Welsh Neonatal Network

Clinical Guideline:
All Wales Enteral Feeding Guideline for Preterm Infants

Authors: Isabel Fraser, Paediatric Dietitian, CAVUHB

Jo Males, Paediatric Dietitian, ABUHB

Kate Harrod-Wild, Paediatric Dietitian, BCUHB

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1.0 Introduction

As survival rates for preterm infants improve, increased emphasis is being put on improving the quality of outcomes by concentrating on optimising nutritional management. Suboptimal nutrition commencing in the early neonatal period contributes to postnatal malnutrition and accumulation of growth deficits, especially in the smallest most immature infants. Delayed introduction of enteral nutrition can result in nutritional deficits and reduced 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 Welsh Government is committed to giving every child a good start in life and a key aspect of this work is to encourage and support more breastfeeding across Wales. This includes increasing the number of mothers choosing to express their breast milk as well as breastfeeding rates on discharge from hospital. As such they are committed to neonatal units achieving accreditation with the UNICEF (United Nations Children’s Fund) Baby Friendly Initiative for Neonatal Units (2). The goals of nutritional support in the preterm 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 long-term outcomes.

There are marked differences in nutritional management in neonatal units across the Network. This was highlighted by a scoping exercise on feeding practices undertaken across Wales in March 2013. The time to start feeding varied; the majority of infants born <32 weeks gestation started feeding on ≥day 2 compared to the majority of >32 week gestation infants who started feeding on day 0 or 1. Other variations across the network identified feed increased by volumes regardless of weight, in some cases resulting in the smaller infants having greater increases compared to the larger infant. This variation is not unique to Wales; in the United States (US), differences in practice were found to be greatest between Neonatal units, although they also existed between individual Neonatologists within the same units (3).

Although there is uncertainty around the definitive practice of nutritional support in preterm infants, standardisation of practice across the Welsh Neonatal Network is recommended for two reasons:

- a significant and prolonged decline in the incidence of NEC, nearing virtual elimination in some centres, has been reported consistently since the implementation of a standardised feeding regimen (SFR) in the form of clinical practice guidelines (4)
- quality improvement literature suggests that a continuing cycle of process planning, consistent implementation, review and audit of practice is highly effective in clinical medicine (5).

A number of preterm infants are cared for in more than one neonatal unit in Wales – a standardised approach to enteral feeding will support consistency of nutritional care.

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

It is designed to be used in conjunction with individual clinical assessment.
processes where decisions are made regarding the initiation and advancement of feeds in preterm infants. Evidence supporting recommendations can be found in Appendix 2.

### 2.0 Nutritional requirements of the preterm infant.

Nutritional requirements for preterm infant are based on published evidence; the most recent being Koletzko et al 2014 and ESPGHAN (European Society of Paediatric Gastroenterology, Hepatology and Nutrition) 2010 (6, 7).

Nutritional requirements are high in preterm infants; they are born when the in utero growth rates would have been 2-3 times greater compared with a baby born at term. Despite this, the increased nutrient demands in preterm are variable and not evenly spread over time. These variable increases are not met simply by increasing the volume of breast milk provision. Hence the development of specialist formulas and breast milk fortifiers for use in the preterm population.

<table>
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<th>Nutrient</th>
<th>Term infant</th>
<th>Preterm infant (Koletzko 2014)</th>
<th>Preterm infant 1000g–1800g (ESPGHAN 2010)</th>
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<td>3.5–4.5</td>
<td>4.0–4.5 (&lt;1000g)</td>
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</tr>
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</table>

### 3.0 Feeding the preterm infant (see Algorithm 1 & Appendix 5)

#### 3.1 When to start feeding

Start enteral feeding within the first 24 hours of life unless clinically contraindicated (8, 9). There is growing evidence to support early enteral feeding even in high risk infants (10). Feed infants according to Algorithm 1.

- <28 weeks gestation or <1000g birth weight
- preterm small for gestational age (SGA) infants (<2nd percentile and <34⁺⁰ weeks gestation)
- absent or reversed end diastolic flow in infants <34⁺⁰ weeks
• infants re-establishing feeds after an episode of NEC
• perinatal hypoxic-ischaemia with significant organ dysfunction
• infant with congenital gut malformations (e.g. operated gastroschisis)
• hypotensive/unstable ventilated neonates.

Caution should be taken in initiating feeds in the following subgroups. The decision to manage as “high risk” is at the clinician’s discretion.

• severe SGA infants (<0.4th percentile and >34+0 weeks gestation)
• complex congenital cardiac disease
• corticosteroid treatment
• indometacin or Ibuprofen treatment for Patent Ductus Arteriosus (PDA)
• polycythaemic infants.

3.2 Trophic feeding / Minimal Enteral Nutrition (MEN)

Trophic feeds, also known as MEN, are small volumes of milk given to stimulate the bowel. These can be maintained for up to 7 days and are not intended to contribute to nutrition.

• The maximum volume classed as a “trophic feed” is 1ml/kg/hour or 24ml/kg/day (11)
• Trophic feeds should be considered in very preterm or high risk infants in order to utilise maternal colostrum and stimulate gut trophic hormones
• There is no recognised consensus on duration or method of delivery (9)
• Trophic feeds should commence as soon as possible after delivery unless contraindicated
• Trophic feeds can be initiated and advanced during Indomethacin/Ibuprofen treatment (12)
• Trophic feeding of preterm infants with intrauterine growth restriction (IUGR) and abnormal antenatal doppler results may not have a significant impact on incidence of NEC or feeding intolerance (13)
• Individual infants should be assessed at least daily for tolerance and a decision made with regard to continuation of trophic feeding or progression to standard advancement of feeds
• The decision as to whether to include these fluids within the daily fluid requirement is left to the clinician’s discretion.

3.3 Rate of advance of feeding

Current data does not support that slow advancement of feeding in very low birth weight infants reduces the risk of NEC (14, 15). However available evidence and current best practice suggest the following:

• in standard risk infants a rate of increase of 30ml/kg/day is reported safe
• in high risk infants evidence suggests a period of trophic feeds followed by a rate of increase of 10-20ml/kg/day
• there should be a low threshold for withholding stepped increases secondary to intolerance in the high risk infant (15).

