East of England Neonatal ODN
(Hosted by Cambridge University Hospitals)

East of England Neonatal Network

Enteral Feeding of Preterm Infants on the Neonatal Unit.

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For use in: EoE Neonatal Units Guidance specific to the care of neonatal patients

Used by: Medical Staff, Nurses, Dietitians, AHPs, IFLs

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Chairman East of England ODN Board	**Date:** **Signed:**

Audit Standards:

- **100% of babies on the neonatal unit have feeds initiated and advanced in line with algorithm 1 and where deviation exists a documented explanation is provided.**
- **100% of babies on the neonatal unit receive feeds in accordance with algorithm 2 and where deviation exists a documented explanation is provided.**
- **100% of babies who meet the criteria for human milk fortification receive fortified milk in accordance with algorithm 2 and where deviation exists a documented explanation is provided.**
- **100% of babies on the neonatal units have their anthropometric parameters measured in line with this guidance and where deviation exists a documented explanation is provided.**

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Equality, Diversity & Inclusivity Statement

This policy document aims to meet the diverse needs of our service, population and workforce, ensuring that none are placed at a disadvantage over others. It takes into account the provisions of the Equality Act 2010 and promotes equal opportunities for all. This document ensures that no one receives less favourable treatment on the protected characteristics of their age, disability, sex, gender reassignment, sexual orientation, marriage and civil partnership, race, religion or belief, pregnancy and maternity. The East of England Neonatal ODN advocates due regard to the various needs of different protected equality groups in our network. The East of England Neonatal ODN acknowledges the additional challenges that gender identity can have, specifically around the perinatal period and in regards to infant feeding. We are aware that there is not yet universal language that addresses all families accessing maternity and neonatal care. We refer to breastfeeding and breastmilk but recognise terms such as chestfeeding, bodyfeeding, nursing, lactation, or providing human milk may be more preferable for and accurate to some of the families we support. We support mothers to express their breastmilk and to breastfeed their babies, but we also understand that not all birthing parents will identify as women or as mothers. We will always use the individual's preferred language, name, pronouns or terminology that they are most comfortable with, as we recognise the importance of providing inclusive and respectful perinatal information and support to all pregnant women, pregnant people, mothers, parents and families.

Section 1: Introduction

As survival rates for preterm infants improve, more emphasis is being put on improving the quality of outcome by giving more focus to optimising nutritional management.
Suboptimal nutrient provision, commencing in the early neonatal period contributes to postnatal malnutrition and accumulation of growth deficits, especially in the smallest, most immature infants. Delaying the introduction of adequate and appropriate enteral luminal nutrition exacerbates nutritional deficits and reduces resistance to infection. Conversely, over nutrition and excessive growth acceleration may lead to adverse health issues such as diabetes, obesity and cardiovascular disease in later life (1).
The goals of nutritional support in the preterm infant include:

- Achieving an acceptable standard of short term growth.
- Meeting the recognised nutritional requirements of the preterm infant.
- Preventing feeding-related morbidities, especially the prevention of Necrotising Enterocolitis (NEC).
- Optimising longterm health and developmental outcomes.

The majority of preterm infants receive either enteral nutrition (EN) or a combination of parenteral nutrition (PN) and EN with a time of transition in between, which is influenced by local feeding practices and assessments of feeding and metabolic intolerances (2-4).

Although early progressive PN and EN strategies have been shown to reduce the cumulative energy and protein deficits that occur during the first weeks of life (5,6) the time of transition can be a critical period for poor growth (7). The use of standardised feeding guidelines and protocols, especially through the transition phase (8,9) can help in reaching nutritional goals (10). Additionally, data from observational studies suggest that standardising feeding practice allows preterm infants to achieve full enteral feeds faster, shorten both the time on PN and length of hospital stay, decrease the rates of NEC, and improve growth and neurodevelopment (11,12-19).
The East of England ODN has had standardised guidance in place for parenteral nutrition since 2013 EOE ODN PN guidelines and enteral feeding since 2011. This document, alongside the accompanying Nutrition Care Pathway represent the fourth update of this network wide guidance. Together they meet the 2022 recommendation from the European Society of Paediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN) that states that all neonatal units establish a standardised feeding protocol that defines the:

- duration of minimal Enteral Feeds (MEF)
- daily advancement of milk feeds
- definition and management of gastric residuals
- definition, and approach to feeding intolerance
- breast milk fortification strategy
- nutritional definition of full enteral feedings. (20)

This guideline aims to use available evidence alongside national best practice to provide, within a practical reproducible framework, both optimal nutritional care and the individual nutritional needs of infants born prematurely in the East of England.

It is designed to be used in conjunction with:

- **Individual clinical assessment processes where decisions are made regarding the initiation and advancement of feeds.**
- **Families and parents, who should be involved in decisions relating to nutritional care.**
- **Existing network guidelines and policies that support the establishment of oral feeding of preterm infants and the implementation of the WHO Baby Friendly Initiative Standards and Code of Practice.**
- EOE Oral Feeding Guideline
- EOE Neonatal Feeding Guideline

Section 2.0: Nutritional Requirements of the Preterm Infant.

Evidence based estimations form the basis of published nutritional requirements for preterm infants, the most recent being ESPGHAN 2022 (20)

These calculated requirements are higher than those of a term infant as preterm infants are born at a time of rapid nutrient deposition, and where in utero growth rates would have been 2-3 times greater than those of an infant born at term. However, these increased nutrient demands are not the same for every nutrient and are therefore not met by a simple straight increase in volume of human milk provision. This inequity of demand has led to the development of specialist formulas and human milk fortifiers for use in the preterm population.

Nutrient	Term infant	Preterm infant <1800g ESPGHAN 2022
Energy (Kcal/kg)	95 -115	115 - 140 (-160)
Protein (g/kg)	2	3.5 - 4.0 (- 4.5)
Protein:energy ratio g/100Kcal		2.8 – 3.6g / 100Kcal
Fat (g/Kg)		4.8 – 8.1
Carbohydrate (g/kg)		11 – 15 (-17)
Sodium (mmol/kg)	1.5	3.0 – 5.0 (-8.0)
Potassium (mmol/kg)	3.4	2.3 – 4.6
Calcium (mmol/kg)	3.8	3.0 – 5.0
Phosphorous (mmol/kg)	2.1	2.2 - 3.7

Table 1 – Selected nutrient requirements for preterm infants (ESPGHAN 2022)

2.1 Energy provision

Energy is required by all cells of the body. The supply of energy for preterm infants is made up of a number of elements:

- Resting energy expenditure (REE) (60-70Kcal/Kg)
- Requirements of any physical activity
- Diet induced thermogenesis
- Tissue deposition in the form of growth (approximately 3.6 – 4.7Kcal/g of new tissue)

Available recommendations for energy, whilst acknowledging that nutritional needs are different in the ex-utero environment, aim to support growth, body composition and nutrient retention in line with those of the in-utero fetus (21). They do not consider

changes in energy needs related to acute illness or chronic disease states.

The average, optimal weight gain for a preterm infant is 17-23g/Kg/day. The energy needed for this rate of growth based on an REE of 60-70kcal/kg/day would be 106-138kcal/kg/day. Allowing for energy lost in stool (5-10%), this equates to a total energy intake of approximately 115-160kcal/kg/day, with a range of 115-140kcal/kg/day sufficient for adequate growth. (20)

It is important to try and ensure that any weight gain represents a proportional balance between the accretion of fat free mass (FFM) and fat mass (FM), as this may have implications for long-term health (22,23). Delivery of energy and protein intakes within the recommended ranges and with the correct protein:energy ratio (PER) is vital to this process. Studies suggest that the optimal enteral PER for preterm infants is 2.8 - 3.6g/100kcal (24, 25), with PERs at the higher end of this range associated with improved weight gain and FFM accretion.

Recommendations:

- **The recommended energy intake for most healthy, growing preterm infants is 115-140Kcal/Kg/day.**
- **Energy intakes of 140 – 160Kcal/Kg/day (alongside appropriate and adequate protein provision) may be needed for infants where growth is suboptimal.**
- **A protein to energy ratio of 2.8-3.6g/100kcal is recommended when intakes of both are within the recommended ranges.**

2.2 Protein provision

Protein intake (in the presence of adequate energy) is the main driver for the accumulation of fat free mass (FFM). Protein requirements for preterm infants are based on the following:

- An assumed protein accretion rate of 2.5 g/kg/day in infants weighing 500 g and 2.2 g/kg/day in infants weighing 1800 g
- Obligatory nitrogen losses (~1 g protein/kg/d)
- Suboptimal dietary protein absorption & intestinal utilisation of amino acids (0.5 g/kg/d)

Unfortunately there is no easy way to determine the protein requirements for individual infants. Based on these factors however, an extremely preterm infant requires approximately 4g/Kg/day of enteral protein to achieve intrauterine accretion rates (45). Plasma urea levels have been used to try and inform on optimal intakes. Although there is a strong correlation between urea levels and protein intake, there is limited evidence to suggest urea levels inform on actual protein synthesis. Regular monitoring can however be useful in managing protein intake.

Recommendations:

- **The recommended protein intake for preterm infants is at least 3.5 to 4.0 g protein/kg/d (alongside adequate and appropriate energy provision)**

- **Protein intake may be increased to 4.5 g/kg/d where growth is slow, provided there are no other causes for suboptimal growth.**

- **Plasma urea should be monitored at regular intervals (ideally 2x week)**

    - **Urea concentrations (after the first couple of weeks of life) that are lower than local laboratory references ranges (generally 3.5-5.7mmol/L), may indicate inadequate enteral protein intake.**

    - **Urea concentrations (after the first couple of weeks of life) that are higher than local laboratory reference ranges (generally 3.5-5.7mmol/L), may suggest the need to reduce protein intake if in the absence of fluid or renal derangements.**

Section 3: Feeding the Preterm Infant (Algorithm 1)

3.1 When to start feeding and the role of minimal enteral feeds (MEF)

The objective of early feeding is to reduce time on parenteral nutrition, with its associated infectious and metabolic risks, and to stimulate gut maturation, motility and hormone release.
Trophic feeding or minimal enteral feeding (MEF) refers to the introduction of small amounts of nutritional insignificant enteral feeds (preferably colostrum/breast milk) at intakes of 12–24 ml/kg/day without any advancement in feed volumes during the first three (26) to seven days after birth (27). The rationale behind this feeding strategy is to "prime" the gastrointestinal mucosa in anticipation of feed advancement.
Concerns exist however that introducing enteral feeds early (within the first few days of life) may lead to feed intolerance and increase the risk of NEC.

