MCN for Neonatology

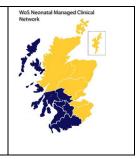
West of Scotland

Neonatal Guideline

Enteral Feeding of Preterm Babies

Contents

- Introduction
- Background
- What is adequate growth for a preterm baby?
- Growth monitoring in the neonatal unit
- Nutritional requirements of a preterm baby
- Feeding the preterm baby
 - When to start milk?
 - Benefits of buccal colostrum
 - Practicalities of buccal colostrum administration
 - Minimal enteral nutrition
 - Rate of feed advancement
- Method and frequency of feeding
 - Bolus versus continuous feeds
 - Nasogastric versus orogastric tubes
 - When to stop parenteral nutrition and remove vascular access?
- Assessing feed tolerance
 - Gastric residual volumes / aspirates
 - Signs of feed intolerance
- Differing milks and their indication for use
- Maternal expressed breast milk
 - Donated human milk
 - o Breast milk fortification
- Preterm formula
- Nutrient enriched post discharge formula
- Nutritional supplements
- Probiotics
 - o Practicalities of introducing probiotics into clinical practice
 - Criteria for use
- Appendix 1: Guide to the assessment of a baby with poor growth
- Appendix 2: Initiating and advancing feeds
- References
- Authorship



Introduction

This guideline describes enteral feeding practices for babies born at \leq 34 week's gestational age (GA) and / or \leq 1800 grams birth weight. It should be used in conjunction with local Parenteral Nutrition (PN) guidance.

It advocates for consistency of approach across neonatal units and networks. These recommendations must always be used in combination with individualised clinical assessment and are **NOT** applicable to:

- 1. Babies with congenital anomalies of the gastrointestinal (GI) tract
- 2. Babies commencing enteral feeding after GI surgery
- 3. Babies commencing enteral feeding after an episode of medically managed necrotising enterocolitis (NEC)

This guideline is applicable to all healthcare professionals caring for preterm babies in Scottish neonatal units.

Background

With improved survival increased emphasis is now placed on ensuring the highest quality outcomes for babies born prematurely. Early nutrition plays an important role in achieving optimised short and longer term health, and the aims of nutritional management are to:

- 1. Achieve an adequate standard of short and longer term growth
- 2. Meet the increased nutritional requirements of the preterm baby
- 3. Avoid feeding-related morbidities, especially NEC
- 4. Optimise longer term health outcomes such as neurodevelopmental attainment

A consistent approach to enteral feeding is advocated because data from multiple observational studies suggest that the use of a standardised feeding guideline positively impacts a number of clinical outcomes including¹⁻⁵:

- Reduced time taken to achieve full milk feeding
- Shortened time on PN
- Shortened length of hospital stay
- Reduced NEC rates
- Improved growth and neurodevelopmental attainment

There is good evidence that both consistency of practice and growth outcomes are improved with a multidisciplinary team (MDT) approach to nutritional care; weekly nutrition specific ward rounds including neonatologists, dieticians, pharmacists and nursing staff are advocated by centres with excellent growth outcomes e.g. Southampton⁶.

The recognised benefits of MDT working are reflected in national recommendations for the optimal provision of neonatal care e.g. British Association for Perinatal Medicine (2022) *Service and Quality Standards for Provision of Neonatal Care in the UK* (<u>https://www.bapm.org/resources/service-and-quality-standards-for-provision-of-neonatal-care-in-the-uk</u>).

What is adequate growth for a preterm baby?

It is generally accepted that there are two phases of postnatal growth; loss of extra cellular fluid (ECF) and therefore weight in the first few days after delivery (first phase), followed by growth after commencing early and optimal nutrition (second phase).

Early weight loss due to ECF contraction is inevitable, therefore on average a baby will generally be lower than birth centile, but when ECF contraction is complete they should grow parallel to a centile. Early fluid / weight loss can be mitigated by the appropriate and early use of PN, with figures for acceptable day seven weight loss including <5% of birth weight or <0.5 standard deviation score (SDS) lower than birth weight. If a stable baby continues to grow along their day seven centile this would usually be viewed as adequate.

There may be times when it is not possible to meet a baby's nutritional requirements e.g. if they are fluid restricted for medical reasons. In addition critically unwell babies won't grow in the first few days of their illness, and these factors have to be taken into considerations when reviewing overall growth trajectory **S**ee *Appendix 1* for a more detailed description of how to assess a baby who is failing to achieve adequate growth.

Enabling a small amount of catch up growth after illness is generally viewed as desirable, although there is very little data on the impact of this on longer term outcomes.

Growth monitoring in the neonatal unit

Growth monitoring is a key component to assessing nutritional status. Anthropometric measurements should include weight, head circumference (OFC) and length because no one measurement in isolation is sufficient to fully evaluate proportional body growth. All measurements should be plotted regularly on an appropriate growth chart.

Weight

All babies should be weighed at birth with a note taken of any oedema or other fluid collection (e.g. hydrothorax) present. Thereafter weight should be measured as clinically / developmentally appropriate every two days for the purpose of growth monitoring and feed / fluid calculations. Birth weight should be used for these calculations until it has been regained. Daily weights may be requested when closer assessment of fluid balance is indicated. For babies unable to be weighed an estimated weight should be calculated at least weekly using their anticipated weight trajectory on their growth chart. **An increase of 15–20 grams/kg/day is ideal to follow a centile line.**

Head circumference (OFC)

OFC should be measured on the day of birth and weekly thereafter. An increase of 0.9 cm/week is ideal to follow a centile line.