3.4 Assessing feed tolerance
Careful clinical assessment is essential to prevent unnecessary limitations of enteral feeds, which may lead to reliance on parenteral nutrition, delay to full feeding and poor growth. Therefore as aspirate volumes may vary in the early stages of feeding, significant increases in aspirate volume should not be used in isolation when deciding to limit advancement of feeds (1). Gastric residual volumes and bloody residuals in combination represent an early relevant marker for the detection of NEC in very low birth weight (VLBW) infants (16). Do not use diluted feeds.

**Signs of intolerance:**

- vomiting
- gastric residuals >50% of previous 4 hours feed volume, particularly if persistent or increasing in volume
- abdominal distension / increasing abdominal girth.

**Signs of NEC:**

- bilious / bloody aspirates
- visual bowel loops / abdominal discolouration
- grossly bloody / watery or abnormal stools
- clinically unstable or acute deterioration.

**Suggested interventions if signs of intolerance present:**

- medical review
- consider septic screen and/or abdominal x-ray
- consider continuing with trophic feeds rather than nil enterally unless worried about NEC.

Available recommendations suggest undigested milk residuals (gastric aspirates) should be re-fed and feeding continued if residual volumes <25% of previous 4 hour feed volume.

### 3.5 Method and frequency of feeding

**Bolus versus continuous feeding:**

There is insufficient evidence to support one method of administration over the other, however best practice (1) suggests that:

- bolus feeding may be more physiological in the preterm infant (17)
- bolus fed infants may experience less feed intolerance and have a greater rate of weight gain (18)
- growth may be compromised in continuous feeding as human milk fat adheres to the tubing (19)
- consider placing expressed breast milk (EBM) in a rocket pump beneath the cot level, that delivers milk upwards to allow the fat in the milk to be delivered first and achieve better growth
- continuously fed infants take the same length of time to achieve full feeds as bolus feds (20)
- higher behavioural stress responses have recently been reported in bolus fed infants (21).
Gastric administration of feeds is preferred. Transpyloric feeding is not routinely recommended in preterm infants as no benefits have been found and they have been associated with a greater incidence of gastrointestinal disturbance (22).

Feed frequency in trophic feeding has not been evaluated and is limited by the small volumes involved. Furthermore debate is even greater with how to advance feeds. In general, infants <32\textsuperscript{+0} weeks should receive 1-2 hourly feeds moving to 3 hourly as they grow (23).

4.0 Milks and Indications for use (see Algorithm 2)

4.1 Breast Milk

Breast milk expressed by the infant’s own mother is the gold standard for preterm infants (24, 25).

In the first few weeks of lactation, preterm breast milk contains higher concentrations of protein, fat, energy and sodium but these will drop to the same levels as mature term milk within 2-3 weeks of birth. A preterm infant can meet its energy requirements from breast milk alone if expressing techniques and milk handling are optimised (e.g. use of hind breast milk), but not the protein requirements. Infants born <1000g will require 200ml/kg/day to meet requirements for energy. Eventually more protein will be required in the form of multi nutrient Breast Milk Fortifier (BMF), especially in infants <1500g birth weight (26-29). Moreover infants born <1000g would require up to 240ml/kg/day to meet the higher requirements for protein, increasing to 330ml/kg/day after two weeks. Clearly these volumes are undesirable and hence fortification is indicated in order to maintain realistic lower feed volumes (See Appendix 1).

Counsel and encourage mothers to breastfeeding or express milk within 4 hours of birth, even if their long term intention is not to breastfeed. In order to sustain exclusive breastfeeding, advise mothers to express as frequently as possible, 8-10 times per day with at least one night expression, aiming for a minimum daily volume of 750ml by day 10-14 after birth (30, 2). All units should have a well-established guideline for skin-to-skin contact to encourage successful breast milk expression. If milk supply is <350ml/day at day 10 further support is recommended (e.g. referral to lactation specialist). Mothers should receive ongoing support to achieve optimal milk expression and to support breastfeeding as the infant progresses.

Preterm infants fed exclusively on breast milk should receive supplementary phosphorus which should be titrated against normal serum phosphate and alkaline phosphatase (ALP) levels.

4.2 Breast Milk Fortification

Nutritional content of EBM decreases after the first 2-3 weeks post-delivery. Therefore, fortification of EBM should be considered using a BMF. The BMFs available in the UK are based on bovine milk protein. BMF based on human milk protein are currently not available in the UK.

BLISS recommends the following (31):
Fortify EBM in all infants <1500g birth weight and <34 weeks gestation.

Consider fortification in infants 1500-2000g birth weight and <34 weeks, and if:

- receiving ≥50% total feeds as breast milk
- tolerating feed volumes at a minimum of 150m/kg/day – preferably 180ml/kg/day
- Serum urea < 4mmol/L and falling.

Infants >2000g birth weight are unlikely to need BMF

UNICEF recommend that infants be tolerating full enteral feeds before BMF is added and not to consider fortification until an infant has received at least 2 weeks of exclusive mother’s milk (2). It is at the discretion of the clinician to introduce BMF before this stage.

To prepare EBM with BMF, add 1 complete sachet of BMF to 50ml of EBM. Storage concerns include the reduction of anti-infective components (32), increased bacterial loads (33) and increasing osmolality over time secondary to hydrolysis of glucose polymers by human milk amylase. Many of these effects can be reduced by adding BMF as close to feeding as possible (34, 35).

Check plasma urea levels weekly to monitor levels and the effect of BMF.

BMF does not need not be added if more than half of the feed requirement is provided by a preterm formula. However it can be considered if there is associated poor growth and tolerance of volume. In practice this would depend on having adequate volumes of milk to fortify accurately.

Do not add BMF as a supplement to preterm formula.

Criteria for stopping BMF (31):

- on <50 % total feeds as EBM and growth satisfactory
- if growth not satisfactory, continue BMF until <25 % total feeds EBM
- able to fully demand breast feed
- at discharge together with satisfactory growth
- assess infants individually to see if BMF post discharge may be of benefit.

BMF is not prescribable in the community and is generally discontinued at the time of discharge.

4.3 Donor breast milk (DBM)

In the absence of a mother’s own EBM, the milk of choice for a high risk infant should be DBM, if available. However, the feasibility of use and role of donor milk in current neonatal practice remains to be established (36). The use of DBM throughout Wales is inconsistent. Indications for use of DBM include:

- gestational age <28+0 weeks
- ELBW < 1000g
- previous proven NEC
- <32+0 weeks and IUGR
• <34\(^{+0}\) weeks and with absent/reversed end diastolic flow.

DBM has a variable nutritional profile compared to maternal EBM (37); premature DBM should be used where available.

