
 - Day 7- 150 ml/kg

These daily volumes should include any intravenous fluids in babies on combined intravenous/enteral intake and should reflect total ensured delivered volume unless eligible for individualised variation.

Individualised variation of daily intake volumes:

In healthy term babies (≥ 37 weeks) undergoing normal transition who are expected to start taking breast sucking feeds quickly, consider giving up to 30mls/kg/day less than the daily requirements above to encourage establishment of breast feeding.

Volumes lower than the above daily amounts should **NOT** be given to any baby with risk factors for hypoglycaemia or in any baby who has had documented hypoglycaemia (≤ 2.0 mmol/l in first 24 hours or ≤ 2.5 mmol/l after 24 hours).

4.5 What should be the final feed volume?

As shown in [table 1](#), 150 ml/kg of fortified breast milk provides nutrients within the lower range of requirements for several factors and below requirements for some factors, most importantly protein. The more immature and the smaller the baby, the more important these nutritional limitations will be. Most feeding regimens aim for a final feed volume between 150 and 200 ml/kg/day.

At RPAH we conducted a randomised trial in babies born before 30 weeks comparing remaining at a final feed volume of 150 ml/kg/day to advancing to 200 ml/kg/day.¹⁷ The 200 group gained weight more quickly but there was no difference in other growth parameters. But about half the 150 group failed to gain weight adequately and about half the 200 group had to have feed volumes reduced (to a mean of 180 ml/kg/day) due to feed intolerance or fluid overload.

The important message we drew from this study was the need to individualise final feed volumes to the baby by titrating against the weight gain and history of feed intolerance.

Summary of recommendations on final feed volume:

In babies born before 33 weeks or 33 and 34 weeks and less than 10th centile (33w <1600g; 34 weeks <1800g), the target total feed volume should be 180 ml/kg/day. This should be achieved by:

1. Increasing hourly bolus feeds with unfortified EBM, DBM or preterm formula to 150 ml/kg/day as described above.
2. After 24-48 hours of tolerance with unfortified EBM or DBM at 150 ml/kg/day, add FM85 to 26cals/30ml.
3. After 48-72 hours of tolerance of fortified EBM or preterm formula, increase to 180 ml/kg/day in three daily steps of 10 ml/kg. Consider going faster than this in more mature babies.

In babies born after 32 weeks and birth weight above than 10th centile (33w >1600g; 34 weeks >1800g), the target total feed volume should be 150 ml/kg/day.

In all babies, the final feed volume should be titrated against weight gain and feed tolerance. Weight gain once on full feeds should be about 15g/kg/day (range 10-25g/kg/day). Less than this suggests calories need increasing by increasing volume or calorie content of the milk. Weight gain more than 25g/kg/day should raise the possibility of fluid retention particularly in babies with chronic lung disease.

4.6 Vitamin Supplementation.

The last trimester is an important time for transfer of vitamins to the fetus. The preterm infant misses out on this transfer and because breast milk has low vitamin concentrations, the vitamins contained in breast milk fortifier are important. As can be seen from table 1, fortified EBM at 180 ml/kg/day largely meets vitamin requirements with the exception of vitamin D and vitamin A.

Vitamin D: Vitamin D is important for supporting a range of physiological processes, particularly bone mineralization and calcium absorption from the GI tract. The study of Bronner et al¹⁸ suggested that preterm infant calcium absorption was largely independent of Vitamin D level, however two more recent studies have questioned this, both showing better calcium absorption

rates in preterm babies supplemented with 1200 IU of Vitamin D a day.^{19,20}

Because of these findings the ESPGHAN recommendations are that Vitamin D should be supplemented in preterm babies to 800-1000IU per day (note **not** per kg/day) during the first months of life.

Vitamin A: Vitamin A is a group of fat soluble compounds used by the body for regulation and promotion of growth and differentiation of many cells, including cells in the retina of the eye and the cells that line the lung. Preterm infants have low vitamin A levels at birth. This may contribute to an increased risk of developing chronic lung disease.

