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IMPROVING OUTCOMES BY OPTIMISING NUTRITION FOR PRETERM INFANTS

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Preterm infants are defined as being born before 37 weeks (term). The smaller and more preterm the infant, the more vulnerable they are nutritionally, as they have not had the opportunity to develop nutritional reserves, as this would usually mostly occur during the third trimester of pregnancy. Therefore, provision of optimal nutrition must be a high priority on the neonatal unit.

The nutritional requirements of preterm infants are higher than for infants born at term and the reasons are multifactorial:

- Low nutritional reserves/stores
- Immature organ systems - leading to increased work of breathing and reduced digestion and absorption of nutrients, for instance
- Increased risk of infection (due to immature immune system)

Care on the neonatal unit is designed to minimise the impact of these deficits; for instance, ventilation supports immature lungs where necessary and babies are nursed in incubators or hot cots to minimise the heat loss from immature skin. Comparison of nutritional requirements can be found in Table 1, from which it can be seen that nutritional requirements are significantly higher in preterm infants relative to size, with additional difficulties in meeting these requirements.

Embleton et al (4) established that preterm infants accrue an inevitable protein deficit that is strongly correlated with postnatal growth retardation on the neonatal unit. Growth velocity in preterm neonates has been related to risk of cerebral palsy, subnormal mental development index and neurodevelopmental impairment (5). Neurological examination performed at 5.4 years by a neurologist blinded to perinatal outcome, found cognitive deficits were associated with intrauterine growth retardation (measured as weight at birth), poor neonatal weight gain and lower post-discharge head circumference. Improved protein and energy intakes in just the first week were associated with improved neurodevelopmental scores at 18 months (6). Time taken to stabilise respiratory status, delays in starting and increasing parenteral and enteral feeds and episodes of sepsis leading to feeds being stopped, all contribute to deficits in nutritional status for preterm babies while on neonatal units.

There has been an increased emphasis on standardised feeding regimes in neonatal units. Although there is still much research needed on optimal feeding regimes, standardised feeding regimes have been found to reduce rates of necrotising enterocolitis (NEC), a potentially devastating complication of prematurity which can lead to gut necrosis, gut resections and even death. Where standardised feeding regimes have been introduced, NEC rates have reduced and NEC has been virtually eliminated in some centres (7). As a re-

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sult, neonatal networks have worked to develop enteral feeding guidelines to use across their networks, the most well-known of which is the East of England Network guideline. The Welsh Neonatal Network has been working on an enteral feeding guideline for our preterm infants, which is based on the East of England guideline (8). This launches in October 2014 at the Wales Neonatal Network Audit Day. An important principle once such a guideline is introduced is that a continuing cycle of process planning, consistent implementation, review and audit of practice is prioritised and implemented (9).

Most infants under <1,500g will not tolerate full nutritional requirements enterally from Day 1 and will need parenteral nutrition; this too will take several days to meet the infant's full nutritional requirements. The immaturity of the preterm gut means that enteral feeds need to be advanced cautiously. However, it is important that enteral feeds are introduced as early as possible to prevent gut atrophy, leading to an increased risk of infection via the gut. However, advancing enteral feeds too fast risks NEC. Therefore, trophic feeding (up to 24mls/kg/d) is increasingly standard practice on neonatal units; giving small amounts of feed enterally to keep the gut patent while building up parenteral feeds, until the infant is stable enough to increase enteral feeds.

A recent large prospective study (10) found that early introduction of enteral feeds in growth-restricted preterm infants, results in earlier achievement of full enteral feeding and does not appear to increase the risk of NEC. However, concerns regarding the risk of NEC mean that any change in practice around early feeding is likely to be viewed very conservatively. A new large multi-centred trial in the UK and Ireland undertaken by SIFT group (Speed Increasing Feeds Trial), aims to recruit 2,500 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.

Prospective, longitudinal nutritional studies in preterm infants started in the 1980s (11), evaluating the influence of early dietary practices on clinical and neurodevelopmental outcomes. Infants were randomised to receive either donor breast milk (DBM) or a preterm formula; either as whole diet or supplementary to mother's breast milk. Only the infants fed preterm formula maintained their birth centile by discharge and at nine months corrected age, the mean developmental quotient was 0.25 standard deviation scores (SDS) lower for infants fed DBM compared with preterm formula (12). However, by 18 months corrected age (13), no differences were seen in developmental indices between the groups. It was concluded that, despite the relatively low nutrient content of breast milk - and particularly DBM (<50kcals/100mls vs 68kcals/100mls for term formula and 80kcals/100mls for preterm formula (14)) - it contained factors to promote neurodevelopment and offset any detrimental effects of poor nutrition.