Length

Linear growth is a good indicator of true body growth and is associated with lean tissue mass. Length should be measured once stabilised after birth and weekly thereafter, along with OFC.

An increase of 1.4 cm/week is ideal to follow a centile line.

Nutritional requirements of a preterm baby

Preterm delivery results in reduced nutrient stores at birth and increased postnatal nutrient requirements, creating a risk of accumulating nutritional deficits and postnatal growth failure. Early, adequate nutrition is essential to mitigate this risk and optimise outcomes.

The European Society for Paediatric Gastroenterology Hepatology and Nutrition's (ESPGHAN) position paper on enteral nutrition in preterm infants provides an expert consensus approach to feeding in this population (2022 Enteral Nutrition in Preterm Infants: ESPGHAN Position Paper | ESPGHAN)⁷. ESPGHAN acknowledge that whilst many of their recommendations are based on high quality evidence significant gaps remain and there is a need for further research, especially into longer term functional outcomes.

	Term baby	Preterm baby				
		(ESPGHAN 2022)				
Fluid volume	150 ml/kg	150-180 ml/kg				
Energy	96-120 kcal/kg	115-140 kcal/kg; may increase up to 140-160 kcal/kg if growth faltering despite optimal protein / other nutrient intakes				
Protein	2.1-2.6 grams/kg	3.5-4 grams/kg; may increase up to 4.5 grams/kg if growth faltering despite optimal energy / other nutrient intakes				
Sodium	1.9 mmol/kg	3-5 mmol/kg; may increase up to 8 mmol/kg in babies receiving high energy and protein intakes, or with large sodium losses				
Potassium	4.2 mmol/kg	2.3-4.6 mmol/kg				
Calcium	13.1 mmol/day	3-5 mmol/kg				
Phosphate	13.1 mmol/day	2.2-3.7 mmol/kg				
Iron	1.7 mg/day	2-3 mg/kg				
Vitamin A	1166 IU/day	1133-3300 IU/kg				
Vitamin D	340 IU/day	400-700 IU/kg (max dose of 1000 IU)				

Table 1. Recommendations for fluid, macro and micronutrient intake

Feeding the preterm baby

When to start milk

The early introduction of milk enhances gut maturation, motility and hormone release, as well as shortening the time to full milk feeding and discharge⁸. It does not increase the risk of feeding-related morbidities, in particular NEC⁸. We recommend that stable babies of any gestation with no other contraindications should receive maternal colostrum as close to birth as possible. To facilitate this it is important that neonatal units have policies and processes in place to support maternal breast milk expression in labour ward.

Benefits of buccal colostrum

Oropharyngeal or buccal administration of freshly expressed colostrum

- Promotes the absorption of maternal antibodies and anti-inflammatory substances which can protect against disease and infection⁹
- Provides bactericidal, antiviral, anti-inflammatory and immunomodulatory protection¹⁰
- Provides a positive oral experience
- Supports early sensory development of taste and smell

Practicalities of buccal colostrum administration

- Commence as soon as possible after birth, always use colostrum in the order it was expressed
- Insert the tip of colostrum syringe into the buccal pouch (do not use a swab as colostrum will be absorbed)
- Give a maximum of 0.15mls in each side
- Use a gloved finger to gently massage the colostrum in, observing baby for signs of stress

Minimal enteral feeds

Minimal enteral feeds (MEF), also known as trophic feeds are defined as nutritionally insignificant, small volumes of milk (typically 12–24 mL/kg/day) administered without advancing for a period of 3–7 days. There is **NO** clear benefit of MEF with delayed advancement compared to initiating small volumes as soon as possible after birth and advancing as clinically tolerated^{11, 12}.

Rate of feed advancement

Meta-analysis and systematic review demonstrate that faster feed progression (generally defined as 30-40 mL/kg/day) versus slower (15-25 mL/kg/day) reduces the time to full enteral feeds, without increasing the incidence of NEC or all-cause mortality^{13, 14}. Included in these analyses is the large **S**peed of **I**ncreasing milk **F**eeds **T**rial (*SIFT*) which compared daily increments of 18mL/kg/day with 30 mL/kg/day. It is worth noting that the median enrolment age of four days in *SIFT* may not adequately inform the relative safety of these increments at an earlier age, in addition the actual daily increment was slower than targeted in both arms of the study¹⁵.

An accepted approach to advancing feeds is to assess each baby's risk of developing feeding-related morbidities (see the colour coded boxes in Figure 1 below), and to use this to inform a standardised rate of increment (see *Appendix 2*). Any approach to feed advancement must be underpinned by regular assessment of feed tolerance

Figure 1. Assessment of a baby's risk of developing feeding-related morbidities

Highest risk babies

- <28 weeks gestational age or birth weight <1000 grams
- Small for gestational age (<2nd percentile) especially if associated with absent or reversed end diastolic flow
- Perinatal hypoxic-ischaemic insult with evidence of end organ injury
- Hypotensive / unstable ventilated babies
- Additional risk factors for gut hypoperfusion e.g. haemodynamically significant ductus arteriosus, co-existing congenital heart disease