Restrict DBM to either:

• establishing feeds in the ‘at risk’ infant with the gradual introduction of alternative feeds once full volumes are achieved, or
• for the short term support of a preterm infant whose mother is establishing milk expression.

4.4 Preterm formulas

Infants born <34\(^{+0}\) weeks and/or with a birth weight <2000g should be fed preterm formula when breast milk is unavailable. There is no evidence to support the use of term, semi-elemental or elemental formulas in these infants.

Requirements:
• feed to initial volume of 150ml/kg/day increasing as indicated by weight gain and volume tolerance
• infants born >1000g will have their protein requirements met by 165ml/kg/day
• infants born ≤1000g will have their protein requirements met by 180ml/kg/day
• volumes >180ml/kg/day are not usually necessary and other reasons for poor growth should be sought before further volume increases are introduced (Appendix 1).

There are no recommendations for infants born between 34\(^{+0}\) and 37\(^{+0}\) weeks gestation. Nutrient stores are better and these infants are likely to establish feeding quicker than those born <34\(^{+0}\) weeks gestation so maternal breast milk is the feed of choice. In the absence of this, use a term infant formula.

Assess growth restricted infants born between 34\(^{+0}\) and 37\(^{+0}\) on an individual basis as they can be offered a term infant formula. For infants with poor growth, consider using a high energy term infant formula. Growth restricted term infants >37\(^{+0}\) weeks should also be offered term infant formula in the absence of maternal milk (38).

Refer infants who have faltering growth to a paediatric dietitian for assessment and advice.

If a combination of formula feed is required in addition to EBM, it can be given either:

• until the next expression of breast milk, or
• when supplies of EBM are no longer available, or
• as a mixed feed of EBM and formula, or
• alternating fortified EBM and formula feeds.

There is no evidence to support one practice over another, but the method that is easiest in practice and that involves the least amount of milk handling is likely to be the best for individual infants.
4.5 Nutrient Enriched Post Discharge Formulas (NEPDF)

Maternal choice and the difficulties some mothers face trying to maintain breastfeeding will result in some infants requiring some or all formula milk by the time of discharge. Infants born prior to 34+0 weeks and <2000g at birth, who are not breastfed or who will require supplementary feeding at discharge, should change to NEPDF when they reach 1800-2000g.

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

On discharge from hospital, units provide infants who require NEPDF with a supply of powdered milk. However, powdered infant formulas (PIF) are not sterile and are at risk of contamination with Salmonella and Enterobacter sakazakii (E sakazakii can survive for at least 1 year in dry PIF) (39). E. sakazakii has caused diseases in all age groups but by far the majority of cases are seen in infants less than 4-6 weeks of age, especially preterm infants, underweight, immunocompromised or from immunocompromised mothers. European guidance recommends that the most effective control measure to minimise risks of Salmonella and E. sakazakii in high risk infants (preterm, underweight, immunocompromised) would be to use commercial sterile liquid formula (40). This is not currently common practice in units across Wales.

NEPDF can be continued until catch up growth has been achieved then changed to a standard formula. Stop these milks by 6 months corrected age. In general when an infant has been weaned and is having 3 meals per day the NEPDF can be discontinued. If catch up growth has not been achieved during this time consider referral to a paediatric dietitian.

4.6 Specialist term formulas (Appendices 3 and 4)

Specialist term formulas are not designed for use in the preterm population so will not fully meet their nutritional requirements. Energy needs might be met by increased volumes, but are often poorly tolerated. Formulas can be concentrated but this will not address the nutrient imbalance. Infants requiring these feeds may include post-surgery infants and infants with suspected cow's milk allergy.

Some units choose to use hydrolysed formulas when breast milk is not available. However, there is little evidence to support or refute this practice at present.

These specialist formulas need to be reconstituted from powder. They will be non-sterile and have potentially inconsistent composition. All powdered feeds should be made up in accordance with the Food Standards Agency ‘Guidelines for making up special feeds for infants and children in hospital’ (39).

Specialist formulas 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 hereditary lactase deficiency or as part of a vegan diet (41).

All infants born <35+0 weeks will need vitamin and iron supplementation according to local health board policy.
Algorithm 1 - Initiating and advancing enteral feeds

This algorithm is to be used in conjunction with Algorithm 2 (Choice of milk) and Appendix 5 (Feed Volume Ready Reckoner).

Enteral feeding should start within the first 24 hours of life unless clinically contraindicated.

Initiate trophic feeds in high risk infants as soon as possible and increase feeds according to algorithm below as soon as clinically indicated.

Infants can move between risk categories following individual clinical assessment.

High risk defined as:
- <28\(^{\text{th}}\) weeks gestation or < 1000g birth weight
- preterm SGA infant (<2nd percentile and <34\(^{\text{th}}\) weeks gestation)
- absent or reversed end diastolic flow in infants <34\(^{\text{th}}\) weeks
- re-establishment of feeds following NEC
- perinatal hypoxic-ischaemia with significant organ dysfunction.
- congenital gut malformations (e.g. operated gastroschisis)
- hypotensive/unstable ventilated infants

Caution should be taken when initiating feeds in the following subgroups. The decision to manage as ‘high risk’ is at the clinician’s discretion.

Moderate risk defined as:
- severe SGA infants (<0.4\(^{\text{th}}\) percentile and >34\(^{\text{th}}\) weeks gestation).
- complex congenital cardiac disease
- corticosteroid treatment
- indometacin or ibuprofen treatment for PDA
- polycythaemic infants

High risk

See above

Step 1:
First day of Feeding

- 10-20ml/kg/day as 1-2 hourly trophic feeds

Increase by 10ml/kg/day every 12 hours as 1 or 2 hourly feeds according to tolerance

Continue to increase by 10ml/kg/day every 12 hours as 1 or 2 hourly feeds until full feeds achieved. Increase beyond 180ml/kg\(^*\) only after assessment of growth.

Step 2:
Advance as indicated

- 20ml/kg/day as 1-2 hourly feeds

Increase by 15ml/kg/day every 12 hours as 2 hourly feeds

Continue increasing at this rate until full enteral volume achieved

Step 3

- 30-60ml/kg/day as 1-3 hourly feeds

Increase by 30ml/kg/day as 3 hourly feeds

Moderate risk

28\(^{\text{th}}\) – 31\(^{\text{st}}\) weeks

- 20ml/kg/day as 1-2 hourly feeds

Increase by 15ml/kg/day every 12 hours as 2 hourly feeds

Standard risk

≥32\(^{\text{th}}\) weeks

- 30-60ml/kg/day as 1-3 hourly feeds

Increase by 30ml/kg/day as 3 hourly feeds

\(\ast\) >180ml/kg/day should rarely be required in infants receiving preterm formula or fortified EBM. Alternative reasons for poor growth should be examined before volumes >180ml/kg/day are implemented.
Algorithm 2 – Choice of milk

Fresh maternal breast milk is the first milk of choice for all infants unless clearly contraindicated.