A meta-analysis of a number of studies from the 1990s (28) considered the impact on feeding, morbidity and mortality of enteral fasting versus MEF in VLBW infants. In these studies MEF commenced within the first three days of life and continued to day 7-10. MEF was found to be safe in comparison to complete enteral fasting. A second review, originally conducted in 2013 and updated in 2022, focused on the prevention of NEC when comparing enteral fasting with delayed (4-7 days) versus early (up to 4 days) introduction of progressive enteral feeding. This meta-analysis did not detect any effect on the risk of NEC or mortality related to introduction of enteral feeding and concluded that delaying the introduction of progressive enteral feeds beyond 4 days of life did not reduce the risk of NEC in very preterm or very low birthweight preterm infants, including growth restricted infants. The authors also concluded that delaying the introduction of feeds may slightly reduce feed intolerance, however delay may also increase the risk of invasive infection and prolong the establishment of full enteral feeding by 2-4 days (29,30).

The ADEPT trial indicated that growth restricted preterm infants born after absent or reversed end-diastolic flow who are fed from the second day after birth achieve full feeds earlier than those commencing feeds on day 6, with no increase in the incidence of sepsis or NEC (31).
Two more recent RCTs have investigated early progressive feeding without MEF compared to delayed progressive feeding after a 3 to 4-day course of MEF, and found conflicting results in relation to time to full feeds and growth (32,33).

It remains unclear whether maintaining MEF for a number of days has any advantage when compared to initial, early progressive feeding. A balanced view should therefore be taken between the evidence linking a lack of luminal nutrients to gut atrophy, and the lack of evidence associating early progressive feeds with adverse effects in preterm, low birth weight infants. This view would support the introduction of early progressive feeding in extreme, very preterm and low birth weight infants to support their gut development and transition from parenteral to enteral nutrition. (20)

Recommendations:

- **There is no clear beneficial effect of MEF of any duration compared to advancing feeds immediately after birth, therefore for most preterm infants, including those considered "high risk" (see section 3.2), start enteral feeds as soon as possible after birth and advance as clinically indicated.**

Were a decision is taken to commence MEF, ensure that:

- **Maternal colostrum is utilised wherever possible**
- **MEFs are commenced as soon after delivery as possible**
- **MEF are maintained for no more than 3-7 days**
- **MEFs are initiated during Indomethicin/Ibuprofen treatment.(34)**

3.2 Rate of advance of feeding

Retrospective analysis of NEC cases undertaken in the early 90s led to the recommendation of limiting feed advancement to 20ml/kg/day (35), whereas a later study comparing 15ml/kg/day with 35ml/kg/day found that infants in the faster group achieved full feeds and weight gain quicker with no increase in the incidence of NEC (36).
A recent Cochrane review published in 2021 sought to review the impact rate of feed advancement had on NEC prevention in VLBW infants (37). The review identified 14 randomised controlled trials in which a total of 4033 infants participated (2804 infants were participants in the Speed of Increasing milk Feeds trial SIFT). Although most participants were stable, very preterm infants of birth weight appropriate for gestation, about one-third were extremely preterm or extremely low birth weight (ELBW), and about one-fifth were small for gestational age (SGA), growth-restricted, or had demonstrated absent or reversed end-diastolic flow velocity (AREDFV) on antenatal doppler. The included trials typically defined slow advancement of feed as daily increments of 15 to 20 mL/kg, and faster advancement as daily increments of 30 to 40 mL/kg.

The authors of the Cochrane review concluded that available trial data do not provide evidence that advancing enteral feed volumes at daily increments of 15 to 20 mL/kg (compared with 30 to 40 mL/kg) reduces the risk of NEC or death in very preterm / VLBW infants, extremely preterm / ELBW infants, SGA /growth-restricted infants, or infants with antenatal AREDFV.
They also concluded that infants who had slow advancement of feed volumes established full enteral feeding and regained birth weight several days later than infants who had faster rates of advancement of feed volumes (there was no evidence of effect on length of hospital stay). The clinical importance of these effects however is unclear, as longer-term growth outcomes were not assessed.
Developmental outcomes were only reported as part of the SIFT trial. Analysis suggested that slow advancement of enteral feed volumes probably does not affect the risk of moderate or severe disability but does suggest that slow advancement of enteral feed volumes may slightly reduce the risk of cerebral palsy. In addition there was an unexpected, unexplained increase in the risk of moderate to severe motor impairment in the faster increment group that needs to be considered. (38).

Evidence to this point suggests that there is little benefit in advancing feeds in increments less than 30ml/kg/day in all preterm infants, however in none of the studies is the practical aspect of tolerance of such volumes in extremely preterm/ extremely low birthweight infants clearly defined. A meta-analysis carried out within the Cochrane review of 9 of the trials (719 infants) (37), demonstrated that slow advancement of enteral feeds may slightly increase the risk of feed intolerance. However only a small number of the reviewed studies included infants <1000g, and the SIFT trial, which accounted for the vast majority of infants in the review, did not report on either feed tolerance and associated feed interruption at all.

A follow up analysis from the ADEPT trail in 2013 sought to describe the feeding and gastrointestinal outcomes in growth restricted < 29 weeks gestation infants and to define the rate of feed advancement best tolerated by the group (39). Analysis demonstrated that 90% of babies <29 weeks had feed intolerance and 39% developed NEC. (This latter risk was reduced by the use of human milk as the majority feed during advancement). This high risk group were very slow to tolerate enteral feeds. The median volume of feed tolerated was much lower in the first 10 days of life than the target trial regimen, and the subsequent rates of advancement remained lower than targeted throughout, with a median age of 28 days to reach full feeds. The group concluded that although the benefits of starting feeds early in growth restricted preterm infants are well established, they may require a slower rate of feed advancement in order to facilitate gut adaptation.

Publication of the full SIFT trial (38) demonstrated that advancing milk feeds at a faster 30ml/kg/day rate compared to a slower 18ml/kg/day does not affect survival without moderate or severe neurodevelopmental disability at 24 months corrected for gestational age. Nor did it affect risk of late onset sepsis, NEC or death in VLBW infants. However, care needs to be taken when interpreting the SIFT data as infants were a median of 4 days old at time of randomisation - the trial therefore may not adequately inform the relative safety of these feeding volume increments during the first few days of life.

In addition, a further economic evaluation that ran alongside the SIFT trial suggested that a faster rate of increase in feed volume for VLBW infants was more costly overall and less effective in achieving the primary outcome of survival without moderate or severe neurodevelopmental disability when compared to a slower rate of advance. The study concluded that based on the results of the economic evaluation carried out, increasing milk feed volumes at a faster rate in VLBW infants is not a cost effective strategy and cannot therefore be recommended. (40).

In light of the evidence and the fact SIFT neither informed on the impact of feed rates before day 4 of life, nor reported on feed intolerance and feed interruption, a pragmatic approach to the rate of feed advancement in the most at-risk group of infants has to be considered. These considerations have been built into the steps recommended in the East of England Standardised Enteral Feeding Regimen.

Recommendations:

- **In medium and standard risk infants advance feeds at a rate of 30ml/kg/day.**

- **In selected high risk infants advance feeds at a rate of 20ml/kg/day.**

Infants considered high risk should include:

- **<28 weeks gestation or <1000g birth weight**
- **infants re-establishing feeds after an episode of necrotising enterocolitis (NEC) or following gastrointestinal surgery**
- **perinatal hypoxia-ischaemia with significant organ dysfunction**
- **hypotensive/unstable ventilated neonates**
- **absent or reversed end diastolic flow in infants <34 week**

Caution should be taken when initiating feeding in the following subgroups. Treatment should be as medium / high risk depending on individual clinical assessment.

- **preterm SGA infants (<2nd percentile and <34 weeks gestation)**
- **severe term SGA infants (<0.4th percentile and >34 weeks gestation).**
- **complex congenital cardiac disease**
- **dexamethasone treatment**
- **indomethecin or Ibuprofen treatment for PDA**
- **polycythaemic infants**

3.3 Assessing feed tolerance

Feeding tolerance is the ability of the newborn to ingest and digest milk without complications; feeding intolerance is a common issue in preterm infants.
Clinical signs of intolerance may include vomiting, increased abdominal girth, abdominal tenderness, the presence, absence or quality of bowel sounds, and/or the presence of abnormal stools. However, all of these signs can also occur in a healthy

premature infant tolerating feeds (42). It is therefore extremely important to put these findings into a clinical context.
Gastric residuals (GR) are frequently used in the assessment of feed tolerance, with an implicit assumption that a low volume of milky aspirates should be used as confirmation that it is safe to advance feeds. There are however, no good data that support GR as a predictive marker of feeding tolerance and no clear definitions of what constitutes a "clinically significant" GR, particularly in the early stages of feed introduction. Available studies refer to a range in volume between >2mL (43) to 5 mL/kg (44) or from >33% (45) of the volume of previous feed up to >50% (46).

Physiologically, gastric residuals are likely a benign consequence of delayed gut maturation and gastric motility in VLBW infants. They are dependent on a number of factors, including size and position of oral/nasal gastric tubes, aspiration technique, infant position between feeds (residuals are increased with supine and left lateral positioning), and type of enteral feed, making them, in isolation, an unreliable marker of feed tolerance.

The presence of large GR volumes or green-coloured residuals prior to feeding often prompts subsequent feedings to be withheld or reduced because of concerns around possible NEC, however few studies have explored the clinical importance of GR in the context of NEC. Evidence from available studies suggest that routine monitoring of GR increases the risk of feed interruption episodes, the time taken to reach full enteral feeds, the number of PN days and time to regain birth weight, but does not have an impact on NEC incidence. (47-49). These findings are supported by a larger retrospective study (50) and a recent Cochrane review (51), however the number of studied infants remain relatively low, so these resources have a limited power to determine a true effect on NEC.
In summary, there is no data on the volume and/or colour of GRs that definitively indicate feeding intolerance, or that are predictive of NEC (38). However the following chart may be useful when assessing aspirate colour.

True bile-stained vomit that requires immediate attention is DARK GREEN like these last three colours:	Milk Lemon Lime Avocado Pea Spinach

Taken from Management of Bilious Vomiting in the Newborn Period and Radiological Support for Neonatal Services – A Framework for Practice Feb 2024 BAPM

NB Colostrum may appear yellow, pale/clear/dark orange or brown in colour

GRs may be present prior to NEC but are likely to be more helpful when assessed in combination with other classic signs.
Available evidence is not sufficient to either support or refute refeeding of GRs in preterm infants.