Introduce buccal colostrum as soon as possible after birth Start minimal enteral feeds @ 12-24 mL/kg/day as 2 hourly boluses as soon possible thereafter Advance feeds once tolerated after 24 hours old @ 30 mL/kg/day (see *Appendix 1*) Continue to monitor feed tolerance regularly with cares

Moderate risk babies

- 28 to 31⁺⁶ weeks gestational age without additional risk factors

Introduce buccal colostrum as soon as possible after birth Start minimal enteral feeds @ 24 mL/kg/day as 2 hourly boluses as soon possible thereafter Advance feeds as tolerated @ 30-40 mL/kg/day (see *Appendix 1*) Continue to monitor feed tolerance regularly with cares

Standard risk babies

- ≥32 weeks gestational age without additional risk factors

Introduce buccal colostrum as soon as possible after birth Start full enteral feeds @ 60-90 mL/kg/day as 2 to 3 hourly boluses as soon possible thereafter Advance feeds as tolerated @ 30-40 mL/kg/day (see *Appendix 1*) Continue to monitor feed tolerance regularly with cares

Method and frequency of feeding

Bolus versus continuous

Current evidence does not support the firm recommendation of one particular method over another, however published data indicate that¹⁶⁻¹⁹:

- Bolus feeds promote the cyclical release of GI tract hormones which stimulate gut maturity and motility
- Babies fed continuously take slightly longer to achieve full feeds compared to those bolus fed
- Growth may be compromised by continuous feeding as human milk fat adheres to the tubing and nutrients may be lost
- There is no significant difference in somatic growth and incidence of NEC between continuous and bolus feeding

In general **we recommend starting with two hourly bolus feeds in most babies²⁰.** One hourly volumes or continuous feeds may be considered if feed tolerance is problematic. Progression to three hourly volumes should occur when tolerance permits.

Nasogastric versus orogastric tubes

Nasogastric (NG) and orogastric (OG) feeding tubes are both used in practice. NG tubes may increase nasal airway resistance especially in the smallest babies²¹, which can theoretically have an impact on their work of breathing^{22, 23}. However systematic reviews show no consistent effects on feed tolerance or frequency of desaturation / bradycardia / apnoea²⁴. OG tubes may be more prone to vagal stimulation which can provoke bradycardia due to tube movements in the hypopharynx²⁵. Adverse effect of both NG and OG tube placement have been described (misplacement, laryngeal perforation). They must be inserted, and their position checked in line with local guidance.

When to stop parenteral nutrition and remove vascular access

The majority of babies' <32 weeks GA receive both parenteral and enteral nutrition, with a transitional period in between which is influenced by local feeding practice^{26, 27}. This transition phase is a critical time period for poor growth, although early progressive parenteral and enteral nutrition strategies, such as earlier fortification may lead to reductions in the cumulative energy and protein deficits that occur during the first weeks of life²⁸⁻³¹.

Administration of PN requires venous access and a balance needs to be struck between optimised nutritional intake and the infection risk associated with indwelling vascular access. NICE recommend consideration of stopping PN within 24 hours of³²:

- Babies <28 weeks GA tolerating milk volumes of 140 to 150 mL/kg/day
- Babies ≥28 weeks GA tolerating milk volumes of 120 to 140 mL/kg/day

Following discontinuation of PN, babies should then continue to increment milk volumes at the same rate until they reach around 165 mL/kg/day.

Assessing feed tolerance

Gastric residual volumes / aspirates

The residual volume (RV) aspirated from the stomach prior to a feed is one factors used to assess feed tolerance. However gastric emptying can be influenced by a number of variables including positioning of the baby and the type of milk feed, with maternal expressed breast milk (MEBM) emptied almost twice as fast as formula³³⁻³⁵. For these reasons RV alone should not be used to determine whether milk feeding is stopped.

Evidence from relatively small studies suggests that routine monitoring of RV increases the risk of feeds being stopped and slows the time taken to reach full milk volumes, without having any impact on adverse outcomes such as NEC^{36, 37}. Currently routine measurement of RV in a stable preterm baby is not recommended and existing practice in many neonatal units is to simply obtain a small volume of gastric aspirate to ensure the correct position of a gastric tube prior to each use. This approach is being evaluated further in the neoGASTRIC trial (neoGASTRIC | NPEU (ox.ac.uk); a multi-centre study comparing no routine measurement of RV with routine (up to six hourly) measurement. The primary outcome is time to full feeds and secondary outcome is NEC.

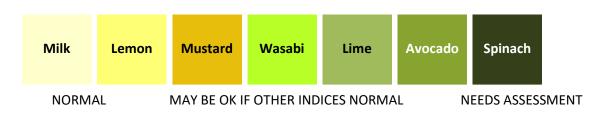
If RV are measured there is no consensus on whether to re-feed or discard the aspirate. If re-feeding is practiced the following should apply:

- RV consist of undigested milk
- RV are present during low volume / trophic feeding
- There are no clinical concerns see below

Colour of gastric residual volumes

The colour of gastric RV can vary significantly and it is good practice to visualise these and compare them to a standardised chart (see Figure 1 below) if concerns are raised.