**Infants <34\(^{+0}\) weeks gestation**

- **Weight <2000g at birth**
  - EBM increases to 150ml/kg/day as per algorithm 1
  - Infant <1500g at birth
    - Once tolerating 150ml/kg/day EBM for 24 hours consider BMF
    - Increase as tolerated up to 180ml/kg/day EBM+BMF
  - Infant ≥1500g and <2000g at birth
    - Increase as tolerated to 180ml/kg/day EBM
    - Increase volume if weight gain poor
    - Consider BMF if:
      - poor tolerance of volume
      - poor weight gain persists
      - serum urea <4mmol/l and falling
      - IUGR < 9\(^{th}\) centile

**Infants ≥ 34\(^{+0}\) weeks gestation**

- **Weight ≥ 2000g at birth**
  - Breast feeding or EBM increases to 165ml/kg/day as per algorithm 1
  - Increase as tolerated to 180ml/kg/day EBM if weight gain poor
  - Increase up to 220ml/kg/day EBM if required to achieve weight gain
  - If insufficient EBM use term infant formula

* >180ml/kg/day should rarely be required in infants receiving preterm formula or fortified EBM. Alternative reasons for poor growth should be examined before volumes >180ml/kg/day are implemented (appendix 1).

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Appendix 1 - Growth

Appropriate weight for gestational age

Low birth weight infants (LBW) (<2500g) born at term have nutritional requirements that differ from those of appropriate weight infants born at term. These requirements differ from those of infants who are preterm and appropriate weight for gestational age, as well as those who are preterm and small for gestational age. Actual requirements are unknown. An infant who is small at term is likely to have better stores of some nutrients compared to the infant born prematurely but of a similar weight. Comparatively the infant who is both preterm and small for gestation is likely to have the poorest stores of all nutrients. Some infants born small for gestation appear to catch up in weight; others do not. Whether improving their nutritional intake is of benefit or harm is unclear, but evidence suggests maternal breast milk achieves the best outcome (38). Until more evidence is available it seems appropriate to recommend breast milk to all growth restricted term infants, with a term infant formula as first option if breast milk is not available.

Infants who are preterm and growth restricted should follow advice for preterm infants.

Expected weight gain

The weekly completion of an appropriate growth chart is the best indicator of growth for an infant; however parents frequently ask how much weight their infant is expected to gain on a daily basis. The most frequently used range is 15–20g/kg/day, but a good guide for an infant born during what would have been their third trimester would be 18g/kg/day up to 2000g then 30g/day thereafter.

Growth monitoring

All growth parameters should be plotted on an appropriate growth chart as a minimum. Within Wales the Badgernet system is used to record data for these infants and this information is transferrable between units in Wales.

Weight
All infants should be accurately weighed at birth with note taken of any oedema present. Weight should be measured two to three times per week for the purpose of growth. All weights are to be recorded on end of bed charts and plotted weekly on the growth chart. Although weight is a poor measure of growth by itself, it is the only practical day to day measure that can be employed. It is needed for calculation of feeds and medications and is seen as an important indicator of progress by an infant's parents. As such measurements should be taken and plotted as accurately as possible.

Head Circumference
Head circumference should be measured on the day of birth and weekly thereafter.

Length
Length measurement is an additional growth monitoring tool, though a difficult measurement to obtain accurately. Frequency of measurement, method and equipment used is at each unit’s discretion, though as a minimum, length should be measured and
recorded at point of discharge. Ideally, all measurements should be performed by one identified trained individual with a helper in order to maintain standardised practice. However, as a minimum, all lengths should be measured by suitably trained individuals. Suitable equipment is available e.g. Leicester Incubator Measure.

Growth failure

Infants born preterm accumulate significant nutrient deficits by the time of discharge from hospital (42, 43). These can manifest as growth deficits that persist through infancy and early childhood (44) into adolescence (45). Factors contributing to nutrient deficits are numerous, though fluid restriction is often the greatest contributor. Most infants will meet their nutritional requirements between 150ml/kg/day and 180ml/kg/day of an appropriate feed, therefore interruption and reductions in feeds to below 150ml/kg/day should be minimised. Where prolonged fluid restrictions are unavoidable in the older formula fed infant, e.g. cardiac disease, consideration should be given to the use of nutrient dense term formula.

Conversely volume increases above 180ml/kg/day should only be implemented once consideration has been given to the range of other factors known to impact on growth:

- use of the most appropriate feed for the infant
- adequacy of human milk fortification
- potential sodium depletion
- anaemia
- sepsis/trauma in the short term
- steroid treatment, which can delay length growth for 3-4 weeks after stopping
- high energy requirements secondary to cardiac/respiratory condition
- low serum urea as an indicator of protein status
- organic causes of growth failure.

Breast milk composition is variable and all strategies should be explored to optimise the nutritional value of the EBM (see breast milk handling and storage section for more information).

In an infant exclusively fed on fortified EBM at maximum tolerated volumes, a combination of poor growth and a serum urea level of <4mmol/l and falling, may be an indicator of inadequate protein intake secondary to low protein levels in the EBM. These infants may benefit from a short period of time on a combination of fortified breast milk and preterm formula. If available, EBM with a higher protein content that has been frozen and stored earlier in the infant’s neonatal course should be considered.
Appendix 2 - Evidence supporting Enteral Feeding Guidelines

When to start feeding

The objective of early feeding is to stimulate gut maturation, motility and hormone release. As starvation leads to atrophy of the gut, withholding feeds may render subsequent feeding less safe and lengthen the time to reach full enteral feeding (3). One study suggested that trophic feeding had several benefits including greater energy intake, improved growth, improved milk tolerance, reduced parenteral nutrition, less sepsis, fewer days of oxygen and were discharged from hospital earlier (46). A Cochrane systematic review in 2013 (11) concluded that early introduction of feeding did not increase the incidence of NEC. Another Cochrane review in 2013 that assessed the effect of delayed rather than early introduction of milk feeds for the very preterm or very low birth-weight infant concluded that there was no evidence that delaying enteral feeding reduces the risk of NEC (47). The ADEPT trial (Abnormal Doppler Enteral Prescription Trial) concluded that growth restricted preterm infants born after abnormal umbilical dopplers (absent or reversed end-diastolic flow in the umbilical artery) 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 (10). No work has yet addressed whether initial feeds should be exclusively breast milk (mother’s own or donor) or whether initial feeds should be delayed if only formula is available. Most evidence suggests that any enteral feed given early is better than gut starvation (9).