Recommendations:

- **Routine monitoring of gastric residuals in clinically stable infants is not recommended (20).**

- **Assessment of GR should be performed only when other clinical signs associated with feeding intolerance or NEC are present such as :**
  - **Bilious/ bloody aspirates**
  - **Visual bowel loops/abdominal discolouration.**
  - **Grossly bloody/watery or abnormal stools**
  - **Clinically unstable or acute deterioration (20)**

3.4 Mode of Feed delivery – continuous or bolus feeds?

The clinical benefits and risks of continuous versus bolus tube feeding cannot be reliably discerned from the limited information available from randomised trials to date (52).

However data suggests that:

- Bolus feeding may be more physiologic in the preterm infant (53)
- Higher behavioral stress responses have been reported in bolus fed infants (54)
- Fat may adhere to the inner wall of the delivery set and feeding tube during continuous feeding when compared to bolus feeding. However, despite two studies showing a loss of energy and fat content after continuous feeding (55,56), the most recently available meta-analysis showed that no significant effects were observed on growth (weight, length or head circumference) (57).
- The 2011 Cochrane review concluded that there was no difference in time to achieve full enteral feeds between the two feeding methods (52), however a more recent meta-analysis described a longer time to reach full enteral feeding in infants fed continuously compared with infants receiving bolus feeds. (58).
- There any no significant differences in the incidence of NEC between the two feeding methods (52)
- Some studies demonstrate an association of a higher number of apnoeas and apnoea related hypoxic episodes during continuous feeding (59,60), whilst others do not (61-63).

Due to the small volumes associated with MEF, evaluation of feed frequency on this practice is not possible, therefore debate is focused on the optimal feed frequencies to use when advancing feeds. Available evidence shows there are marked variations in feeding interval protocols for infants <28 weeks' gestation (64) but would suggest that 3 hourly feeding is comparable to 2 hourly feeding in VLBW infants, and that ELBW infants reach full enteral feeds earlier when fed 2-hourly compared with 3-hourly (65).

Recommendations:

- **There is no evidence to say which method of feeding (bolus or continuous) is best for preterm infants.**

- **Infants born <32 weeks should receive 1-2 hourly feeds moving to 3 hourly as they grow.**

- **Four hourly feeds is probably not physiologic in babies receiving human milk and therefore not recommended in the neonatal unit (65)**

3. 5 Management of Gastroesophageal reflux disease (GORD)

Gastroesophageal reflux (GOR), is generally defined as the passage of gastriccontents into the oesophagus and described as "posseting" or "overt regurgitation". It is an almost universal phenomenon in preterm infants that can be attributed to oesophageal immaturity, slower gastric emptying and incomplete peristalsis during swallowing. The fact that infants spend their time lying flat and ingest relatively large volumes of milk during feeding also contribute to the incidence of GOR. The presence of nasogastric/orogastric tubes may also result in greater lower oesophageal sphincter (LOS) relaxation and therefore more frequent episodes of overt regurgitation. (66)

Gastroesophageal reflux disease (GORD) can be defined as GOR that is associated with "bothersome symptoms or complications" (67). In the neonatal unit this can include:

- Gastrointestinal symptoms (eg. regurgitation, vomiting, abdominal distension)
- Cardiorespiratory symptoms (eg. desaturation, apneas, tachycardia, bradycardia)
- Somatosensory symptoms (eg. irritability, back arching, crying, grimacing)
- Aerodigestive symptoms (eg. swallowing and feeding difficulties, sneezing, coughing)

Attributing these symptoms solely to GOR is however, controversial (66). Given the physiological nature of GOR in preterm infants it is important to carefully consider whether the presenting symptoms and/or complications are pathological GORD which would benefit from treatment. Most preterm infants will not require anything more than simple positioning approaches. When considering when to escalate treatment beyond simple positioning or alteration of the feed regime, it is important to consider carefully the risk:benefit ratio of any proposed treatment.

3.5.1 Feeding strategies

3.5.1.1 Continuous and bolus feeds

Continuous feeding is generally thought to cause less gastric distension and offer less pressure to the lower oesophageal sphincter whilst permitting significantly faster gastric emptying when compared to bolus feeding. However delayed gastric emptying does not appear to play a contributory role in GOR in preterm infants, as those demonstrating symptomatic GOR do not appear to have delayed gastric emptying when compared with other infants.(66)

Bolus feeding is purported to affect greater gastric distension as a result of the quick delivery of a larger feed volume, that subsequently weakens the lower oesophageal sphincter, resulting in GOR.
However a Cochrane review from 2021 did not find any randomised trials that evaluated the effects of continuous versus bolus tube feeding on GORD in preterm and low birthweight infants (68), therefore recommendations as to the best method of feed delivery in respect of GORD management cannot be made.

3.5.1.2 Gastric and transpyloric feeding

The delivery of milk feeds directly to the small bowel (transpyloric feeding) rather than the stomach (gastric feeding) has the theoretical advantage of decreasing the potential for GOR and GORD, however there are also potential problems (69).

On a practical level transpyloric feeding tubes are difficult to position and, unlike gastric tubes, have to have their position confirmed with imaging. There is also a significant risk of tube migration back into the stomach.
Clinically, digestion in the stomach is by-passed and potentially pathogenic organisms (which would have been neutralised by stomach acid) may be delivered directly into the upper small bowel thereby contributing to a possible higher risk of necrotising enterocolitis in infants fed via the transpyloric route (70).

Although two observational studies have suggested that transpyloric feeding may reduce the frequency or degree of GOR and GOR-related apnoea (71,72) the most recent Cochrane review (69) did not find any evidence to support this view. The authors of this review also concluded that there is some evidence of harm associated with transpyloric feeding, including a higher risk of gastrointestinal disturbance and mortality, however these findings should be interpreted and applied cautiously because of methodological weaknesses in the included trials.

3.5.1.3 Feeding strategies – Thickeners and alginates

Thickeners

The following discussion relates to the use of feed thickeners for the management of GORD only. The use of feed thickeners in the management of swallowing difficulties is outside the remit of these guidelines and should be managed in conjunction with the unit peech and language therapist.

Feed thickeners are thought to prevent the reflux of gastric content into the oesophagus by increasing the ‘stickiness’ and weight of a feed, thereby retaining the feed in the stomach. Maintaining the correct feed consistency is however challenging due to variables such as the type of liquid the thickener is added to, the temperature of the feed and the stomach dwell time. Thickeners may also increase the energy density and osmolarity of feeds, leading to an increase in the frequency of relaxation of lower oesophageal sphincter and a delay in gastric emptying. Ironically this has the potential to actually increase regurgitation episodes and worsen GOR.(69)

Thickening of feeds is often used in the management of GOR in the neonatal unit. Available thickeners include cereal-based thickeners made from rice or maize, gum-based thickeners from guar, carob or locust bean, and carboxymethyl cellulose. The most frequently used product in the EOE is Carobel®, a powdered thickener based on carob bean gum and maltodextrin. Although the product's manufacturers do not recommend use in preterm or low birthweight infants due to a lack of clinical data supporting its use in these populations, Carobel® is used by a number of units within the EOE for the management of GOR.

Only small trials have been conducted comparing thickened feeds with standard feeds in preterm infants. One trial demonstrated that the number of GOR episodes was the same in both groups, with less total lower oesophageal acid exposure for the infants receiving thickened feeds. No assessment was made as to whether this reduction in acid exposure had any effect on associated GOR symptoms (73) However, preterm infants are less likely to suffer oesophageal mucosa injury as the high frequency of milk feeds renders gastric contents only weakly acidic.

Despite a lack of clear evidence, and the fact that available studies have found no reported link between thickened feeds and undesirable gastrointestinal effects in term infants, (74 75) there is a growing clinical concern regarding the use of thickened fluids in populations with still developing GI systems (ie preterm infants) and the incidence of NEC. In 2004 a link was proposed between the use of carob bean thickener and the development of NEC in two extremely low birthweight infants in the UK (76) and in the USA in 2011/2012 concerns were raised over the use of xanthan gum and the incidence of late onset colonic NEC (77,78) in preterm and ex-preterm infants. These reports led to a US Food and Drug Administration consumer advisory warning (79) and a case series investigation that concluded that there was sufficient evidence to propose that the use of xantham gum, or similar gum thickeners in preterm infants can significantly increase their risk of developing NEC. (77)
Concerns have also been raised about nutritional consequences, such as impaired adsorption of nutrients from feed that has been thickened with indigestible complex carbohydrate thickeners (80)

Alginates

Alginate preparations work by precipitating into a viscous gel when they come into contact with gastric acid, which then acts as a physical barrier to the gastric mucosa. When combined with sodium bicarbonate, (as in Infant Gaviscon®) a carbon dioxide foam forms which is the first to reflux into the oesophagus during a GOR episode, thereby protecting the lower oesophagus from acid damage.
Infant Gaviscon: suggested dosing regimen

Small studies in preterm infants show that sodium alginate preparations decrease both the total number of GOR acidic episodes (81) and the frequency of regurgitations (82). However the long-term safety of these preparations has yet to be evaluated. (66 67)

There is some evidence that links alginate thickeners (such as Infant Gaviscon®) with the formation of lactobezoars or milk curd plugs in the GI tract of preterm infants, especially those fed via NGT.(83 84). A similar picture has been seen in the USA as a

rare consequence of feeding preterm infants nutrient dense milk feeds (including fortified breast milk) (85).

These incidents have led to a consensus that the combined effect of alginate thickeners and breast milk fortifiers, when administered/added to milk feeds at the same time, can increase the risk of over thickening of the stomach content, the potential formation of lactobezoars and an increased risk of intestinal obstruction. These concerns have been widely translated into recommendations not to give the two products together without careful consideration between the caring consultant and the neonatal dietitian, as there is a need to balance the risks of potential growth failure following removal of fortifier in order to continue the use of alginate thickeners, with the risk of curd obstruction (especially in very small infants). When a decision is made to use both products in older/larger infants, avoid mixing in the same bottle/container and deliver the alginate after the feed has been completed. HMF delivery can either be as standard fortification, or as concentrated "supplements" before feeds.