Signs of feed intolerance

The definition of feed intolerance includes not only the volume and colour of gastric RV, but also assessment for some or all of the following:

- 1. Any concern that gastric residual volumes resemble or smell like faeces (so called faeculent aspirates)
- 2. Vomiting
- 3. Abdominal distension / visible bowel loops / discolouration / tenderness
- 4. Presence of abnormal or bloody stool

- 5. Clinical instability e.g. apnoea, temperature instability, tachycardia
- 6. Blood results e.g. metabolic acidosis, rising inflammatory markers
- 7. Abdominal x-ray

Dependent on these findings an informed decision to continue milk feeding, reduce milk volumes and review, or stop milk feeding can be made.

Differing milks and their indications for use

Maternal expressed breast milk / mother's own milk

Maternal expressed breast milk (MEBM), also known as mother's own milk (MOM) is the optimal feed for preterm babies. It confers many short and longer term health benefits which are described in more detail in the recently updated World Health Organisation (WHO) recommendations for the care of preterm and low birth weight babies³⁸ (<u>https://reliefweb.int/report/world/who-recommendations-care-preterm-or-low-birth-weight-infant)</u>.

Donor human milk

In the absence of sufficient MEBM donor human milk (DHM) is recommended in preference to infant formula (IF) for babies <32 weeks GA and / or <1500 grams^{38, 39, 40}. High quality evidence of benefit from DHM is limited, but a consistent finding when compared to IF is that DHM reduces the incidence of preterm NEC^{41, 42}.

It is important to acknowledge that DHM is fundamentally different to MEBM. DHM undergoes multiple processes e.g. freezing, transportation and pasteurisation prior to being fed, which have an impact on the biochemical, immunological and nutritional composition when compared to fresh and frozen MEBM. Parents should always be counselled of the differences between MEBM and DHM, highlighting that optimal outcomes are based on MEBM, and that DHM is ideally a bridge to achieving this. Ongoing maternal lactation support should always be provided in conjunction with DHM use, and parental consent for use must be obtained. Further information on DHM, the existing evidence base and ongoing uncertainties is available in the updated British Association of Perinatal Medicine Framework for Practice on Donor Human Milk Use in Neonates³⁹ (The Use of Donor Human Milk in Neonates | British Association of Perinatal Medicine (bapm.org))

Ideally DHM is replaced by MEBM once maternal lactation is established, but in the continued absence of sufficient MEBM the options include continuing with DHM beyond the highest risk window for NEC i.e. >34 weeks corrected GA or grading over to a preterm formula (PTF). If DHM is continued fortification should be considered as per MEBM (see below).

There is insufficient evidence to make specific recommendations about either duration of DHM use or routine fortification of DHM. However it is important than neonatal units and networks work collaboratively to produce and adhere to guidelines that ensure DHM use is consistent. See the BAPM recommendations below³⁹.

BAPM recommendations for donor human milk use

- DHM may be considered in babies born at <32 weeks gestation and/or <1500 grams to establish enteral feeding when mother's own milk (MOM) is unavailable or insufficient to meet their baby's requirements.
- Parents must provide informed consent for the use of DHM; as part of the consent process they should be counselled regarding the differences between both DHM and infant formula when compared to MOM, including benefits, risks and ongoing uncertainties.
- DHM use must be supported by adequate lactation support and appropriate staff training.
- There is insufficient evidence to make specific recommendations about duration of DHM use, fortification of DHM and use of DHM in moderate/late preterm and term babies.
- Neonatal units and networks must work collaboratively to produce guidelines that ensure DHM use is consistent.

Multicomponent breast milk fortification

The benefits of MEBM have been described above, however human milk alone (maternal and / or donor) at volumes of \leq 200 ml/kg does not have the nutrient density, particularly of protein, calcium and phosphorus to meet the increased nutritional requirements of a preterm baby⁴³. For this reason supplementation with a multicomponent breast milk fortifier (BMF) is recommended. It should be noted that although most studies of BMF show slightly greater weight, length and head growth, and no demonstrable increase in NEC there is no consistent data showing improvements in longer term developmental outcomes⁴⁴.

Which babies should receive breast milk fortification?

There is insufficient evidence to make specific recommendation on which subgroups of preterm babies may benefit most from BMF and we therefore recommend that fortification should be considered in all babies born \leq 32 weeks GA or \leq 34 weeks GA with a birthweight of \leq 1800 grams.

Fortification may not be required if \geq 50% of the feed requirement is provided by preterm formula, although it can be considered if there is poor growth and suboptimal tolerance of volume. **BMF should never be added as a supplement to preterm formula.**

When should breast milk fortification be started?

The optimal time to start BMF is not clear and practice varies across the UK. Early fortification seems to be as safe as delayed fortification and it may reduce accrued nutrient deficiencies, positively influencing bone metabolism⁴⁵. ESPGHAN suggest starting BMF when enteral intakes reach 40–100 mL/kg/day⁷ however this is considerably earlier than most neonatal units in Scotland have traditionally introduced fortification.

We recommend a move towards earlier consideration of fortification once milk volumes ≥120 mL/kg/day have been tolerated for at least 24 hours. This will help to mitigate the recognised reduction in nutritional intake and associated growth failure when PN stops²⁸⁻³¹.

Which breast milk fortifier?

Currently bovine based, multi-nutrient BMF are recommended for routine clinical practice. The following are both produced in powder form and packaged into sachets:

- Nutriprem BMF (Cow & Gate) contains extensively hydrolysed protein, carbohydrate, vitamins and minerals. Halal & Kosher certified
- SMA BMF (Nestle) contains partially hydrolysed protein, carbohydrate, vitamins and minerals, including iron. Halal certified

Human milk derived BMF are now commercially available either as concentrated liquids or lyophilized powders which make an exclusive human milk diet possible. They are expensive when compared to bovine based fortifiers and to date systematic reviews do not show clear benefit of their use over current practice of using a bovine based fortifier, and they are not routinely recommended at this time⁴⁶.