Trophic feeding

Trophic feeds are small volumes of milk given to stimulate the gut that are maintained for up to 7 days and not intended to contribute to nutrition. The maximum suggested volume is 1ml/kg/hour or 24ml/kg/day (11). There is no recognised consensus on duration or method of delivery (9). One paper suggested starting trophic feeds early and keeping volumes at trophic levels for some days before advancing feed volumes relatively rapidly, however, the authors recommend that further research is needed (48). Another study showed no advantage for trophic feeding in an extremely low birth weight population in a randomised control trial (49). Another paper concluded that the duration of trophic feeds and the rate of advancement of feed volumes may be modifiable risk factors for NEC in preterm infants (50). The study in 2010 on trophic feeding suggests that early trophic feeding of preterm infants with IUGR and abnormal antenatal doppler may not have a significant impact on incidence of NEC or feed intolerance, though the standard of evidence presented in this paper leaves its conclusions open to criticism (13). None of the papers make recommendations for optimal duration of trophic feeds and all call for further research.

Rate of advance of feeding

Retrospective analysis of NEC cases undertaken in the 1990s led to the recommendation of limiting feed advancement to 20ml/kg/day (51), 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 (52). However a study of prolonged trophic feeding before advancement was closed early because of significantly increased NEC in the advancing feed group (53). Current data does not provide evidence that slow advancement of feeding in very low birth weight infants reduces the risk of NEC,
showing no advantage in increasing at 15-20ml/kg/day compared to 30-35ml/kg/day (14, 15). Although time to full feeds was longer in the slowly advanced group, there was no statistical difference in length of stay between the two groups.

A review of nutritional practices in the US in 2006 showed earlier initiation of feeds and higher volume increases than a similar review undertaken in 2001 (9). The range of feed increase was between 5-30ml/kg/day with the majority advancing at 10-20ml/kg/day. The authors commented that this is likely to be too cautious a figure for the majority of infants. In standard risk infants a rate of increase of 30ml/kg/day is reported safe, whereas data is more limited in the high risk infant. Evidence points towards several days of trophic feeds followed by a rate of increase of 10-20ml/kg/day. There should be a low threshold for withholding stepped increases secondary to tolerance concerns in the high risk infant.

A new large multi centred trial in the UK and Ireland undertaken by SIFT group (Speed Increasing Feeds Trial) aims to recruit 2500 very preterm or VLBW infants to compare advancement of feeds at either 30ml/kg/day or 18ml/kg/day. This trial will recruit infants who are fed either human or formula milk. Initial results are awaited.

Assessing feed tolerance

In the first few days following birth, gastric residuals are extremely common and are rarely associated with NEC (54, 55). The volume of feed aspirated from the stomach prior to a feed is one of the factors used to judge tolerance of feeding. Although volume and colour of aspirate may indicate level of gut maturity rather than gut dysfunction, they are still important signs for feed advancement when used in conjunction with other parameters. The paradoxical motility, which is responsible for most of the residuals, transitions more rapidly to a normal progressive pattern if feeds are started early and are persistently offered, than when feeds are withheld (1). Despite this, feeds are frequently stopped, or advances held on the basis of “feed intolerance”. The use of diluted feeds is not recommended.

The definition of intolerance includes not only the presence and colour of gastric residuals, but also vomiting, increases in abdominal girth or abdominal tenderness, presence of abnormal or blood stained stool, presence of bowel sounds, abdominal wall discolouration, or a combination of any (1, 55). As all of these can occur in the healthy preterm infant who is tolerating feeds (54) careful clinical assessment is essential to prevent unnecessary limitations of enteral feeds, reliance on parenteral nutrition, and delay to full feeding resulting in poor growth. Use of diluted feeds has been suggested for preterm infants, however intestinal motility responses have been shown to occur earlier and to persist longer following use of full strength formula in comparison to one third and two third dilutions (56). Clearly defining feed intolerance and a standardised feeding regimen can lead to dramatic improvements in nutritional outcomes (57). Gastric residuals up to 2ml in infants ≤ 750g and up to 3ml in infants 750g – 1500g were treated as normal (55). Maximum gastric residuals in premature infants who develop NEC have been shown to be 40% of feed volume compared to 14% in those who did not develop NEC, with residuals increasing dramatically over the three days before the onset of NEC (58). For the early detection of VLBW infants at risk for NEC, both gastric residual volumes and bloody residuals represent an early relevant marker (16).

As residuals vary so much in the early stages of feeding, significant increases should not be used in isolation when deciding to limit advancement of feeds (1). Guidelines are based on the California Perinatal Quality Care Collaborative Toolkit 2008.
Method and frequency of feeding

Feeds given by intermittent bolus method promote a cyclical surge of gut hormones similar to that in adults and term infants so are considered more physiological in the preterm infant (17). They also experience less feed intolerance and have a greater rate of weight gain when fed a bolus regimen compared to continuous infusion (18). Some authors recommend bolus or modified bolus feeding, given over an extended period of time, for the majority of very low birth weight infants (1, 59). One study demonstrated that continuously fed infants achieved full feeds more quickly than those receiving bolus feeds (19), however no assessment was made of growth and feed tolerance in the longer term. Higher behavioural stress responses in bolus fed infants have recently been reported by the same group (21); these findings need balancing against the advantages reported for bolus feeding. There are risks associated with continuous feeds that growth could be compromised as human milk fat adheres to the tubing during continuous feeding (59). A recent Cochrane review showed no differences in time to achieve full enteral feeds or the incidence of NEC and concluded that there was insufficient evidence to determine the best feeding method for low birth weight premature infants. They recommended that more research is required in this area (20).

Occasionally intolerance is seen in a bolus fed preterm infant with duodenal motility decreasing following a feed (60), however a bolus feed administered over a longer period of time results in a return of motility and improved tolerance (61).