Cochrane review of trials of vitamin A supplementation in preterm babies showed reduced incidence of oxygen requirement at 36 weeks corrected age and an insignificant trend to less retinopathy of prematurity.²¹ The intervention in the included trials involved intramuscular injections of vitamin A. In the one trial where vitamin A was used orally, the dose was 1500 µg/day. ESPGHAN highlights the risk of potentially toxic levels of vitamin A at doses above 1200 µg/day thus they recommend a dose between 400 and 1000 µg/kg/day.¹

Vitamin A and D in TPN: The TPN regimen at RPAH provides 160 IU/kg/day of Vitamin D and 276 mcg/kg/day (920 IU/kg/day) of Vitamin A at 3gms/kg/day of lipid infusion.

Vitamin A and D in EBM fully fortified with FM85 at 180 ml/kg/day will deliver about 290 IU of Vitamin D and 756 µg of Vitamin A.

Vitamin A and D in S26 low birth weight formula at 180 ml/kg/day will deliver about 240 IU of Vitamin D and 333 µg of Vitamin A.

4.7 Mineral Supplementation

Sodium: Most of a preterm baby's mineral and trace element requirements will be met using 180 ml/kg of fortified breast milk or low birth weight formula. The exception will be sodium where the intake will be at the lower end of the recommended range. Sodium chloride supplementation should be titrated to the serum sodium level, starting at 2 mmol/kg (46 mg/kg).

Calcium and Phosphate: Requirements for these minerals will be met at 180 ml/kg/day of fortified EBM/DBM or low birth weight formula but these will need monitoring with blood tests as detailed in the 'Metabolic Bone Disease' guideline. High risk babies for deficiency in these minerals will include:

- Babies with delayed feed tolerance requiring prolonged TPN.
- Babies who do not tolerate FM85.
- Babies who are fed with extensively hydrolysed formula such as Neocate.

Babies with blood test evidence of calcium or phosphate deficiency will need supplementing as detailed in the 'Metabolic Bone Disease' guideline.

Iron: Total body iron in a newborn is approximately 75mg/kg with most of this within the blood volume thus the smaller a baby, the lower their iron stores. Risk of iron deficiency is compounded by losses due to blood tests and low iron content of EBM. On the other hand there are risks of excessive iron supplementation including increased infection risk, poor growth and disturbance of

absorption of other minerals. There is also the potential risk of free oxygen radical formation increasing the risk of ROP.²² For these reasons, we've traditionally delayed administration of enteral iron for 6-8 weeks.

However two trials of early supplementation (when tolerating 100ml/kg) vs no enteral iron supplements have shown no adverse effects of early iron administration and one trial showed less early iron deficiency and lower transfusion rates.^{23,24} Further an RCT of an iron fortified HMF (commenced when tolerating 100ml/kg) showed no adverse effects and a lower transfusion rate with iron fortification of HMF.²⁵

Summary of recommendations for mineral and vitamin supplementation:

In babies <33 weeks or 33 and 34 weeks and birth weight <10th centile.

- **If tolerating 180ml/kg/day of fortified EBM or LBW formula:** Nutritional and vitamin requirements are met with the possible exception of Vitamin D. Our view is that the evidence supporting the ESGHAN Vitamin D recommendation is not strong enough to support routine supplementation of Vitamin D above that provided by FM85.
- **If baby is not tolerating FM85 in EBM or has been changed to Neocate:**
 - Add 1.5 mmol/kg/day of calcium and 1.0 mmol/kg day of phosphate
 - Add Pentavite 0.45ml/day when baby is tolerating 150 ml/kg/day.
 - Add Iron as Ferrous Sulphate (6mg elemental iron per ml) from 28 days of age at 1.2mg elemental iron/kg/day (0.2ml/kg/day) in one dose.

4.8 When to stop FM85 supplementation of human milk or LBW formula and post-discharge nutrition.

Supplementation of human milk with multicomponent fortifiers is associated with short term increases in weight gain, linear and head growth.²⁶ For almost all studies, fortification ceased at a specified weight (generally 1800 to 2000g) or at discharge.²⁶ Limited available data do not provide convincing evidence that feeding preterm infants with multi-nutrient fortified breast milk compared with unfortified breast milk following hospital discharge affects important outcomes including growth rates during infancy.²⁷ However, there is substantial heterogeneity between trials. One trial of multicomponent fortification of half human milk feeds for 12 weeks post discharge reported increased weight, head circumference, bone mineral density and visual acuity in fortified infants.²⁸⁻³⁰ A second trial in which fortifier was given once daily mixed in 20 mL to 50 mL of milk reported no significant influence on growth parameters at 1 year of age compared with unfortified mother's milk.³¹ These trials did not enrol infants with postnatal growth failure or chronic lung disease.