When should BMF be stopped and when should post discharge fortification be considered?

Traditionally BMF have been stopped before discharge once breastfeeding is established. However there is evidence that babies who have not reached term benefit from continued milk fortification to ensure that their intake of critical nutrients (especially protein and minerals) is maintained⁴⁷. This combined with the introduction of home nasogastric feeding policies to facilitate earlier discharge mean that continuation of BMF at home is becoming established into practice.

We recommend that post discharge fortification is considered in the following babies:

- Those <37 weeks CGA and / or ≤1800 grams, especially if there has been inpatient growth faltering and growth parameters have dropped >2 centiles from birth
- When breast feeding is still being established

Fortification is generally not required beyond 6 weeks CGA and if growth remained suboptimal at this stage medical review and dietetic referral should be considered. A guideline to provide greater clarify on the practice is currently being written.

Preterm formula

Preterm formula (PTF) have been designed to meet the increased nutrient requirements of preterm babies and to support adequate growth. They are not recommended for growth restricted term babies and are only available in hospital settings.

PTF are recommended when MEBM and / or DHM are unavailable in babies born <34 weeks GA and are used until babies reach 2000 grams and / or 37 weeks CGA.

- If using SMA Gold Prem 1, volumes should be maintained at 150 mL/kg/day to avoid excessive protein intake
- If using Cow & Gate Nutriprem 1, volumes can be increased up to 165 mL/kg/day as indicated by weight gain and volume tolerance

SMA Gold Prem 1 is partially hydrolysed. Cow & Gate Hydrolysed Nutriprem is extensively hydrolysed however the benefit of hydrolysed milk use in neonatal settings is yet to be substantiated⁴⁸.

Nutrient enriched post discharge formula

Nutrient enriched post discharge formulae (NEPDF) can be considered when a preterm baby reaches >37 weeks CGA and / or >2000 grams if:

- Growth has been poor i.e. growth parameters have dropped >2 centiles from birth and catch-up growth is required
- There are associated co-morbidities, such as BPD which result in a higher nutrient requirement

It should be noted that meta-analyses of NEPDF have not shown any consistent improvements in longer term growth outcomes⁴⁹ and a decision to use it should be discussed within the MDT on a case by case basis. **The majority of preterm babies with normal growth velocity do not require NEPDF.**

There are two NEPDF available in the UK; Nutriprem 2 and SMA Gold Prem 2. Both are available on prescription and should be added to discharge prescription request. Once introduced they are continued until adequate catch-up growth has been achieved or until 6 months CGA.

Term formula

In the absence of MEBM, term formula are indicated for late preterm babies 34-37 weeks GA with normal growth velocity and no requirements for catch-up growth.

Specialised term formula

Specialised term formulae are not designed to meet the requirements for preterm babies and will require modification to ensure individual requirements are met. These should only be used where absolutely necessary and under the direction of a specialist neonatal dietitian.

These are not available as ready to feed preparations, and if reconstituted out with a specialist milk kitchen they need to be prepared in accordance with the Department of Health guidelines^{50, 51}.

Nutritional supplements - vitamins & minerals

Babies born prematurely have lower stores of fat soluble vitamins, and potentially higher requirements for all vitamins and minerals than those born at term. High quality evidence to guide supplementation is lacking which has led to variation in practice. **Please see local monographs for current unit policies.**

Probiotics

Evidence from randomised controlled trials and meta-analysis suggest that administration of probiotics to preterm babies reduces their risk of severe NEC and death^{53, 54}. A variety of probiotic preparations have been studied and although preparations using combinations of organisms appear to confer the greatest benefit there is still uncertainty about which is the optimal preparation⁵⁵.

Probiotics are not licensed as medicines, rather they are characterised as a food product and regulated in a similar way to breast-milk fortifier. The two most commonly used preparations in the UK are⁵⁶:

- Labinic (Biofloratech Ltd, UK) which contains *Lactobacillus acidophilus, Bifidobacterium infantis* and *Bifidobacterium bifidum*. This is a liquid preparation and the dose is 5 drops (0.2ml) daily. The cost is 64p per dose
- **ProPrems (Neobiomics AB, Sweden)** which contains *Bifidobacterium infantis Bifidobacterium lactis* and *Streptococcus thermophiles*. This is a powder preparation and the dose is one sachet (0.5g) mixed into 1-3ml of milk or sterile water daily. The cost is £5.90 per dose

Practicalities of introducing probiotics into clinical practice

- Although not licensed as a medicine in the UK, it is important to ensure appropriate delivery, dosage and governance when introducing probiotics onto the neonatal unit
- They should be prescribed on the neonatal drug prescription chart and administered after checking by two nurses in the same way as for a medicine
- An appropriate information leaflet should be available for families
- Sepsis with probiotic organisms has been described and the local microbiology team should be made aware if probiotics are introduced into practice. These organisms are sensitive to standard antibiotics and grow on conventional culture media