Gastric feeding stimulates digestive processes whereas transpyloric feeding has the potential benefits of delivering nutrients past the pylorus and gastro oesophageal junction for the management of gastro oesophageal reflux (GOR) disease. These feeds have to be continuous, which may account for the reduction in symptoms of GOR. Transpyloric feeding is not routinely recommended in preterm infants as no benefits have been found and they have been associated with a greater incidence of gastrointestinal disturbances and mortality, but findings should be interpreted and applied cautiously because of methodological weaknesses in included trials (22).

Breast milk

Human milk is the preferred feed for preterm infants - in the short term it offers strong protection against infection and NEC, and in the long term improved neurocognitive development. Recent evidence shows the reduction in NEC risk using human milk to be dose dependent (62).

Maternal breast milk handling and storage

The breast should be completely emptied at each expression to ensure the collection of all the fat rich hind milk (63). Optimal expressing technique (e.g. ‘hands on’ expression) will help to ensure this is achieved. Handling cold milk can increase fat losses as the fat solidifies, whilst freezing with subsequent thawing can cause fat loss through the rupture of fat globules during the freezing process. The fat component in expressed breast milk is also prone to separation and adhesion to bottles and tubing thereby reducing the energy content of the milk (64). For further information about optimal breast feeding management see the UNICEF document ‘Breastfeeding and Lactation Management’ (2). Unfortified
EBM can be stored in a suitable fridge (2 – 4°C) for up to 48 hours (up to 24 hours if fortified) or in a freezer at -20°C for up to three months (36).

**Breast Milk Fortification**

Increased preterm nutritional requirements persist beyond the time when early milk composition changes to that of mature milk. This often coincides with a slowing of weight gain and a sequential reduction in serum urea, where a level <1.6mmol/l is indicative of a protein intake of <3g/kg (65).

In order to maintain the benefits of breast milk whilst optimising the nutritional status and growth of preterm infants, multi nutrient BMF have been developed. The two available in the UK are Nutriprem BMF (Cow & Gate) and SMA BMF (Wyeth). Both are based on cow’s milk protein. Neither product has clear indications for introduction or guidance for infant suitability. Therefore practice varies considerably across Wales.

Fortification of EBM using Human Milk Fortifier (HMF) has been studied and showed improved growth (66) but low serum phosphate levels due to inadequate bone mineral concentrations (67).

Concerns with the use of BMFs include tolerance and effects of storage. Most studies have found no significant problems with the tolerance of fortified EBM (68, 67) whilst those investigating gastric emptying have been contradictory (69, 70). Storage concerns include the reduction of anti-infective components (32), increased bacterial loads (33) and increasing osmolality over time, secondary to hydrolysis of glucose polymers by human milk amylase (34). The majority of these effects can be reduced by adding the BMF as close to feeding as possible, though recent work shows osmolality of fortified EBM reaches a peak within 10 minutes of addition and remains consistent to 24 hours of storage (35). A Cochrane review concludes that the use of BMF can lead to short term improvements in weight, length and head circumference and that whilst it is unlikely that further comparative studies with breast milk alone are to take place it recommends further research seeks to evaluate long term outcomes of BMF therapy and identify the optimum composition of BMF products (71). Breast milk is fortified without knowing the nutritional composition of an individual mother’s EBM. As the composition of breast milk, particularly protein concentration varies from one mother to the next and from expression to expression in the same mother; individual analysis prior to fortification would appear to be of value (72). Such analysis is at present impractical in day to day practice. Serum urea has been validated as an indicator of protein adequacy after the first two weeks of life in preterm infants (31) but should be carefully interpreted in infants with severe IUGR due to lower intestinal absorption (73). Studies looking at fixed supplementation against urea determined supplementation have been inconclusive but a study demonstrated improvement in body weight and head circumference where protein fortification was adjusted according to serum urea levels (74).

**Donor breast milk (DBM)**

In the absence of a mother’s own expressed breast milk, donor milk may be the milk of choice for a high risk infant; however access to DBM is variable due to the geography of Wales. The location of the unit will determine which milk bank will be used. Additionally the role of DBM in current neonatal practice and the feasibility, cost and impact of its use on nutrient intake, growth and development remains to be established (36). Observational studies suggest that DBM is similar to mothers own milk with regard to improved feed tolerance (75), anti-infective properties (76) and reduced risk of NEC (77, 76). However in...
these studies infant growth was slower and benefits only seen when breast milk or formula was the sole source of nutrition, whereas current UK practice uses DBM as a supplement to mother’s milk. For indications other than NEC and for long term outcomes, justification for the use of DBM remains anecdotal.

DBM has an average energy content of 46kcal/100ml (compared to 70kcal/100ml for preterm breast milk) as the majority of donated milk tends to come from lactating mothers of older term infants. However, preterm DBM is becoming available and should be used whenever possible. The use of DBM should normally be restricted to establishing feeds in the at risk infant with the gradual introduction of alternative feeds once full volumes are achieved. Some units may use DBM for the short term support of a preterm infant whose mother is establishing milk expression.

It is important to bear in mind that DBM is a human body fluid and as such carries risks of transmission of infective agents. All donor screening, handling, testing and processing of DBM in the Milk Bank is carried out according to NICE Guidelines (78). Documentation and traceability of DBM is essential. The recent NICE Guidelines contain specific recommendations for practice within hospitals receiving DBM from a Milk Bank in addition to recommendations for central processing units.

Preterm Formulas

Preterm formulas are designed to meet the basic nutritional requirements of most preterm infants when fed between 150ml/kg/day and 180ml/kg/day and is used when EBM is not available.

There are currently two formulas available in the UK, Nutriprem 1 and SMA Gold Prem 1. Both are presented in 60ml ready to feed bottles and are for hospital use only. They are not available in the community setting.

Preterm formulas can be used as soon as commencement of enteral feeding is recommended. Term formulas should not be used as they fail to meet the nutritional needs of preterm infants.