The most recent Cochrane Review concludes that there are reported side effects from the use of feed thickeners, including NEC, and that there is insufficient evidence to recommend the use of thickener in the management of preterm infants (86)

3.5.2 Body positioning

Body positioning is widely used as a management approach in infants believed to have GOR.
Placing preterm infants in the left lateral position after feeding and in the prone position may reduce lower oesophageal relaxation and reflux episodes,(87 88 89), whereas placement in the right lateral position may increase reflux episodes after feeding, but also enhances gastric emptying (89). However, evidence would suggest that despite a reduction in reflux episodes in the left lateral position, behavioural manifestations of reflux (crying and/or irritability) did not improve. (90) It therefore remains unclear as to whether positioning techniques can reduce signs of GOR in preterm infants.

One researcher recommends placing infants in the right lateral position immediately after feeding, followed an hour later by placing them in the left lateral position to decrease acid reflux. (90). This should only be considered in the cardiovascularly monitored infant given that lateral and prone positioning also increase the risks of sudden infant death syndrome (SIDS)(91)

Safe sleep approaches, including use of the supine position on a firm, flat surface, should be the management option of choice for all infants >32 weeks gestation who are no longer on monitors and/or with a planned discharge date.(92 86 66).

3.5.3 Pharmacological strategies

Preterm infants who have been clinically diagnosed with GORD are often treated with pharmacologic agents; however, there is a paucity of data about the effect of treatment on either symptoms or short- and long-term outcomes. This lack of data when viewed alongside emerging evidence of significant harm, particularly with gastric

acid blockers, strongly suggests that pharmacological agents used to managed GORD should be used sparingly, if at all, in preterm infants (66)

Prokinetic agents

Prokinetic agents seem to aid gastric emptying, reduce regurgitation and enhance lower oesophageal sphincter tone, however none of these products have been shown to reduce the symptoms of GOR in preterm infants (93 94). All prokinetics have potentially significant adverse effects. These include a greater risk of infantile pyloric stenosis and cardiac arrhythmia (erythromycin) and neurological side effects (domperidone (95) and metoclopramide). For these reasons prokinetics should not be used in preterm infants if the only indication is for the treatment of GOR/GORD.

Histamine -2 Receptor Blockers

Histamine-2 (H2) receptor blockers compete with histamine for the H2 receptor in the stomach, leading to decreased gastric acid secretion and a resultant increase in gastric pH. This is thought to assist in controlling the symptoms of GOR associated with acid reflux, however preterm reflux episodes are only mildly acidic due to their naturally lower gastric acidity and frequent milk feeds, and although preterm infants do have some acidic GOR episodes, oesophageal injury is unlikely to occur.
No work has been done to assess the efficacy of H-2 blockers in the control of GOR symptoms in this population. Several studies have however linked these preparations with an increased incidence of NEC (96) and a higher incidence of late-onset infections and death (97) possibly as a result of an alteration in the preterm intestinal microbiome. (98). Since the withdrawal of ranitidine from the formulary there are no H2 receptor blockers available for use, however it is important to understand their unsuitability for preterm management.

Proton Pump Inhibitors

Proton pump inhibitors (PPIs) block the gastric proton pump, thereby decreasing gastric acid secretion. Given this effect on gastric acid secretion, it is likely that PPIs would have similar potential adverse effects as H-2 blockers in preterm infants, including a potentially increased risk of NEC secondary to reduced gastric acid secretion. PPIs are known to maintain stomach pH >4 in preterm infants, so they may have an effect on any potential acid related pain and discomfort but do not appear to help reduce regurgitation or vomiting. In randomised double blind placebo controlled trials both omeprazole andlLansoprazole were ineffective in reducing signs of GOR in infants, with lansoprazole associated with the highest rate of adverse events. (99) PPIs have been associated with increased respiratory and gastrointestinal infections (67) and may also impair vitamin and mineral absorption.

Recommendations:

GOR is almost universal in preterm infants. It is a physiologic process that will resolve with maturation. Available data does not support the association of

the perceived signs of GORD with either acidic or nonacidic reflux episodes in preterm infants. Parents should be reassured that the signs will usually improve with time without treatment.

- **No recommendation can be made as to the best method of feed delivery or preferred route of feeding for the management of GOR/GORD.**
- **Feed thickeners should not be used for the management of GOR/GORD in preterm infants.**
- **Alginates can be considered, though their longterm effect is unknown.**
- **Alginates should not be used in conjunction with human milk fortifiers for infants <37weeks.**
- **Cardiovascularly stable and monitored infants may benefit from placement in the right lateral position immediately after feeding, followed an hour later by placement in the left lateral position to decrease acid reflux.**
- **Safe sleep approaches, including use of the supine position on a firm, flat surface, should be the management option of choice for infants >32 weeks gestation who are no longer on monitors and/or with a planned discharge date.**
- **Pharmacological preparations, including prokinetics and proton pump inhibitors should be used sparingly in all preterm infants, and preferable not at all in infants < 34 weeks.**
- **Where used, proton pump inhibitors administered via an enteral feeding tube must be in a formulation that is appropriate for preventing tube blockage.**

Section 4. Types of milk and indications for use (Algorithm 2)

4.1 Human Milk

Despite slower in hospital growth rates compared to formula fed infants (100), preterm infants fed human milk appear to demonstrate a positive impact on long-term neurodevelopmental outcome (101-104) as well as lower rates of neonatal morbidities including NEC and (potentially) bronchopulmonary dysplasia (BPD) (105-107). Human milk, expressed by an infant's own birth parent, is therefore the standard of care for all infants born preterm (106 -108) provided it is adequately fortified in line with national and network guidance (21).

Birth parents should be counselled and encouraged to breastfeed or express milk as soon after birth as possible, even if their long term intention is not to breastfeed. They

should express as frequently as possible as a minimum daily volume of 750 – 900ml by day 10-14 after birth is required in order to sustain exclusive breastfeeding (109).

Preterm milk contains higher concentrations of protein, fat, energy and sodium in the first weeks of lactation, but these drop to the same levels as mature term milk within 2 weeks of birth. At this point, in order to meet the high requirements of preterm infants, maximise growth potential and minimise the cumulative nutritional deficits seen in the early weeks of life, more nutrients will be required in the form of human milk fortifiers, especially in those with a birth weight <1800g (21).

Colostrum, produced in the first few days after preterm delivery, is particularly rich in immuno-protective, anti-infective agents and growth factors (110, 111). Oropharyngeal tissue may play an important role in developing the immune system, but is bypassed when orogastric/nasogastric tubes are utilised. Administering colostrum directly onto the buccal mucosa may therefore serve to protect the infant from infection, stimulate the development of the gastrointestinal tract and modulate the immune system (112). Although recent studies suggest that the administration of buccal colostrum in the first few days of life has no clinical benefits (as mortality and NEC rates remain unchanged) (113-118), the practice does increase parental involvement, provide early positive oral experiences in order to support long term feeding outcomes and help to increase milk provision.(119)

For further information on lactation management in the preterm population, see local EOE Infant Feeding Guidelines

For information on the handling and storage of human milk, see local guidelines EOE Milk Handling Guidelines

Recommendations:

- **Human milk expressed by an infant's own birth parent is the standard of care for all infants born preterm**
- **All infants should be considered for mouth care in line with the current network guidelines EOE Mouthcare Guidelines**

4.2 Human Milk Fortification

Human milk initially contains levels of protein of up to 2g/100mL, but this declines to the levels found in mature human milk within the first two weeks of lactation. Mature human milk has an average content of 1.2g/100mL and 67Kcal/100mL, with significant variability of macronutrient composition - not only between parents, but also within the same parent. Published nutrient contents range from 0.5 – 2.0g/100mL for protein and from 45 - 90 kcal/dl for energy content (120-123).

Neonatal growth rates are known to be linearly related to protein and energy intakes (124, 125). In order to compensate for the term infants' immature renal concentration capacity and to meet their expected growth rates (5-10g//Kg/day) and nutritional

requirements (1.6-2.5g protein/kg/day and 85-110Kcal/kg/day), the composition of human milk has evolved to meet the needs of the majority of term infants in 150-165ml/kg/day.

Preterm infants however, experience significantly higher growth rates of up to 17 - 23 g/kg/day. In order to achieve these rates they require a protein intake of 3.5 to 4.0 (4.5) g/kg/d and a corresponding energy intake of 115 to 140 (160) kcal/kg/day. In the neonatal care setting "normal" fluid allowances of 150-165mL/kg are often extended to 180 – 200ml/kg in stable infants, however these volumes are still not adequate to meet the needs of the very low birth weight infants when fed as unfortified human milk. (126). As an example a 1000g baby would require approximately 200mL/kg/day in the first two weeks of life to meet their protein requirements, and 360m – 400mL/kg/day of mature milk thereafter. Most infants would be unable to tolerate this volume. In addition, the energy provision would be excessive (180-200Kcal/kg/day) leading to an unbalanced protein:energy ratio, potential metabolic derangement and an unfavourable body composition. (127)

In order to maintain the benefits of human milk and meet the nutritional and growth requirements of preterm infants, a method was sought to enable the adaptation of the composition of human milk to meet these increased needs. Commercial human milk fortifiers were first introduced in the 1980s and have now become part of the standard nutritional care for preterm infants in most NICUs. From a scientific perspective the physiological and nutritional basis for the use of human milk fortifiers is quite strong (125) however evidence from clinical trials is limited. Available studies reviewing multicomponent and protein supplementation suggest some improvement in weight and anthropometric indices, (128,129,130) whilst those reviewing potential side effects conclude that fortification can be considered a safe process with respect to incidence of NEC, feeding intolerance and osmolality. (21, 131, 132) No trials have compared the effect of human milk fortification on neurodevelopmental outcome (133).

The two fortifiers available in the UK are Nutriprem Human Milk Fortifier®(Danone) and SMA Gold Prem Breast Milk Fortifier® (Nestle). Both are bovine-based, multi-nutrient fortifiers containing varying amounts of hydrolysed protein, energy, minerals, vitamins, electrolytes and trace-elements (SMA Gold Prem BMF contains iron, whereas Nutriprem HMF does not). The recent addition of lipids to multi-nutrient fortifiers has not only provided an effective source of essential fatty acids (134), the consequent reduction in carbohydrate content has also resulted in a product with a lower osmolar load than previous versions. (135)

Although the quality of the fortifiers and the methods of human milk fortification have improved over time, the recipes used to formulate these fortifiers are based on two assumptions that have meant that with current practice, nutrient fortification remains suboptimal for some infants. These assumptions are that:
(i) individual milk composition is represented by an average macronutrient content and so doesn't allow for variations.
(ii) the average enteral fluid intake of preterm infants is 150 - 165 ml/kg/d.