The available data (7 trials, 631 infants) do not provide strong evidence that feeding preterm infants following hospital discharge with nutrient-enriched formula compared with standard term formula affects growth rates or development up to 18 months post-term.³² There are no data from randomised controlled trials to determine whether feeding preterm infants following hospital discharge with nutrient-enriched formula milk versus human breast milk affects growth and development.³³ Again, These trials did not enrol infants with postnatal growth failure or chronic lung disease.

A single trial in infants with bronchopulmonary dysplasia comparing an isocaloric protein and mineral enriched formula to a standard formula reported greater linear growth, lean and bone mass

in the enriched formula group.³⁴ ESPGHAN notes that infants discharged with a subnormal weight for postconceptional age are at increased risk of long-term growth failure, and recommends the human milk they consume be supplemented with a human milk fortifier to provide an adequate nutrient supply.³⁵

Summary of recommendations on when to change LBW formula to term formula or when to stop fortifying EBM:

Once a baby is feeding at the breast there are practical limitations to providing nutritional supplementation and not enough evidence to support routine supplementation. This will need individualising in babies not growing adequately.

Prior to establishment of sucking feeds at breast or bottle, we will stop breast milk fortification or change low birth weight formula to normal term formula in:

1. AGA infants with normal growth velocity ($\geq 15\text{g/kg/day}$) may cease multicomponent fortification when they reach 2200g.
2. AGA infants with normal growth velocity who have achieved 3 sucking feeds for 2 consecutive days may cease multicomponent fortification between 1800g to 2200g.
3. Continued fortification, at least until a post-conceptional age of 40 weeks, and possibly until about 52 weeks post-conceptional age, should be considered in the following groups of babies:³⁵
 - Infants with postnatal growth failure (weight percentile $<10^{\text{th}}$),
 - Infants with low growth velocity (weight gain $<15\text{g/kg/day}$), and
 - Infants with increased energy requirements including those infants with chronic lung disease with increased work of breathing.

4.9 Post-discharge iron and vitamins supplementation:

Iron: The recent trial of Berglund et al³⁶ suggested that all babies, breast and formula fed, born less than 2.5kg would benefit from early iron supplementation. This randomised controlled trial enrolled 285 babies birth weight between 2 - 2.5kg to one of three arms; placebo, iron at 1mg/kg/day and at 2mg/kg/day from 6 weeks to 6 months. The main outcome was the iron deficiency anaemia rate at 6 months. This was 10% with placebo, 2.7% with 1mg/kg/day and 0% with 2mg/kg/day. Benefits were greatest in babies exclusively breast fed and preterm.

Pentavite: There is little evidence on this though it is apparent that breast milk does not have adequate vitamins for preterm babies in the post discharge period. Vitamins are added to infant formula but it is less clear whether these standard formulas contain adequate vitamins for preterm babies. Table 3 below shows vitamin intake at 150ml/kg of S26 gold compared to the ESPGHAN recommendations. It can be seen that A and D are low and the others are in the lower end of the recommended range.

Recommendation: That for consistency we provide routine post-discharge iron and vitamin supplementation to all babies who are born before 35 weeks (e.g 34 weeks and less) with birth weight less than 2.5 kg. Supplementation can be considered on an individual basis for babies born

after 34 weeks if they are very growth restricted.

Regimen: Pentavite 0.45ml/day and Ferrous Sulphate (6mg elemental iron per ml) at 1.0ml/day both as a once daily dose to be started when stopping breast milk fortification or changing from LBW to Term formula in the smaller babies.

If babies of 33 and 34 weeks >10th centile (e.g babies not getting fortified BM or LBW formula) are slow in establishing sucking feeds then Pentavite and Ferrous Sulfate should be started in day 28 at the latest.