Specialist Formulas

There is no evidence to support the use of term elemental/semi-elemental formulas in the early stages of feeding unless there is a compelling clinical reason to do so. Hydrolysed Nutriprem was introduced into the UK market in April 2014 but experience of use has not been determined. This product has a similar composition to Nutriprem 1. A partially hydrolysed preterm formula has recently been introduced to the US market, but there is currently no published information as to its safety or efficacy (1).
Appendix 3: Specialist infant formulas used in the neonatal unit

(NB: Products are listed in alphabetical order of the manufacturer)

<table>
<thead>
<tr>
<th>Formula</th>
<th>Manufacturer</th>
<th>Indications</th>
<th>Nutrient Modification</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hydrolysed Preterm Formula</td>
<td>Cow &amp; Gate</td>
<td>For preterm and LBW infants who require a hydrolysed protein feed.</td>
<td>50% whey; 50% casein; osmolality = 405mOsm/kg water</td>
</tr>
<tr>
<td>Hydrolysed Nutriprem</td>
<td>Cow &amp; Gate</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Extensively Hydrolysed Protein Formula (EHF)</td>
<td>Abbott Abbott</td>
<td>Cow’s milk protein intolerance</td>
<td>hydrolysed casein; low lactose; 30% MCT; osmolality = 274mOsm/kg water</td>
</tr>
<tr>
<td>Similac Alimentum</td>
<td>Abbott</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Extensively Hydrolysed Protein Formula (EHF) with approximately 50% MCT fat</td>
<td>Danone</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aptamil Pepti 1</td>
<td>Danone</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nutramigen Lipil 1</td>
<td>Mead Johnson</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Althera</td>
<td>Nestle</td>
<td>hydrolysed whey; contains lactose; osmolality = 281mOsm/kg water</td>
<td></td>
</tr>
<tr>
<td>Extensively Hydrolysed Protein Formula (EHF) with approximately 50% MCT fat</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pepti-Junior</td>
<td>Cow &amp; Gate</td>
<td>Malabsorption; post NEC; post GI surgery; conjugated hyperbilirubinaemia</td>
<td>whey based; minimal lactose; osmolality = 210mOsm/kg water</td>
</tr>
<tr>
<td>Pregestimil Lipil</td>
<td>Mead Johnson</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Infatrini Peptisorb</td>
<td>Nutricia</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Amino Acid Formula</td>
<td></td>
<td></td>
<td>osmolality = 350mOsm/kg water</td>
</tr>
<tr>
<td>Nutramigen Puramino</td>
<td>Mead Johnson</td>
<td>Severe malabsorption; allergy</td>
<td>osmolality = 350mOsm/kg water</td>
</tr>
<tr>
<td>Alfamino</td>
<td>Nestle</td>
<td></td>
<td>osmolality = 360mOsm/kg water</td>
</tr>
<tr>
<td>Neocate LCP</td>
<td>Nutricia</td>
<td></td>
<td>osmolality = 360mOsm/kg water</td>
</tr>
<tr>
<td>High Energy Formula</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Similac HE</td>
<td>Abbott</td>
<td>Increased requirements or fluid restricted infants</td>
<td>1kcal/ml; osmolality = 333mOsm/kg water</td>
</tr>
<tr>
<td>Infatrini</td>
<td>Nutricia</td>
<td></td>
<td>1kcal/ml; osmolality = 345mOsm/kg water</td>
</tr>
<tr>
<td>SMA High Energy</td>
<td>SMA</td>
<td></td>
<td>0.9kcal/ml; osmolality = 387mOsm/kg water</td>
</tr>
<tr>
<td>MCT Formula</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Monogen</td>
<td>Nutricia</td>
<td>Use when a diet low in long chain fats is indicated</td>
<td>80% MCT; 20% LCT osmolality = 280mOsm/kg water</td>
</tr>
<tr>
<td>Renal Formula</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Renastart</td>
<td>Vitaflor</td>
<td>Renal insufficiency</td>
<td>low in protein, calcium, chloride, potassium, phosphorus and vitamin A; 1kcal/ml at standard 20% solution osmolality = 198mOsm/kg water</td>
</tr>
<tr>
<td>Kindergen</td>
<td>Nutricia</td>
<td>Renal insufficiency</td>
<td>low in potassium, chloride, calcium, phosphorus and vitamin A. 1kcal/ml at standard 20% solution osmolality = 215mOsm/kg water</td>
</tr>
<tr>
<td>Low Calcium Formula</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Locasol</td>
<td>Nutricia</td>
<td>Disorders causing high blood calcium levels e.g. Williams Syndrome; hypophosphatasia</td>
<td>very low in calcium and vitamin D osmolality = 310mOsm/kg water</td>
</tr>
<tr>
<td>Formulas used in Inherited Metabolic Disorders (IMD)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>There are a variety of specialist infant formulas used in IMD dependent upon the specific condition. These should be used following discussion with your metabolic, neonatal or paediatric dietitian.</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
### Appendix 4 - Nutritional Composition of Milks and Supplements

Values are given per 100ml ‘ready to feed’ formula (where products are available in this format). All other feeds are per 100ml of reconstituted formula at standard concentration.