Criteria for use

- Start probiotics in babies <32 weeks GA or <1500 grams within 48 hours of commencing enteral feeds
- Continue probiotics until 34 weeks CGA
- Withhold daily dose in babies who are seriously unwell / septic due to the potential risk of translocation of probiotic bacteria in this situation
- Withhold daily dose in babies who are nil by mouth for a suspected gastrointestinal surgical diagnosis

Appendix 1. Guide to the assessment of a baby with poor weight gain

Multiple factors contribute to nutrient deficits and poor weight gain in a preterm baby including:

- Late / inadequate nutrient provision e.g. delayed introduction of parenteral nutrition or breast milk fortifier
- Multiple interruptions to intravenous or enteral nutrition e.g. around blood transfusions
- Periods of poor milk tolerance
- Fluid restriction for medical reasons
- Medical co-morbidities

Routine growth monitoring enables the early identification and management of growth faltering. This should include:

- Regular measurement of developmentally appropriate anthropometry (weight, OFC and length), with accurate plotting and interpretation of results
- Interpretation of biochemical markers including plasma urea, electrolytes, calcium, phosphate, alkaline phosphatase and albumin, and urinary sodium

This information can be used to inform a detailed nutritional assessment and develop management strategies. Factors that should be taken into consideration include:

- Optimised protein to energy intake to ensure that protein is utilised for growth and not as a source of energy
- Appropriate feed volumes to achieve recommended nutritional intake
- Assessment of total body sodium stores to exclude sodium depletion; this requires assessment of urinary sodium as well as serum sodium (low urinary levels suggest inadequate total body stores)
- Treatment of anaemia / sepsis
- Recognition of the impact of medication e.g. steroids can delay length growth for 3-4 weeks after cessation of therapy
- Recognition of high energy requirements secondary to co morbidities
- Low serum urea as an indicator of protein insufficiency
- Organic causes of growth failure

Appendix 2. Guide to rate of feed advancement

The tables below provide a guide to the frequency and volume of feed increments

Weight	30 mL/kg/day increments			40 mL/kg/day increments		
(grams)	High risk			Moderate risk		
	Increase	Frequency of increment		Increase	Frequency of increment	
	(mL/day)			(mL/day)		
		1mL/feed	2mL/feed		1ml/feed	2ml/feed
		every	every		every	every
≤500	15mL/day	20 hour				
600	18mL/day	16 hour				
700	21mL/day	14 hour				
800	24mL/day	12 hour				
900	27mL/day	11 hour				
1000	30mL/day	10 hour		40mL/day	8 hour	
1100	33mL/day	10 hour		44mL/day	8 hour	
1200	36mL/day	8 hour		48mL/day	6 hour	12 hour
1300	39mL/day	8 hour		52mL/day	6 hour	12 hour
1400	42mL/day	8 hour		56mL/day		10 hour
1500	45mL/day	6 hour	12 hour	60mL/day		10 hour
1600	48mL/day	6 hour	12 hour	64mL/day		8 hour
1700	51mL/day	6 hour	12 hour	68mL/day		8 hour
1800	54mL/day		10 hour	72mL/day		8 hour
1900	57mL/day		10 hour	76mL/day		8 hour
≥2000	60mL/day		10 hour	80mL/day		8 hour

Table 1. Two hourly feeding regimen

Table 2. One hourly feeding regimen

Weight (grams)	30 mL/kg/day increments High risk			40 mL/kg/day increments Moderate risk		
	Increase (mL/day)	Frequency of increment		Increase (mL/day)	Frequency of increment	
		0.5mL/feed	1mL/feed		0.5mL/feed	1mL/feed
		every	every		every	every
≤500	15mL/day	19 hour				
600	18mL/day	16 hour				
700	21mL/day	14 hour				
800	24mL/day	12 hour				
900	27mL/day	11 hour				
1000	30mL/day	10 hour		40mL/day	7 hour	
1100	33mL/day	9 hour		44mL/day	7 hour	
1200	36mL/day	8 hour		48mL/day	6 hour	12 hour
1300	39mL/day	7 hour		52mL/day	6 hour	12 hour
1400	42mL/day	7 hour		56mL/day		10 hour
1500	45mL/day	6 hour	12 hour	60mL/day		10 hour
1600	48mL/day	6 hour	12 hour	64mL/day		8 hour
1700	51mL/day	6 hour	12 hour	68mL/day		8 hour
1800	54mL/day		10 hour	72mL/day		8 hour
1900	57mL/day		10 hour	76mL/day		8 hour
≥2000	60mL/day		10 hour	80mL/day		8 hour

References

1. Butler TJ, Szekely LJ, Grow JL. A standardized nutrition approach for very low birth weight neonates improves outcomes, reduces cost and is not associated with increased rates of necrotizing enterocolitis,

sepsis or mortality. J Perinatol 2013;33:851-7.

2. Jadcherla SR, Dail J, Malkar MB, et al. Impact of process optimization and quality improvement measures on neonatal feeding outcomes at an all-referral neonatal intensive care unit. *J Parenter Enteral Nutr* 2016;40:646–55.

3. Johnson MJ, Leaf AA, Pearson F, et al. Successfully implementing and embedding guidelines to improve the nutrition and growth of preterm infants in neonatal intensive care: a prospective interventional study. *BMJ Open* 2017;7:e017727.

4. Barrett CE, Thornton K, Boateng B. A retrospective review of the incidence of necrotizing enterocolitis in very low birth weight neonates before and after the establishment of feeding guidelines. *J Invest Med* 2011;59:450–1.