Both of these assumptions can provide challenges when seeking to make recommendations for network practice, as rather than adopting a "Standard fortification" approach, it is now accepted that an optimal approach to fortification is to

provide each baby with their individual needs, which might be different from the average of the group (21 44 132). This can be achieved through "individualised fortification", delivered either as "adjustable" fortification following a programme of standard fortification or as "targeted" fortification.
Although individualised fortification is now considered optimal practice, a pragmatic approach that reflects the safest strategy based on the availability of suitably skilled staff is required when considering network recommendations.

Table details the three methods of fortification and their advantages/disadvantages–

Fortification method	Principle	Advantages	Disadvantages
Standard Fortification	Fortification method currently in use in most neonatal units. A fixed amount of fortifier is added to a fixed volume of HM according to the manufacturers' instructions.	Practical and easily reproducible in standardised guidance.	Some VLBW infants continue to receive suboptimal levels of protein and many continue to have suboptimal growth.
Adjustable Fortification (21 131 141)	Protein adequacy is monitored by serum urea levels twice weekly. Normal laboratory levels are generally reported as 3.5-5.7mmol/L. If the level is lower than reference range and showing a downward trend, extra protein is added to the standard fortification.	Practical, not too labour intensive. Doesn't need expensive devices. Monitors protein intake of each infant & takes into consideration each infant's protein requirement. Safeguards also against excessive protein intake Effective in optimising growth and protein intake.	Requires regular, skilled dietetic support to ensure protein adequacy and accurate protein:energy ratios. Requires blood monitoring.
Targeted Fortification (21 131 141)	Macronutrient concentrations in HM are analysed and based on the results milk is supplemented with extra protein and/or fat to recommended intake levels.	All macronutrients can be supplemented.	Bedside human milk analysers are required. May be labour intensive Supplementation is based on published nutrient recommendations and does not take into consideration that each individual infant's requirement may be different.

(adapted from reference 131 Fortification of Human Milk for Preterm Infants: Update and Recommendations of the European Milk Bank Association)

There is no consensus as to when to start fortification of human milk (136). The current practice of first introducing at half strength when enteral feeds reached 150 ml/kg/d and then advancing to full strength 48 hours later is well accepted but has no strong evidence to support it (137). It also has the disadvantage of delaying the time needed to meet nutrient needs, thereby increasing the risk for growth faltering. An individual clinical decision may occasionally be made to commence fortification at half strength, especially in the extreme preterm infant. Where adopted, half strength fortifier should be used for no more than 24-48 hours before progression to full strength.

Current evidence would suggest that fortification is tolerated from day one and leads to reduced parenteral nutrition intake (138). One recent review discussed two trials that compared introductory time points of 20 vs 100 ml/kg/d and "first feeding" vs. 75 ml/kg/d (139-141). Although there were no differences in growth rates, there were also no differences in adverse outcomes, suggesting that early fortification may be as safe as delayed fortification.

Current published European recommendations are to commence full strength fortification in all infants birth weight <1800g once an infant is tolerating 40-100ml/kg/day (21 132 142)

Recommendations:

- **Human Milk Fortifiers (HMF) should be added to human milk for all infants born <1800g once they have tolerated 80- 100ml/kg/day for 24 hours.**

- **HMF should be used at full strength (1g/25ml milk) from the commencement of fortification for the majority of infants.**

- **Serum urea concentrations should be monitored regularly (ideally 2x per week) until discharge.**

- **Standard full fortification is 150 - 165mL/kg/day full strength fortified human milk. If growth is suboptimal on standard fortification, increase volume to 180mL/kg in conjunction with regular serum urea monitoring and ongoing dietetic supervision.**

- **Adjusted fortification can be considered for infants who growth falter on standard fortification, but only where regular serum urea monitoring is in place and where adequate, dedicated dietetic staff are available to calculate feed composition and monitor progress.**

- **There is currently insufficient evidence to recommend the use of human milk derived fortifiers.**

- **HMF should be added to human milk using one of the two recommended processes outlined in appendix 1**

- **HMF should never be added to preterm formula.**

- **HMF is not recommended if more than half of the feed requirement is provided by preterm formula, though fortification of the human milk component should be considered if there is associated poor growth and tolerance of volume.**

- **Combination feeds, when required, can be given either:**

- **Alternating feeds of fortified milk and preterm formula.**
- **Preterm formula used once the daily supply of expressed human milk has either run out or until the next expression.**
- **Mixed together if feeds are delivered by continuous infusion, as the fat in human milk is held in suspension and is less likely to coat the sides of the container.**

There is little evidence to support one practice over the other, however there is some evidence to suggest mixing human milk with cow's milk formula decreases the number of lysozymes in human milk and potentially increases E.coli. (143).
The method that involves the least amount of milk handling and is easiest for each unit practice is likely to be the best for individual infants.

4.3 Additional Protein Supplements

Nutriprem Protein Supplement® is a bovine based, hydrolysed protein supplement that can be used, as part of an adjusted fortification strategy, to meet the high protein needs of selected infants who fail to grow appropriately on a standardised fortification regimen.

The product is available in 1g sachets and provides an additional 0.82g protein per sachet. It has been designed for use with Nutriprem Human-milk Fortifier, but can be used with SMA Breast Milk Fortifier in line with the guidance below. Nutriprem Protein Supplement should never be added to unfortified human milk.

Table 2 Suggested use of Adjusted fortification after the first 2 weeks of life (adapted from Koletzko 2021)(142)

Serum urea level (range 3.5-5.7mmol/L)	**Adjustment required**
<3.0mmol/L + evidence of downward trend	Increase protein fortification up to 2 steps dependent on serum urea level
Normal reference range	No change
>5.7mmol/L in the absence of fluid or renal derangement	Decrease protein fortification

Nutriprem Protein supplement®	**Step 1**	**Step 2**
	0.5g (½ sachet) / 100mL mature human milk	1g (1 sachet) /100mL mature human milk
	0.41g additional protein/100mL	0.82g additional protein/100mL

Mature milk = milk expressed 10-14 days post partum.

The required dose of Nutriprem Protein Supplement® should be weighed and added to fortified milk. Once added it should be used immediately, or within 4 hours if not warmed. EOE Milk Handling Guidelines

Nutriprem Protein Supplement® has an osmolality of 40 mOsmol/kg H20 per 1g of protein, which will contribute to the overall osmolality of the total feed.

Recommendations:

- **Consider using additional protein supplements as part of an adjusted fortification strategy for infants who fail to grow appropriately on a standardised fortification strategy.**
- **Additional protein supplements should only be used in conjunction with regular serum urea monitoring.**
- **Additional protein supplements should only be used under the guidance of a dedicated neonatal dietitian.**
- **Never add additional protein supplements to unfortified human milk.**

4.4 Donor Human Milk (DHM)

Donor human milk reduces the risk of NEC by about half in very preterm or VLBW infants when given in preference to formula milk. Although there is probably little or no effect on late-onset invasive infection or all-cause mortality before hospital discharge. (144). In their most recent publications, the World Health Organisation, ESPGHAN and the British Association of Perinatal Medicine (BAPM) state that when milk from a birth parent is either not available or only available in insufficient volumes to meet an infant's needs, pasteurised donor human milk should be used as an alternative. (21, 145,146)

See the East of England Donor milk guidelines for supporting evidence and further guidance. EOE Donor Milk Guidelines

Recommendations:

- **DHM should be used for very preterm (< 32 weeks' gestation) or very LBW (< 1.5 kg) infants when parental milk is either unavailable, contraindicated or insufficient to meet an infant's needs**
- **DHM may be used for babies >32 weeks gestation or >1.5Kg birth weight, where they meet the additional High Risk criteria in the EoE Nutrition Care Pathway (see section 3.2)**
- **DHM may be used for late/moderately preterm infants resident on neonatal units or transitional care facilities within the EoE if:**
  - **They have a birthweight <1.5kg.**
  - **They meet any of the additional high risk criteria in the EOE Nutrition Care Pathway (see section 3.2).**

- **There is a need to "bridge" milk supplies for any late/moderately preterm infant where there is a clear parental intention to establish breastfeeding**.

- **Babies born <1500g or <32 weeks gestation in receipt of DHM should be given milk that has been fortified with a multi-nutrient human milk fortifier (Nutriprem HMF or SMA BMF) in preference to preterm formula. Full strength fortifier should be added when babies are tolerating 80-100ml/kg DHM**

- **Babies <1800g with a gastrointestinal surgical diagnosis should not receive fortified DHM without discussion with the caring surgical team.**

- **The use of DHM must be discussed with parents and verbal consent for the use of donor breast milk must be documented in the infant's notes.**

- **DHM must be sourced from a suitably regulated human milk bank - for units in the EOE this is either the Rosie Milk Bank or the Herts Milk Bank.**

- **DHM must be stored and handled in line with the EOE Milk Handling Guidelines EOE Milk Handling Guidelines**

- **When providing DHM, staff must continue, at all times, to raise and maintain awareness of the benefits of a parent's own milk over both DHM and preterm formula. Regular, ongoing support must be made available to parents, in the form of lactation support, in order to ensure maximal volumes of MOM provision and establishment of effective breastfeeding.**

4.5 Preterm Formulas (Appendix 2)

Preterm formulas are designed to meet the nutritional requirements of most preterm infants weighing <1800g when fed between 150 and 165ml/kg.

There are currently three formulas available in the UK. They are presented in 70ml or 90mL ready to feed plastic bottles and are for hospital use only. They are unavailable in the community setting.

Preterm formulas can be used as soon as enteral feeding is indicated if parental milk is not available or the criteria for DHM are not met. Term formulas should not be used in preterm infants as they fail to meet the nutritional needs of premature infants.

Nutriprem 1 (2.7g protein /100mL and 80Kcal/100mL)

Whole protein formula designed to meet the nutritional requirements of preterm infants. Protein and energy requirements are met when fed at 150ml/kg, however volumes can be increased to 165ml/kg if growth rates are suboptimal. Volumes in excess of this will exceed maximum protein recommendations and should only be considered in consultation with a neonatal dietitian.
Nutriprem 1 has Halal certification and Kosher approval.