<table>
<thead>
<tr>
<th>Milk</th>
<th>Energy (kcal)</th>
<th>Protein (g)</th>
<th>Fat (g)</th>
<th>CHO (g)</th>
<th>Na (mmol)</th>
<th>K (mmol)</th>
<th>Fe (mg)</th>
<th>Ca (mmol)</th>
<th>P (mmol)</th>
<th>Vit A (µg)</th>
<th>Vit D (µg)</th>
<th>Osmolality (mosm/kg H2O)</th>
</tr>
</thead>
<tbody>
<tr>
<td>EBM - preterm</td>
<td>70</td>
<td>1.8</td>
<td>4.0</td>
<td>7.0</td>
<td>1.3</td>
<td>1.5</td>
<td>ns</td>
<td>0.6</td>
<td>0.5</td>
<td>ns</td>
<td>ns</td>
<td>~276</td>
</tr>
<tr>
<td>EBM – preterm &gt;2 weeks</td>
<td>70</td>
<td>1.3</td>
<td>4.2</td>
<td>7.4</td>
<td>0.7</td>
<td>1.5</td>
<td>ns</td>
<td>0.9</td>
<td>0.5</td>
<td>58</td>
<td>ns</td>
<td>~270</td>
</tr>
<tr>
<td>EBM + Nutriprem BMF</td>
<td>86</td>
<td>2.5</td>
<td>4.2</td>
<td>10.2</td>
<td>2.3</td>
<td>2.1</td>
<td>ns</td>
<td>2.6</td>
<td>1.7</td>
<td>290</td>
<td>5</td>
<td>~340</td>
</tr>
<tr>
<td>EBM + SMA BMF</td>
<td>85</td>
<td>2.3</td>
<td>4.4</td>
<td>9.8</td>
<td>1.5</td>
<td>2.2</td>
<td>ns</td>
<td>3.2</td>
<td>1.9</td>
<td>328</td>
<td>7.6</td>
<td>~343</td>
</tr>
<tr>
<td>Nutriprem 1 (LBW formula)</td>
<td>80</td>
<td>2.6</td>
<td>3.9</td>
<td>8.4</td>
<td>3.0</td>
<td>2.1</td>
<td>1.6</td>
<td>2.35</td>
<td>2.0</td>
<td>361</td>
<td>3.0</td>
<td>375</td>
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<tr>
<td>SMA Gold Prem 1</td>
<td>82</td>
<td>2.2</td>
<td>4.4</td>
<td>8.4</td>
<td>1.9</td>
<td>1.9</td>
<td>1.4</td>
<td>2.5</td>
<td>2.0</td>
<td>185</td>
<td>3.4</td>
<td>272</td>
</tr>
<tr>
<td>Nutriprem 2</td>
<td>75</td>
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<td>4.0</td>
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<td>1.2</td>
<td>2.2</td>
<td>1.5</td>
<td>100</td>
<td>1.7</td>
<td>310</td>
</tr>
<tr>
<td>SMA Gold Prem 2</td>
<td>73</td>
<td>1.9</td>
<td>3.9</td>
<td>7.5</td>
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<td>1.2</td>
<td>1.8</td>
<td>1.4</td>
<td>100</td>
<td>1.5</td>
<td>312</td>
</tr>
<tr>
<td>Cow &amp; Gate First Infant Milk</td>
<td>66</td>
<td>1.3</td>
<td>3.4</td>
<td>7.3</td>
<td>0.8</td>
<td>1.7</td>
<td>0.6</td>
<td>1.3</td>
<td>0.9</td>
<td>55</td>
<td>1.2</td>
<td>310</td>
</tr>
<tr>
<td>SMA First</td>
<td>67</td>
<td>1.3</td>
<td>3.6</td>
<td>7.3</td>
<td>0.7</td>
<td>1.7</td>
<td>0.6</td>
<td>1.0</td>
<td>0.8</td>
<td>66</td>
<td>1.2</td>
<td>280</td>
</tr>
<tr>
<td>Aptamil First</td>
<td>66</td>
<td>1.3</td>
<td>3.4</td>
<td>7.3</td>
<td>0.7</td>
<td>1.7</td>
<td>0.5</td>
<td>1.4</td>
<td>1.0</td>
<td>54</td>
<td>1.2</td>
<td>335</td>
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<td>(powder information)</td>
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<td></td>
<td></td>
<td></td>
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<tr>
<td>Hydrolysed Nutriprem</td>
<td>80</td>
<td>2.6</td>
<td>4.0</td>
<td>8.4</td>
<td>3.0</td>
<td>2.2</td>
<td>1.6</td>
<td>2.6</td>
<td>1.9</td>
<td>325</td>
<td>3.0</td>
<td>405</td>
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<td>Similac Alimentum</td>
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<td>1.9</td>
<td>3.8</td>
<td>6.6</td>
<td>1.3</td>
<td>1.8</td>
<td>1.2</td>
<td>1.8</td>
<td>1.4</td>
<td>61</td>
<td>1.0</td>
<td>274</td>
</tr>
<tr>
<td>Aptamil Pepti 1</td>
<td>67</td>
<td>1.6</td>
<td>3.5</td>
<td>7.1</td>
<td>0.9</td>
<td>1.9</td>
<td>0.53</td>
<td>1.2</td>
<td>0.8</td>
<td>53</td>
<td>1.2</td>
<td>280</td>
</tr>
<tr>
<td>Nutramigen Lipil 1</td>
<td>68</td>
<td>1.9</td>
<td>3.4</td>
<td>7.5</td>
<td>1.4</td>
<td>2.1</td>
<td>1.2</td>
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<td>1.7</td>
<td>60</td>
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<tr>
<td>Althera</td>
<td>67</td>
<td>1.7</td>
<td>3.4</td>
<td>7.3</td>
<td>0.8</td>
<td>1.8</td>
<td>0.7</td>
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<td>0.7</td>
<td>79</td>
<td>1.0</td>
<td>281</td>
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</table>
### Appendix 4 Continued - Nutritional Composition of Milks and Supplements

Values are given per 100ml 'ready to feed' formula (where products are available in this format). All other feeds are per 100ml of reconstituted formula at standard concentration.

<table>
<thead>
<tr>
<th>Milk</th>
<th>Energy (kcal)</th>
<th>Protein (g)</th>
<th>Fat (g)</th>
<th>CHO (mmol)</th>
<th>Na (mmol)</th>
<th>K (mmol)</th>
<th>Fe (mg)</th>
<th>Ca (mmol)</th>
<th>P (mmol)</th>
<th>Vit A (µg)</th>
<th>Vit D (µg)</th>
<th>Osmolality (mosm/kg H2O)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pepti-Junior</td>
<td>66</td>
<td>1.8</td>
<td>3.5</td>
<td>6.8</td>
<td>0.8</td>
<td>1.7</td>
<td>0.8</td>
<td>1.2</td>
<td>0.9</td>
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<td>Pregestimil Lipil</td>
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<td>3.8</td>
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<td>1.3</td>
<td>1.9</td>
<td>1.2</td>
<td>2.0</td>
<td>1.7</td>
<td>77</td>
<td>1.3</td>
<td>280</td>
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<tr>
<td>Infatrine Peptisorb</td>
<td>100</td>
<td>2.6</td>
<td>5.4</td>
<td>10.1</td>
<td>1.4</td>
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<td>1.0</td>
<td>2.0</td>
<td>1.3</td>
<td>81</td>
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<td>350</td>
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<td>Nutramigen Puramino</td>
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<td>1.9</td>
<td>3.6</td>
<td>7.2</td>
<td>1.4</td>
<td>1.9</td>
<td>1.2</td>
<td>1.6</td>
<td>1.1</td>
<td>61</td>
<td>0.9</td>
<td>350</td>
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<tr>
<td>Alfamino</td>
<td>69</td>
<td>1.8</td>
<td>3.4</td>
<td>7.9</td>
<td>1.1</td>
<td>2.0</td>
<td>0.7</td>
<td>1.4</td>
<td>1.2</td>
<td>91</td>
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References

32. Quan R. et al. 1994. The Effect of Nutritional Additives on Anti-Infective Factors in Human Milk. Clinical Pediatrics,
33(6), pp.325-328.
Human Milk Protein or with a Bovine Milk Protein Preparation. Journal of Pediatric Gastroenterology and Nutrition, 13(2), pp.150-154.


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