5. Patole SK, de Klerk N. Impact of standardised feeding regimens on incidence of neonatal necrotising enterocolitis: a systematic review and meta-analysis of observational studies. *Arch Dis Child Fetal Neonatal Ed* 2005;90:F147-F151.

6. Andrews ET, Ashton JJ, Pearson F, et al. Early postnatal growth failure in preterm infants is not inevitable.

Arch Dis Child Fetal Neonatal Ed 2019;104:F235-F241.

7. Embelton ND, Moltu SJ, Lapillonne A et al. Enteral Nutrition in Preterm Infants (2022): A Position Paper From the ESPGHAN Committee on Nutrition and Invited Experts. *J Pediatric Gastroenterol Nutr* 2023;76:248-268.

8. Chitale R, Ferguson K, Talej M, et al. Early enteral feeding for preterm or low birth weight infants: a systematic review and meta-analysis. *Pediatrics* 2022;150 (Suppl 1). doi:10.1542/peds.2022- 057092E.

9. Scholarly articles for Lee J et al. Oropharyngeal colostrum administration in extremely premature infants: An RCT. *Paediatrics* 2015;135.

10. Gephart SM, Weller M. Colostrum as oral immune therapy to promote neonatal health. *Adv Neonatal Care* 2014;14(1):44-51.

11. Morgan J, Young L, McGuire W. Delayed introduction of progressive enteral feeds to prevent necrotising enterocolitis in very low birth weight infants. *Cochrane Database Syst Rev.* 2014:CD001970.

12. Bozkurt O, Alyamac Dizdar E, Bidev D, et al. Prolonged minimal enteral nutrition versus early feeding advancements in preterm infants with birth weight </=1250 g: a prospective randomized trial. *J Matern Fetal Neonatal Med* 2020;1:7.

13. Oddie SJ, Young L, McGuire W. Slow advancement of enteral feed volumes to prevent necrotising enterocolitis in very low birth weight infants. *Cochrane Database Syst Rev* 2017;(8):CD001241.

14. Yang WC, Fogel A, Lauria ME, et al. Fast feed advancement for preterm and low birth weight infants: a systematic review and meta-analysis. *Pediatrics* 2022;150(Suppl 1). doi:10.1542/peds.2022-057092G.

15. Dorling J, Abbott J, Berrington J, et al. Controlled trial of two incremental milk-feeding rates in preterm infants. *N Engl J Med* 2019;381:1434–43.

16. Wang Y, Zhu W, Luo BR. Continuous feeding versus intermittent bolus feeding for premature infants with low birth weight: a meta-analysis of randomized controlled trials. *Eur J Clin Nutr* 2020;74:775–83.

17. Bozzetti V, Paterlini G, De Lorenzo P et al. Impact of continuous vs bolus feeding on splanchnic perfusion in very low birth weight infants: a randomized trial. *J Pediatr* 2016;176:86–92 e2.

18. Aynsley-Green A, Adrian TE, Bloom SR. Feeding and the development of enteroinsular hormone secretion in the preterm infant: effects of continuous gastric infusions of human milk compared with intermittent boluses. *Acta Paediatr Scand* 1982;71:379-83.

19. Davis T, Fiorotto M, Suryawan A. Bolus versus Continuous Feeding to Optimize Anabolism in Neonates. *Curr Opin Clin Nutr Metab Care* 2015;18(1):102-108.

20. Razak A. Two-hourly versus three-hourly feeding in very low-birthweight infants: a systematic review and meta-analysis. *Am J Perinatol* 2020;37:898–906.

21. Stocks J. Effect of nasogastric tubes on nasal resistance during infancy. *Arch Dis Child* 1980;55:17–21.

22. Purcell M. Response in the newborn to raised upper airway resistance. *Arch Dis Child* 1976;51:602–7.

23. Tonkin SL, Partridge J, Beach D et al. The pharyngeal effect of partial nasal obstruction. *Pediatrics* 1979;63:261–71.

24. Watson J, McGuire W. Nasal versus oral route for placing feeding tubes in preterm or low birth weight infants. *Cochrane Database Syst Rev* 2013:CD003952.

25. Lagercrantz H, Edwards D, Henderson-Smart D et al. Autonomic reflexes in preterm infants. *Acta Paediatr Scand* 1990;79:721–8.24.

26. Klingenberg C, Embleton ND, Jacobs SE et al. Enteral feeding practices in very preterm infants: an international survey. *Arch Dis Child Fetal Neonatal Ed* 2012;97:F56–61.

27. Miller M, Vaidya R, Rastogi D et al. From parenteral to enteral nutrition: a nutrition-based approach for evaluating postnatal growth failure in preterm infants. *JPEN J Parenter Enteral Nutr* 2014;38:489–97.

28. Spath C, Zamir I, Sjostrom ES et al. Use of concentrated parenteral nutrition solutions is associated with improved nutrient intakes and postnatal growth in very low-birth-weight infants. *JPEN J Parenter*

Enteral Nutr 2020;44:327–36.

29. Miller M, Donda K, Bhutada A et al. Transitioning preterm infants from parenteral nutrition: a comparison of 2 protocols. *JPEN J Parenter Enteral Nutr* 2017;41:1371–9.