4.10 Special Situations.

Preterm and growth restricted babies with absent or reversed end-diastolic flows on antenatal Doppler:

Observational studies, including one from this unit, have pointed to reversed EDF as being a risk factor for the development of NEC.^{37,38} This association led to a range of feeding practices in these babies such as withholding feeds for a period after birth. This has now been tested in the multicentre ADEPT trial in the UK where 404 babies born before 34 weeks, under the 10th centile and with antenatal Doppler changes were randomised to early (day 1/2) or late (day 5/6) introduction of feeds. There was no difference in the NEC rate (note: preliminary conference presented data as not published yet).¹³

Thus we should follow similar principles to other high risk babies such as the extremely premature.

- Insert a peripheral IV after birth to allow slow introduction of feeds.
- Aim to establish early central venous line access and start TPN.
- Initially use only EBM as it becomes available.
- Consider supplementing with formula in babies born after 30 weeks after 72 hours if EBM supply is slow.

Prolonged enteral feed intolerance: Intolerance of enteral feeds is very common in preterm babies and the initial response is to titrate feed volumes to the tolerance e.g. advance feeds in babies with minimal aspirates and no vomiting and hold at current volumes or reduce volumes in babies with large aspirates and/or vomiting. There is no magic cure for this problem other than continue parenteral nutritional support and patience and time. But further action should consider the following.

1. **Lack of evidence for Prokinetics:** There is no evidence to support the preventative or therapeutic use of prokinetics such as erythromycin. The Cochrane meta-analysis of 10 randomised trials on the use of erythromycin as a prokinetic found no evidence of benefit in either prevention or treatment of enteral feed intolerance.³⁹ We do not routinely use prokinetics at RPAH.
2. **Need to exclude surgical cause:** This is rare but needs to be considered in any baby with prolonged feed intolerance, particularly if there is associated bile stained aspirates and abdominal distension. Consultation about need for contrast imaging of the GI tract should be through the RPAH Paediatric Surgeon on call.
3. **Extensively hydrolysed formula milk e.g Neocate:** Sometimes, for reasons that are not clear, babies will tolerate an extensively hydrolysed formula when they won't tolerate breast milk or low birth weight formula. This should be considered in babies with very prolonged intolerance but should only be initiated by senior medical staff. There are important

considerations in terms of undermining mother's confidence in her breast milk and it needs to be emphasised to the parents that this will most likely be a temporary change.

RPA Newborn Care SUMMARY FEEDING GUIDELINES

Term infants who are well and are expected to start sucking feeds early may commence on 30mls/kg/day less than the defined volumes below – However lower volumes should NOT be given to any baby with risk factors for hypoglycaemia or who has had BSL $\leq 2.0\text{mmol/l}$ before 24 hours or $\leq 2.5\text{mmol/l}$ after 24 hrs.

Which milk?

First choice milk: Maternal expressed breast milk (EBM). If maternal EBM not available, neonatologist may advise human donor milk (HDM) in high risk babies. Fortify with BMF if born before 33 weeks and 33 to 34 week infants who are less than the 10th centile – *see tables*.

Second choice milk: Low birth weight formula (S26 LBW) for babies born before 33 weeks and 33 to 34 week infants who are less than the 10th centile – *see table*.

Gestation	BMF or S26 LBW formula if:
33 weeks	<1600g
34 weeks	<1800g

Normal term formula (S26) is used in babies born after 32 weeks who are over the 10th centile – *see table above*.

Partially hydrolysed formula (NAN Ha) is used for babies born after 32 weeks who are over the 10th centile who will be breastfeeding.