SMA Gold Prem 1 (2.9g protein/100mL and 80Kcal/100mL)

SMA Gold Prem 1 contains higher amounts of protein than Nutriprem 1. It has been formulated to meet the maximum protein recommendations of 4.5g/kg required by some extremely low birth weight infants, and those who individually require additional protein when fed at 150ml/Kg.
Due to its higher protein content SMA Gold Prem 1 should not be delivered in volumes >150mls/kg/day without consultation with a neonatal dietitian.
SMA Pro Gold Prem 1 contains a degree of partially hydrolysed protein and contains 24% of its fat as medium chain triglycerides (MCT). It can be a useful formula to use in the preterm surgical infant where either parental milk is not available or where feed tolerance is an issue.
Halal and Kosher suitability – contact SMA Careline for information 0800 081 80

Hydrolysed Nutriprem (2.7g protein /100mL and 80Kcal/100mL)

A preterm formula that contains extensively hydrolysed protein that has been formulated for infants with a compromised ability to break down or absorb whole protein, or who are not tolerating standard preterm formula. The nutritional composition is comparable to Nutriprem 1.
Nutriprem 1 has Halal certification and Kosher approval.

Recommendations:

- **Preterm formulas can be used for infants born preterm (<37 weeks) with a birthweight <1800g where parental milk/DBM is unavailable or not indicated.**
- **Feed to a volume of 150-165ml/Kg.**
- **Do not exceed 150ml/kg SMA Gold Prem 1 or 165ml/Kg Nutriprem 1 without consultation with a neonatal dietitian.**

4.6 Extensively Hydrolysed Protein Formulas

Hydrolysed protein has been made increasingly available within preterm infant formulas and fortifiers in recent years, however there is no agreement as to whether,

in the absence of human milk, avoiding whole bovine protein and replacing it entirely with a hydrolysed product is of benefit. (21)

In term infants hydrolysed protein formulas have been used for the prevention and treatment of allergic disease, however in preterm infants there are no good data suggesting benefit for allergy prevention (147).

Preterm formulas with hydrolysed protein (for example Hydrolysed Nutriprem®) have been introduced on the basis that early feeding tolerance might be better in small preterm infants and that their use might be associated with lower rates of other complications such as NEC. However, no adequately powered studies have been conducted to explore this. (148) Although several studies have shown faster gastrointestinal transit with hydrolysed protein formulas (149 – 151) and accelerated time to achieve full enteral feeds (152) use is also known to increase osmolality and possibly reduce nutrient bioavailability (150).

Term extensively hydrolysed formulas should not be used in preterm infants unless there is a clear clinical indication for use, due to their high osmolar load and inappropriate nutritional composition. These formulas will require concentration by an experienced paediatric/neonatal dietitian in order to meet preterm macronutrient requirements.

Although the use of hydrolysed preterm infant formulas appears generally safe, there is insufficient evidence to recommend routine use, no data to determine the optimal degree of hydrolysis and no data to show routine use decreases the risk of NEC (147).

Recommendations:

- **Hydrolysed <u>preterm</u> formulas may be used for early enteral feeding in preterm infants, but only if human milk is not available.**
- **<u>Term</u> hydrolysed formulas should not be used for preterm infants unless there is a clear clinical indication for use.**
- **Term hydrolysed and amino acid based formulas should only be used under the direction of a Neonatal Dietitian.**

4.7 Nutrition post discharge (Appendix 2)

Deciding how to feed a preterm infant after discharge can be challenging as there is a desire to "normalise" feeding despite continued high nutritional requirements. Marked differences in individual infant nutritional needs are influenced by variables such as body weight and postconceptional age, the degree of nutrient and growth deficits accumulated during the infant's hospital stay, and clinical conditions that lead to an increased energy requirement, such as pulmonary and cardiac disease. These variations often make it difficult to achieve a growth and body composition equivalent to that of an infant of the same postconceptional age. (21),

The challenges of post discharge feeding can be reduced by effective optimisation of a preterm infant's nutritional care during their neonatal inpatient journey. This will serve to reduce their accumulated deficits in growth and nutrient stores and minimise the need for catch up growth after discharge (142)

For guidance on supporting the nutritional needs of preterm infants who are to be fed Human milk post discharge, see EOE HMF Post Discharge Guideline

Parental choice and the difficulties some parents face trying to maintain breastfeeding will result in some infants requiring some or all formula milk at the time of discharge. Standard infant formula has been designed to meet the requirements of healthy infants born at term. When fed to preterm infants at the time of hospital discharge, standard infant formula – similar to unfortified human milk– fails to meet the calculated nutrient requirements needed to meet intrauterine growth rates. This theoretical deficit led to the development of nutrient enriched post discharge formulas (NEPDF) for use in formula fed preterm infants once at home. However clear evidence of routine benefit is yet to be established.
A 2016 Cochrane report sought to establish whether feeding preterm infants nutrient-enriched formulas (both preterm formula and NEPDF) rather than standard formula after discharge helped to facilitate "catch up" growth or help improve development. The authors concluded that continuing to feed preterm formula rather than changing to standard formula after discharge improved infant growth parameters at 12-18 months corrected age, whereas using NEPDF after discharge showed higher weights and lengths at 9 months, but no statistically significant effects on growth at 12-18 months corrected age. (153). Little data is available on neurodevelopmental outcomes, with no reported significant differences at 18 months after term. A further, larger review, with significant heterogeneity within the included studies, compared use of preterm formula with other formula types after discharge. (154). Several, but not all, studies found enhanced anthropometrics upto 12 months (greater in boys than in girls) and increased lean body mass in infants fed protein and energy enriched feeds, but little difference in neurocognitive development.

Contrary to practices within the neonatal unit, once at home, infants are more likely to be fed on demand in response to hunger and satiation cues (responsive feeding) rather than to a prescriptive regimen. Preterm infants are known to adjust their intake volumes according to the energy density of the formulas provided, so when responsively fed NEPDF they may actually not receive anymore energy or other nutrition than infants fed standard formula.(153, 154). In contrast, where infants are fed to a more prescriptive regimen with nutrient enriched formulas this ability to adjust intake is lost and they are more at risk of catch up growth with accelerated weight gain and crossing of body mass index percentiles. This may be associated with altered body fat distribution and increased risks of insulin resistance and cardiovascular disease in later life. (153)

In summary, available evidence does not suggest that routine feeding of formula fed preterm infants with NEPDF once at home has any significant long lasting effect on growth and development at 18 months of age. There will however be a group of preterm infants who would benefit from a period of feeding with a NEPDF in order to support adequate and appropriate weight gain in the initial period at home.
These include preterm infants with a birthweight <1.8kg who, at discharge have

higher energy requirement (e.g. infants with cardiac conditions or CLD on home oxygen) or who have had ongoing poor growth (e.g. have crossed down > 2 centiles on their growth chart during their neonatal stay). These infants should be considered for NEPDF at home once they are >1.8- 2.0kg and/or just before discharge.

All other preterm infants who do not have clinical conditions requiring enhanced nutritional provision, or who have had adequate growth during their NICU stay can be discharged home on standard term formula.

There are two NEPDFs available in the UK, Nutriprem 2 and SMA Gold Prem 2. Both are available in a ready to feed (RTF) and powdered format. The RTF format is preferable for hospital use.

Nutriprem 2 and SMA Gold Prem 2 are available on prescription for preterm infants until 6 months corrected age, but in practice are only required until an infant is demonstrating appropriate, proportional growth, at which point they should receive standard infant formula. Regular, careful post-discharge anthropometric monitoring of these patients is required to prevent over feeding.

Growth restricted term infants >37 weeks, should be offered ordinary term formula in the absence of human milk (155).

Recommendations:

- **Formula fed preterm infants born <1800g (including those born LMPT) who at discharge have higher energy requirement or who have had ongoing poor growth should be considered for NEPDF once they are >1800-2000g.**

- **Formula fed preterm infants not meeting the above criteria should be offered standard term formula at discharge.**

- **Formula fed, growth restricted term infants >37 weeks should be offered standard term formula at discharge.**

There are no specific nutritional recommendations for those infants born moderate to late preterm (LMPT), though requirements are thought to be higher than those of term infants (156).
Current feeding guidelines for this cohort recommend:

- **All late and moderate preterm infants born <1800g need additional nutritional support and should be managed in line with the recommendations within this guideline (156).**

- **Parents who wish to breastfeed should be fully supported to do so, both prior and following discharge.**

- **Infants receiving HMF at home must be monitored closely.**

- **Iron and vitamin supplementation should be managed in line with current network guidance EOE Vitamin and Iron guideline**

4.8 Specialised Term Formulas (Appendix 3)

These include extensively hydrolysed formula (EHF), amino acid formula (AAF) or Nutrient Dense Term formulas.

Nutrient Dense term formulas are designed to meet the needs of term infants in a reduced volume. Their nutritional profile and protein:energy ratio are unsuitable for use in the preterm population.

Regular extensively hydrolysed formulas (EHF) are products developed for term-born infants and are generally considered appropriate for term infants with allergies.

Because some EHFs also contain dipeptides, no lactose and high amounts of medium chain triglycerides they are commonly used for preterm infants after surgical NEC where there is associated intestinal failure or short bowel syndrome. In recent years, however, these formulas have been also used for infants following medically managed NEC and as a management strategy for perceived feed intolerance.

Amino Acid Formulas (AAF) are also products developed for term infants and are lower in protein, energy and mineral content compared with preterm formulas. AAFs are only recommended for treatment of severe gastrointestinal impairment and/or severe cow's milk protein allergy.

Term EHFs and AAFs do not meet the increased nutritional needs of preterm infants even at volumes of 180mL/kg. Concentration of these formulas may be tolerated, but this will not address the nutrient imbalance. Clinicians should also be aware of the resulting increase in osmolarity when concentrating these formulas and the need for these products to be made up within a Feed Unit/Milk Kitchen environment. They will be non-sterile and have potentially inconsistent composition.

The nutritional management of the surgical preterm infant is outside the remit of this guideline, however current recommendations are that where human milk is not available in sufficient quantity it can be supplemented with formula, in order of preference:

a) standard preterm formula

b) preterm formula with (partially) hydrolysed protein

c) extensively hydrolysed formula (not regular)

d) amino acid-based formula.(157 158)

Recommendations:

- **All powdered feeds should be made up in accordance with the East of England ODN milk kitchen guidelines EOE Milk Kitchen Guidelines**

- **Use of specialised formulas puts preterm infants at risk of inadequate and inappropriate nutrition and are be used with caution. They should only be used where absolutely necessary and always under the**

direction of a Paediatric or Neonatal Dietitian.

- **Soya formulas are not recommended for infants unless specifically required for treatment of galactosaemia or after discussions with parents, as part of a vegan diet (159).**

- **Parents should receive training before discharge on how to prepare powdered feeds and clean equipment in line with current national practice.**

Section 5: Growth

Growth is evaluated by the regular measurement, and plotting on a suitable weight chart, of weight gain, length/height and head circumference.