30. Moltu SJ, Blakstad EW, Strommen K et al. Enhanced feeding and diminished postnatal growth failure in very-low-birth-weight infants. *J Pediatr Gastroenterol Nutr* 2014;58:344–51.
31. Roggero P, Gianni ML, Orsi A, et al. Implementation of nutritional strategies decreases postnatal growth restriction in preterm infants. *PLoS One* 2012;7:e51166

32. NICE guideline: Neonatal parenteral nutrition (NG 154).

33. Ewer AK, Durbin GM, Morgan ME et al. Gastric emptying in preterm infants. *Arch Dis Child Fetal Neonatal Ed* 1994;71:F24–7.

34. Perrella SL, Hepworth AR, Gridneva Z et al. Gastric emptying and curdling of pasteurized donor human milk and mother's own milk in preterm infants. *J Pediatr Gastroenterol Nutr* 2015;61:125–9.

35. Yigit S, Akgoz A, Memisoglu A et al. Breast milk fortification: effect on gastric emptying. *J Matern Fetal Neonatal Med* 2008;21:843–6.

36. Riskin A, Cohen K, Kugelman A et al. The impact of routine evaluation of gastric residual volumes on the time to achieve full enteral feeding in preterm infants. *J Pediatr* 2017;189:128–34.

37. Abiramalatha T, Thanigainathan S, Ninan B. Routine monitoring of gastric residual for prevention of necrotising enterocolitis in preterm infants. *Cochrane Database Syst Rev* 2019;7:CD012937.

38. WHO recommendations for the care of the preterm or low birth weight infant 2022.

39. British Association of Perinatal Medicine Framework for Practice on Donor Human Milk Use in Neonates 2022.

40. Quigley M, Embleton ND, McGuire W. Formula versus donor breast milk for feeding preterm or low birth weight infants. *Cochrane Database Syst Rev* 2019;7:CD002971.

41. Li Y, Chi C, Li C et al. Efficacy of donated milk in early nutrition of preterm infants: a metaanalysis. Nutrients. 2022; 14: 1724.

42. Silano M, Milani GP, Fattore G, et al. Donor human milk and risk of surgical necrotizing enterocolitis: a meta-analysis. *Clin Nutr* 2019;38:1061–6.

43. Arslanoglu S, Boquien CY, King C, et al. Fortification of Human Milk for Preterm Infants: Update and Recommendations of the European Milk Bank Association (EMBA) Working Group on Human Milk Fortification. *Front Pediatr* 2019;7:76.

44. Brown JV, Embleton ND, Harding JE, et al. Multi-nutrient fortification of human milk for preterm infants. Cochrane Database Syst Rev. 2016(5):CD000343.

45. Alyahya W, Simpson J, Garcia AL, et al. Early versus Delayed Fortification of Human Milk in Preterm Infants: A Systematic Review. Neonatology. 2020;117(1):24-32.

46. Premkumar MH, Pammi H, Suresh G, et al. Human milk-derived fortifier versus bovine milk-derived fortifier for prevention of mortality and morbidity in preterm neonates. Cochrane Database Syst Rev. 2019:CD013145.

47. McCormick K, King C, Clarke S, et al. The role of breast milk fortifier in the post-discharge nutrition of preterm infants, British Journal of Hospital Medicine. 2021;82(3):42-48.

48. Ng DHC, Klassen JRL, Embleton ND, McGuire W. Protein hydrolysate versus standard formula for preterm infants. Cochrane Database Syst Rev. 2019:CD012412.

49. Young L, Embleton ND, McGuire W. Nutrient-enriched formula versus standard formula for preterm infants following hospital discharge. Cochrane Database Syst Rev 2016:CD004696. 50. Opinion of the Scientific Panel on Biological Hazards on a request from the commission related to the microbiological risks of infant formulae and follow on formulae.(2004) The EFSA Journal 113, 1-34

51. Guidelines for making up special feeds for infants and children in hospital. (2007). Food Standards Agency.

52. NDIG guideline

53. Morgan RL, Preidis GA, Kashyap PC et al, Probiotics reduce mortality and morbidity in preterm, low birth weight infants: a systematic review and network meta-analysis of randomized trials. *Gastroenterol* 2020;159:467-480.

54. Sharif S, Meader N, Oddie SJ et al. Probiotics to prevent necrotising enterocolitis in very preterm or very low birth weight infants. *Cochrane Database Syst Rev* 2020;10:CD005496. 55. Van den Akker CHP, Van Goudoever JB, Szajewska H et al. Probiotics for Preterm Infants: A Strain-Specific Systematic Review and Network Meta-analysis. *J Pediatric Gastroenterol Nutr* 2018;67:103-122.

56. Karupaiah K, Abdurrazaq A, Quaynor J. Current use of probiotics in neonatal units in England. *Infant* 2023;19:84-86.

Authors:

Dr Judith Simpson, Consultant Neonatologist, RHC, Glasgow Lorraine Cairns, Specialist Neonatal Dietician, RHC, Glasgow Orlaith McGuiness, Specialist Neonatal Dietician, RHC, Glasgow

Other Professionals Consulted

Dr Andrew MacLaren, Consultant Neonatologist, RHC, Glasgow Anisa Patel, Neonatal Pharmacist, RHC, Glasgow

Document Name WoS_EnteralFeeding_Neonates

Implementation / Review Dates

Implementation Date01/06/13 Latest review 19/12/24 Next review 19/12/27