Grading fluid volumes and milk supplements:

Day	Infants < 33 weeks or 33-34 weeks and less than 10 th centile	Infants ≥ 33 weeks and above 10 th centile
1	60 mls/kg/day - IV fluids	60 mls/kg/day
2 - 3	90 mls/kg/day	90 mls/kg/day
4 - 6	120 mls/kg/day	120 mls/kg/day
7	150 mls/kg/day	150 mls/kg/day -
Grading up calories and volume.	<ul style="list-style-type: none"> After 48 hours tolerating 150mls/kg/day of milk Add FM85 to 23 kcal to breast milk, then after 48 hours tolerance; Add FM85 to 26 kcal, then after 48 hrs tolerance; Grade up to 180 mls/kg/day in 10ml/kg daily increments. 	Continue at 150 mls/kg/day unless weight gain is inadequate.
If intolerant of BMF.	For babies not tolerating FM85 added to EBM or are receiving Neocate – feeds will be supplemented with Pentavite, iron, calcium & phosphate as set out in the enteral feeding guideline.	
When to stop BMF or LBW formula.	Cease FM85 or change from LBW to normal formula when: over 2.2kg or sucking three feeds a day on two consecutive days and appropriately grown and gaining weight $>15\text{g/kg/day}$.	

Vitamin and Iron regimen that will be continued after discharge:

Who to supplement? All babies born < 35 weeks with birth weight less than 2.5 kg.

When to start? When sucking 3 feeds a day on two consecutive days (e.g. when the <33 week babies stop FM85 or change from LBW formula).*

What to give? Pentavite 0.45mls/day & Ferrous Sulfate (6mg elemental iron/ml) at 1.0ml/day both as a once daily dose.

*Babies of 33 and 34 weeks (>10th centile) should start on day 28 if they have not established sucking by this time.

Table 1: Comparison of the nutritional provision of breast milk and breast milk supplemented with FM85 human milk fortifier to 23 cal/100ml and 26 cal/100ml. *Note cells shaded red mark those below the recommended intake range.*

Preterm Babies Fluid and Nutritional Requirement: from ESPGHAN 2004	Breast Milk	EBM and new FM 85 23cal 2.5g/100ml	EBM and new FM 85 26cal 5g/100ml		
Energy and Fluid					
	/kg/day				
Fluid (ml)	135 - 200	150	150	150	180
Energy (kcal)	110-135	105	117.5	130	156
Protein (g)	3.5 – 5.0	2.1	2.7	3.3	4.0
Lipids (g)	4.8 – 6.6	6.6	6.6	6.6	7.9
Carbohydrate (g)	11.6 – 13.2	10.2	12.9	15.6	18.7
Minerals and Trace Elements					
Sodium (mg)	69-115	28	43	62.4	75
Potassium (mg)	66-132	72	139	187	225.5
Chloride (mg)	105-177	64	77	90	108
Calcium (mg)	120-140	34	90	147	176
Phosphate (mg)	60-90	20	54	88	106
Magnesium (mg)	8-15	5	7.7	10.7	12.8
Iron (mg)	2-3	0.15	1.05	2	2.4
Zinc (mg)	1.1-2.0	0.3	1.2	2	2.4
Copper (µg)	100-132	45	83	100	120.4
Vitamins					
Thiamin (B1) (µg)	140-300	0	135	255	306
Riboflavin (B2) (µg)	200-400	0.15	195	345	414
Niacin (B3) (µg)	380-5500	450	1050	3330	3996
Pantothenic Acid (mg)	0.3-2.1	0.3	0.6	0.9	1.1
Pyridoxine (B6) (µg)	45-300	0	127	240	288
Cobalamin (B12) (µg)	0.1-0.8	0.15	0.225	0.3	0.36
Folic Acid (µg)	35-100	7.5	38	68	82
Ascorbic acid (mg)	11-46	15	19.5	32.5	39
Biotin (µg)	1.7-16.5	0.9	3.7	6.3	7.6
Vitamin A (µg)	400-1000	75	363	630	756
Vitamin D (IU/day) (µg 1/40)	800-1000	6	122.4	242	290
Vitamin E (mg)	2.2-11	0.9	3.52	6.5	7.83
Vitamin K (µg)	4.4-28	0.45	6.15	12.1	114.6
Choline (mg)	8-55	24	24	24	24

Table 2: Comparison of the nutritional provision of the common low birth weight milk formulas and extensively hydrolysed Neocate. *Note red cells mark those below the recommended intake range.*