Identifying the optimal growth velocity for an individual preterm infants is hard to determine. Slow growth might be a sign of inadequate nutrition but might also be acceptable at certain periods, for example when direct breastfeeding is being established. Rapid growth may be acceptable following periods of clinical care where nutritional supply has been poor, but too rapid weight gain, in particular, may also be harmful. Growth must therefore be seen not simply as achieving increases in anthropometric values but in the context of optimising nutritional status in order to improve short- and long-term functional and neurodevelopmental outcomes.

The neonatal period involves major changes to growth and body composition, determined by the immediate adaptation to ex-utero life, followed by a period of stable growth. In preterm infants this can be described in two phases:
● Phase 1. From immediately after birth until 3-4 days of life. This phase involves a loss of body weight mainly due to a one-time contraction of extracellular water space (160 161). A loss of 7-10% body weight is an acceptable range (4-7% for small for gestational age infants) (162 163)
● Phase 2. From the lowest weight point until discharge, where the growth of each infant follows their current percentile on a chosen growth chart – the "growing phase".

Defining growth standards for preterm infants is challenging as many growth references are simply based on cross-sectional birth weight data. However using growth velocities based on fetal ultrasound estimations can aid evaluation of growth in a stable preterm infant in phase 2 of growth and help guide clinicians to identify the nutritional strategies needed to optimise an individual infant's growth along a chosen growth chart percentile.
World Health Organisation (WHO) in-utero data suggest average fetal weight gain for infants up to 37 weeks and offer a rough guide for clinical application.(21)

WHO Growth velocities:
20–23 g/kg/d during weeks 23–25 of gestation
17–20 g/kg/d during weeks 26–29 of gestation
13–17 g/kg/d during weeks 30–34 of gestation
10–13 g/kg/d during weeks 35–37 of gestation

The key to optimising preterm growth is however regular, effective monitoring of weight, head circumference and linear length. This requires local policies, standardised operating procedures (SOPs) and guidelines, accurate and precise measuring devices, training of health care professionals and the use of an appropriate growth reference chart.

Weight should be measured 2-3 times a week in special care and daily in high dependency and critical care environment, using the same device each time

Head circumference (HC) should be measured on the day of birth and weekly thereafter, using specifically designed measuring tape placed on the same reference points on the head each time, ideally taking three independent measurements and using the highest value of the three readings.

Linear growth measures of crown heel length should be measured weekly and is best performed with two people using a hard surface length board for stable infants, an infant length stadiometer or specially designed measuring equipment suitable for use within an incubator.

All anthropometric measurements are to be recorded on end of bed charts or electronic monitoring records and plotted weekly on an appropriate close monitoring growth chart. Growth velocity should be calculated every 5-7 days and used in conjunction with weekly assessment of an infant's growth chart and nutritional intake to inform on any changes in feeding strategy needed to optimise growth and development.

Growth faltering (GF) is most common in sick infants and describes an infant whose growth slows and does not grow parallel to a centile during phase two of established growth.

Catch-up growth refers to accelerated rates of growth following a period of growth faltering. However, rapid catch-up growth may increase the risk of cardiovascular and metabolic disease in later life especially when it is due to catch-up in weight without equivalent linear or head growth (21). There is no evidence to enable the identification of the optimal degree or duration of catch-up growth in an individual infant. Careful consideration must be given to balancing the well-documented neurocognitive risks of nutrient deficiencies and slow growth in early life, against the theoretical risks from rapid catch-up growth and adverse metabolic programming in later life.

Recommendations:

- **Regular monitoring of weight, head circumference and linear length are recommended in line with the parameters outlined above.**

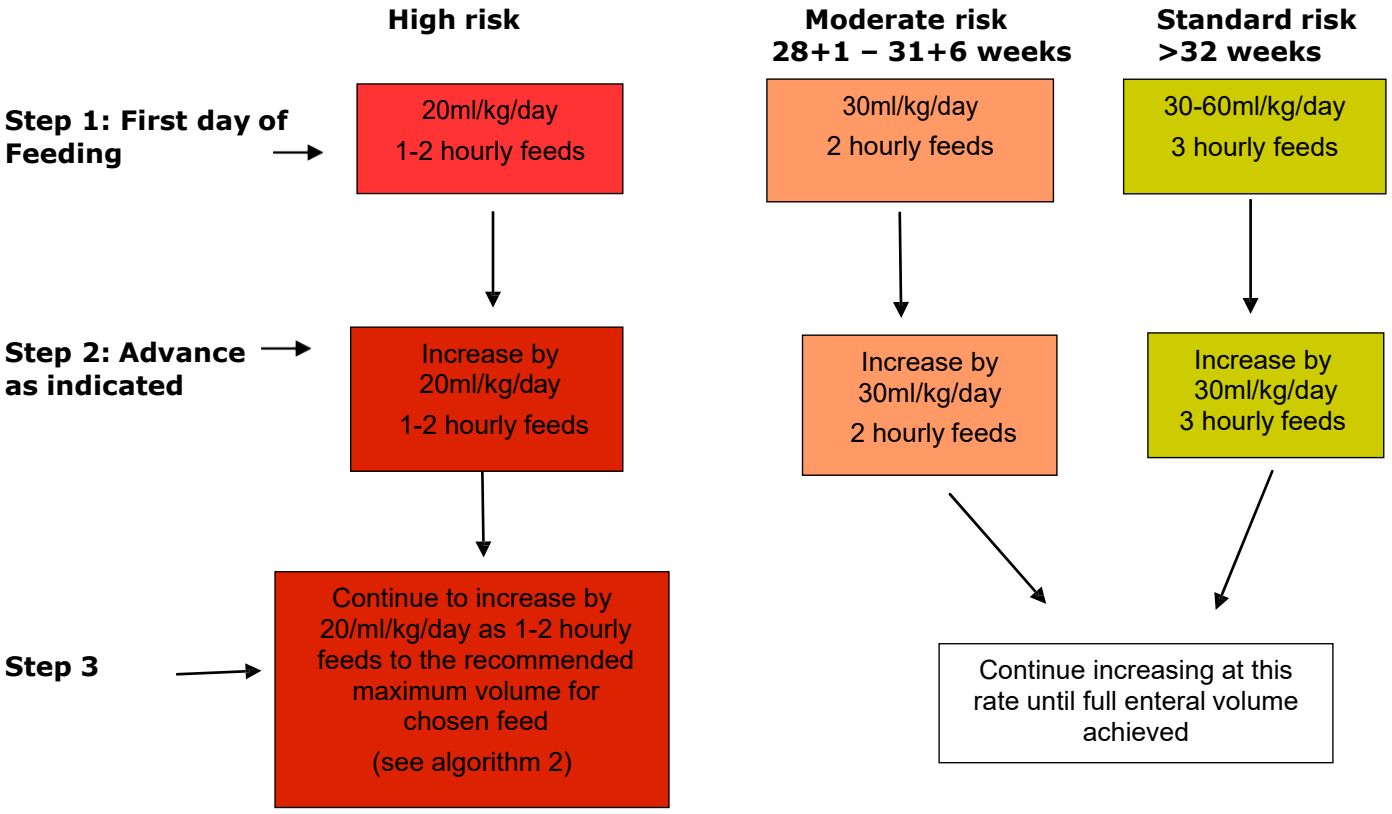
- **After an initial weight loss of 7%–10% by day 3-4, nutritional provision should aim to regain birth weight by 7–10 days of age, then follow along a target centile on a neonatal close monitoring chart.**

- **Infants born with in-utero growth restriction (IUGR) and/or small for gestational age (SGA) should receive nutrition and growth management that is the same as those born actual gestational age (AGA)**

- **Infants with postnatal growth failure should be allowed some catch-up growth. Where catch-up growth is considered too rapid, ensure a nutritional assessment is conducted and that nutrients are within recommended intake ranges**

Algorithm 1 Initiating and advancing enteral feeds.

Use this algorithm in conjunction with algorithm 2 – choice of milk



Commence feeding as close to birth as possible

There is no clear beneficial effect of implementing minimal enteral feeding (MEF) of any duration compared to advancing feeds immediately after birth.

Where a decision is made to initiate MEF, advance as clinically indicated and do not maintain for more than 3-7 days.

Infants can move between risk categories following individual clinical assessment.

High risk defined as:

<28 weeks gestation
< 1000g birth weight
Unstable /hypotensive ventilated neonates
Re-establishment of feeds following NEC or gastrointestinal surgery
Perinatal hypoxia-ischaemia with significant organ dysfunction
Absent or reversed end diastolic flow in infants <34 weeks

Caution should be taken initiating feeds in the following subgroups. The decision to manage as either "high risk" or "moderate risk" is at clinician's discretion.

Severe SGA infants (<0.4th percentile **and** >34 weeks gestation)
Preterm SGA infant (<2nd percentile **and** <34 weeks gestation)
Indomethecin or Ibuprofen for PDA
Complex congenital cardiac disease
Dexamethasone treatment
Polycythaemic infants

Algorithm 2 – choice of milk

Freshly expressed human milk is the first milk of choice for all infants unless clearly contraindicated

Infants born with birth weight < 1800g

Freshly expressed human milk
Increase as per algorithm 1 to 80 - 100mL/kg
Once tolerated for 24 hrs add full strength HMF

↓

Standardised fortification:
Increase to 150 -165 (180*) mL/kg as per algorithm 1.

↓

Target weight gain** achieved?

↓ Yes

Continue :
Standardised fortification
and Growth monitoring

↓ No

Consider **Adjusted fortification***

Serum urea <3mmol/L with downward trend?

↓ *YES*

Add protein*

↓ *NO*

Examine alternative reasons for poor growth

*180ml/kg fortified human milk and adjusted fortification strategies should only be considered where regular serum urea monitoring is in place and where adequate dietetic provision is available to provide regular nutritional monitoring.

If insufficient or no parental milk is available fortified donor milk is the next feed of choice for infants meeting the network donor milk guideline criteria. Those infants born<1800g not meeting the network donor milk guideline criteria should be given preterm formula.

Do not exceed 150ml/kg SMA Gold Prem 1 or 165ml/Kg Nutriprem 1 without consultation with a neonatal dietitian

Infants born with birth weight >1800g

Establish breastfeeding / Freshly expressed human milk increasing to 165mL/kg as per algorithm 1

↓

Increase as tolerated to 180 - 200mL/kg EBM if indicated to achieve required growth.

If insufficient human milk is available following lactation support or if parental choice is not to give human milk, offer standard term infant formula.

** Target weight gain

- 20–23 g/kg/d during weeks 23–25 of gestation
- 17–20 g/kg/d during weeks 26–29 of gestation
- 13–17 g/kg/d during weeks 30–34 of gestation
- 10–13 g/kg/d during weeks 35–37 of gestation
- 8-11g/kg/day during weeks 38 -41 of gestation

Appendix 1 – Techniques for the addition of human milk fortifiers to human milk.

This document recommends two techniques for adding fortifier powder to human milk (fresh / frozen & thawed / donor). These techniques are not the same as manufacturer's guidelines, but provide the most successful methods for ensuring complete and effective dissolving of fortifier. They are techniques employed by a number of trust, and have been practically assessed by members of the National Neonatal Network Dietitian's Group to ensure maximum dissolvability.

Pre-preparation guidance

Fortifier should be added to human milk in accordance with the East of England ODN Preterm Enteral Feeding Guidelines. EOE enteral-feeding-guideline and the ODN ANTT Milk Kitchen Prompt contained in the East of England Milk Kitchen Guidelines EOE preparation-and-handling-of-ebm-dbm-and-pif

1. Collect human milk and sachet(s) of fortifier. If using frozen milk defrost using the Trust's chosen thawing method. Check infant's name, DOB, hospital number and expiry date of milk
2. Check best before date on sachet(s) of fortifier.
3. Gather required equipment: 5ml syringe, gallipot/paper weigh-boat and appropriate syringes/bottle for storing milk
4. Weighing containers should ideally be single use. If using re-usable weighing containers, use one for each baby for a period of 24 hours then sterilise using the unit's chosen sterilisation process.
5. Syringes should be single use only.
6. Never mix fortifier with preterm formula.
7. Do not vigorously shake breast milk as the resultant frothing disrupts the fat globules and has a negative impact on the energy density of the milk.

Technique 1: Weighed Fortification.

The Weighed Fortifier technique is for use with warmed milk for immediate use. Do not store fortified milk that has been previously warmed – any feed left after an hour of commencing an oral feed should be discarded.

Preparation guidance:

1. Switch calibrated digital scales on, place weighing container/gallipot/paper weigh-boat on scales and press TARE to zero.
2. Calculate the amount of Human Milk Fortifier required using 0.04g per mL of feed (see example table below).
3. Weigh out the amount of fortifier required into a single use weighing container/gallipot/paper weigh-boat.
4. Add the weighed amount of fortifier to the measured volume of warmed human milk (try to avoid weighing container /paper weigh boat making contact with the bottle neck), swirl gently to ensure fortifier is dissolved. Do not shake as this disrupts the fat globules in the milk.
5. Label the bottle in accordance with the EOE feed preparation guideline.

6. Discard the paper weigh-boat, or wipe the weighing container with Clinell Universal Wipes. Wipe the scales with Clinell Universal wipes and allow to air dry.
7. Discard opened sachets of fortifier unless it is to be used to make up other feeds which are due at the same time.

Example calculations

1g (per sachet) divided by 25mL (of milk) = 0.04g/mL .
To obtain total weight of fortifier needed, multiply by feed volume (mL)
(If fortifier is required at half strength, halve the total grams needed).

Feed volume (mL)	Multiply by 0.04	fortifier needed (full strength)
10	10 x 0.04	0.4g
18	18 x 0.04	0.74g
30	30 x 0.04	1.2g
38	38 x 0.04	1.52g

Technique 2: Fortifier Concentrate

The fortifier concentrate technique is for use with cold milk where aliquots of fortified milk are to be stored for future use.
To prevent wastage, make up the smallest volume as possible. Fortified milk can be stored in a refrigerator for up to 12 hours, after which any remaining feed must be discarded.
Fortifier concentrate is made up in multiples of 25ml, depending on the volume of feed required.

Preparation guidance (scale for multiples of 25ml):

1. Take the bottle of human milk and gently invert a few times. DO NOT WARM THIS MILK.
2. For every multiple of 25mL, using a 5ml syringe, measure out 5ml human milk into a sterile gallipot.
3. Add 1 sachet of fortifier for each 5ml human milk in the gallipot. Gently swirl the mixture and allow to sit while preparing the feed bottle.

4. For every multiple of 25mL, measure out 20mls of human milk into the sterile bottle (22.5ml if using half strength fortifier).

5. Label the syringe/bottle as "fortified milk" as detailed in the EOE Milk Kitchen guidelines, including date of fortification and time of expiry (12 hours)

6. Return to the concentrate solution. Take the plunger out of the syringe and with the tip of the syringe, gently stir until all the powder is dissolved, ensuring no residue of the powder remains on syringe. This will make approximately 5ml of concentrate solution

7. Add the concentrate solution to the measured volume of human milk (5ml concentrate +20ml measured human milk =25ml full strength fortified human milk).
   (2.5ml concentrate + 22.5ml measured human milk = 25ml half strength fortified human milk).

8. Store either in the bottle (having replaced the lid) or in prescribed feed volumes drawn up into individual labelled syringes.

9. Any syringes/bottles not for immediate use must be stored in the fridge designated for this purpose at temperatures recorded ≤4°C in line with the EOE Milk kitchen guidelines.

Adapted in part from the Once for Scotland Guidance on Addition of Multi-Nutrient Fortifier

Appendix 2 - Preterm formulas

Requirements for infants birthweight <1800g
115-140 (160) Kcal/kg/day and 3.5-4.0 (4.5)* g protein/kg/day

	Nutriprem 1 **2.7g & 80Kcal/100ml**	**Hydrolysed Nutriprem** **2.7g & 80Kcal/100ml**	**SMA Gold Prem 1** **2.9g & 80Kcal/100ml**
Protein	Whole protein (59% whey)	Extensively hydrolysed protein (57% whey)	Partially hydrolysed protein (100% whey)
Protein in 150mL/kg	4.0g/kg	3.9g/kg	4.3g/kg
Energy in 150mL/kg	120Kcal/kg	120Kcal/kg	120Kcal/kg
Protein in 165mL/kg	4.4g/kg	4.3g/kg	4.8g/kg*
Energy in 165mL/kg	132Kcal/kg	132Kcal/kg	132Kcal/kg
Protein in 180mL/kg	4.9g/kg*	4.9g/kg*	5.22g/kg*
Energy in 180mL/kg	148Kcal/kg	148Kcal/kg	148Kcal/kg
lactose	60% of total carbohydrate	60% of total carbohydrate	46% of total carbohydrate
Medium chain Triglyceride (MCT)	8.7% of total lipid	7.2% of total lipid	12.5% of total lipid
osmolality	340mOsmol/kg H^2O	410mOsmol/kg H^2O	367mOsmol/kg H^2O
Suitability	Halal & Kosher compliant	Halal & Kosher compliant	Contact SMA for detail

	Nutriprem 2	**SMA Gold Prem 2**

	72Kcal & 2.0g /100mL	**73Kcal & 2.0g /100mL**
Protein	Whole protein (60% whey)	Partially hydrolysed protein (100% whey)
Protein in 150mL/kg	3.0g/kg	3.0g/kg
Energy in 150mL/kg	108Kcal/kg	110Kcal/kg
Protein in 165mL/kg	3.3g/kg	3.3g/kg
Energy in 165mL/kg	119Kcal/kg	120Kcal/kg
lactose	80% of total carbohydrate	96% of total carbohydrate
Osmolality	320mOsmol/kg H^2O	309mOsmol/kg H^2O
Halal compliant	Halal & Kosher compliant	Contact SMA for details

Nutrient / 100ml	**Preterm human milk**	**Mature human milk**	**SMA BMF (per 1g sachet) Halal compliant**	**Nutriprem HMF (per 1g sachet) Halal & Kosher compliant**
Energy Kcal	67	69	4.3	4
Fat g	3.5	4.1	0.18	0.18
Carbohydrate g	7.3	7.2	0.32	0.37
Protein g	1.62	1.3	0.36	0.33
Vitamin A micrograms	14.4	58	95	58
Vitamin D micrograms	0.2	Trace	1	1.38
Calcium mg	25	34	19	17.3
Phosphorus mg	14.5	15	11	9.5
Magnesium mg	3.5	3	1	1.25
Iron mg	0.09	0.07	0.45	Trace

Nutrient	Preterm human milk +4g SMA BMF	Preterm human milk +4g Nutriprem HMF	Mature human milk +4g SMA BMF	Mature human milk +4g Nutriprem HMF
Energy in 100ml/kg	84.2	84	86.2	85
protein in 100ml/kg	3.06	2.9	2.74	2.6
Energy in 150ml/kg	126	126	129	128
protein in 150ml/kg	4.6	4.3	4.1	3.9
Energy in 165ml/kg	139	139	139	140
protein in 165ml/kg	5.0	4.8	4.5	4.3
Energy in 180ml/kg	151	151	156	153
protein in 180ml/kg	5.5	5.2	4.9	4.7

Appendix 3 Specialist formulas –

To be used under the supervision of a paediatric/neonatal dietitian

Formula	Indication for use	Nutrient modification	Suitable for preterm infants?
Aptamil Pepti Junior	Malabsorption/post GI surgery	Hydrolysed protein/clinically lactose free/MCT fat	No – requires concentration and supplementation to meet preterm requirements.
Aptamil Pepti 1	Cow's milk intolerance	Extensively hydrolysed protein. Contains lactose, so not suitable if malabsorption suspected	No – requires concentration and supplementation to meet preterm requirements.
Nutramigen LGG	Cow's milk intolerance	Extensively hydrolysed protein. Clinically lactose free. Contains probiotics.	No – requires concentration and supplementation to meet preterm requirements. Needs making up with boiling water to denature probiotics.
Neocate /	Severe	Amino acids.	No - requires

Alfamino/Puramino	malabsorption –use only after failure with an extensively hydrolysed formula	Neocate does not contain MCT Clinically lactose free High osmolality	concentration and supplementation to meet preterm requirements.
Similac High Energy/ Infatrini/ SMA High Energy	Infants >37 weeks (>2kg) with increased nutritional requirements/fluid restrictions	Nutrient dense. SMA High Energy contains partially hydrolysed protein	No – formulated to meet requirements of term infants. Protein:energy ratio not suitable for preterm infants.
Infatrini Peptisorb	Infants >37 weeks (>2kg) with increased requirements/fluid restrictions AND Malabsorption	Nutrient dense with extensively hydrolysed protein	No – formulated to meet requirements of term infants. Protein:energy ratio not suitable for preterm infants.
Monogen	Chylothorax	Whole protein 80% fat as MCT	No – requires concentration and supplementation to meet preterm requirements.

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