Preterm Babies Fluid and Nutritional Requirement: from ESPGHAN 2004	S26 LBW		Pre-NAN	Nutri-Prem	Neocate:		
Energy and Fluid							
	/kg/day						
Fluid (ml/kg/day)	135 - 200	150	180	180	180	150	180
Energy (kcal)	110-135	123	148	144	144	106	127
Energy (kcal/30ml)		25.6	25.6	24	24	21.2	21.2
Protein (g)	3.5 – 5.0	3.3	4.0	5.4	4.5	2.9	3.5
Lipids (g)	4.8 – 6.6	6.6	7.9	7.2	7.92	5.3	6.4
Carbohydrate (g)	11.6 – 13.2	12.6	15.12	15.2	13.7	12.2	14.6
Minerals and Trace Elements							
Sodium (mg)	69-115	66	79	92	90	28	34
Potassium (mg)	66-132	128	154	216	148	94	113
Chloride (mg)	105-177	100	120	137	122	64	77
Calcium (mg)	120-140	151	181	209	216	73	88
Phosphate (mg)	60-90	92	110	139	119	52	62
Magnesium (mg)	8-15	12.3	14.8	15	14.2	7.6	9.1
Iron (mg)	2-3	2.1	2.5	3.2	2.5	1.5	1.8
Zinc (mg)	1.1-2.0	1.2	1.4	2.2	1.6	1.1	1.32
Copper (µg)	100-132	135	162	150	144	90	108
Vitamins							
Thiamin (B1) (µg)	140-300	202	242	252	252	90	108
Riboflavin (B2) (µg)	200-400	300	360	360	360	120	144
Niacin (B3) (µg)	380-5500	4305	5166	2880	4320	102	122
Pantothenic Acid (B5) (mg)	0.3-2.1	0.15	0.18	0.14	0.18	0.6	0.72
Pyridoxine (B6) (µg)	45-300	185	222	169	360	120	144
Cobalamin (B12) (µg)	0.1-0.8	0.28	0.34	0.41	0.49	0.3	0.36
Folic Acid (µg)	35-100	43.5	52	74	50	9	11
Ascorbic acid (mg)	11-46	22.5	27	38	23	9	11
Biotin (µg)	1.7-16.5	3.6	13	7.2	5.4	5.8	7.0
Vitamin A (µg)	400-1000	278	333	666	324	118	141
Vitamin D (IU)	800-1000	200	240	268	222	76	91
Vitamin E (mg)	2.2-11	5	6	6.5	5.4	0.75	0.9
Vitamin K (µg)	4.4-28	9.5	11.4	11.5	11	4.8	5.8
Choline (mg)	8-55	22.5	27	36	23	11.25	13.3

Table 3: Compares vitamin provision by S26 milk formula with the ESPGHAN recommended range. Content of Pentavite multivitamin preparation below. (Cells shaded pink; low requirement range: Cells shaded red; below requirement range)

Preterm Babies Fluid and Nutritional Requirement: from ESPGHAN 2004		S26 Normal Formula	
Vitamins			
Iron (mg)	2-3	1.2	1.44
Thiamin (B1) (µg)	140-300	150	180
Riboflavin (B2) (µg)	200-400	225	270
Niacin (B3) (µg)	380-5500	750	900
Pantothenic Acid (B5) (mg)	0.3-2.1	0.45	0.54
Pyridoxine (B6) (µg)	45-300	82.5	99
Cobalamin (B12) (µg)	0.1-0.8	0.3	0.36
Folic Acid (µg)	35-100	12	14.4
Ascorbic acid (mg)	11-46	13.5	16.2
Biotin (µg)	1.7-16.5	3	3.6
Vitamin A (µg)	400-1000	112.5	135
Vitamin D (IU)	800-1000	66	79
Vitamin E (mg)	2.2-11	1.1	1.3
Vitamin K (µg)	4.4-28	10	12
Choline (mg)	8-55	15	18
Pentavite formulation: The standard dose of 0.45 ml Pentavite contains:			
Thiamine (Vit. B1)	540 mcg		
Riboflavine	800 mcg		
Nicotinamide (Vit. B3)	7.1 mg		
Pyridoxine (Vit. B6)	135 mcg		
Ascorbic acid (Vit. C)	42.8 mg		
Cholecalciferol (Vit. D3)	10.1 mcg / 404 IU		
Vitamin A mcg	490 mcg		

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