The advantage of breast milk was still seen at seven and a half to eight years, with children fed breast milk having a significantly higher Intelligence Quotient (IQ), which remained even after adjustment for mother's education and social class. A dose response was seen between amount of milk consumed and subsequent IQ (15). Therefore, mothers' own breast milk is the feed of choice on the neonatal unit for the reasons explained above. Use of breast milk is also well recognised to decrease the risk of NEC. In early studies, any breast milk (MEBM or donor breast milk DBM) was shown to reduce the incidence of NEC by up to tenfold (16). The protective effects of breast milk have been correlated with its anti-inflammatory components (IL-10), growth factors (EGF), erythropoietin, lysozymes and immunoglobulins as well as pre and probiotics which favourably affect gut microflora (17).

Mothers should be given all necessary support to start expressing breast milk within a few hours after birth and encouraged to express at least eight times a day including at night. Techniques such as 'hands on' pump expression can help to maximise volumes and suitably trained midwives and neonatal nurses should provide ongoing support to ensure volumes are maintained and breasts are emptied to ensure the calorie rich hind milk is expressed. Breast milk from the mothers of preterm infants is known

Table 1: Nutritional requirements of preterm infants vs term infants

Nutrient	Term infant (1)	Preterm infant Koletzko 2014 (2)	Preterm infant 1000g–1800g ESPGHAN 2010 (3)
Energy (kcal/kg/day)	95-115	110-130	110-135
Protein (g/kg/day)	2.0	3.5-4.5	4.0-4.5 (<1,000g) 3.5-4.0 (1,000-1,800g)
Sodium (mmol/kg/day)	1.5	3.0-5.0	3.0-5.0
Potassium (mmol/kg/day)	3.4	1.9-5.0	2.0–3.5
Calcium (mmol/kg/day)	3.8	3.0-5.0	3.0-3.5
Phosphate (mmol/kg/day)	2.1	1.9-4.5	1.9-2.9

Table 2: Nutritional content of milks and fortifiers

	Energy (kcals/100mls)	Protein (g/100mls)
Preterm breast milk	70	1.8
Term breast milk	69	1.3
Term breast milk + BMF	84	2.1 -2.3
C&G Nutriprem 1	80	2.5
SMA Gold Prem	82	2.2
Aptamil Preterm	80	2.5

to be higher in protein than the milk of term infants, helping to provide the necessary extra protein intake (Table 2); although, after the first few weeks, protein levels start to fall towards term levels. Where MEBM is not available, donor breast milk is thought to be helpful in reducing the risk of NEC in high risk infants (<28 weeks; <1,000g; IUGR). However, this milk is often drip milk - so called because it drips from one breast while the baby feeds from the other. As a result, donor breast milk can be much lower in calories and protein than standard breast milk, which has adverse consequences for growth. More recently, preterm donor milk has become available from some milk banks, which should be used whenever possible. In addition, some breast milk banks are making nutritional analyses of their donor milk available, which makes it easier to assess the nutritional adequacy of the milk that is being provided.

As a result of the desire to use breast milk to minimise the risk of NEC and also maximise cognitive outcome, breast milk fortifiers (BMF) have been developed, which add calories, protein and vitamins to breast milk, while enabling the full volume of breast milk to be given (see Table 2). Cochrane (18) found evidence of improved short-term weight gain, linear growth and head growth with the use of BMF and no evidence of increased risk of NEC. Nevertheless, care should be taken with addition of breast milk fortifier to minimise any risk of NEC. BLISS recommends that breast milk fortifier is used in infants <1,500g at birth and <34 weeks once they are on full feeds and serum urea is <4.0mmols/l and falling (19). This is because there is a correlation between serum urea and protein content of milk (20).

Where mothers do not wish to, or can't provide breast milk, or produce insufficient volumes, preterm formulas are used, which are formulated to meet the high nutritional requirements of preterm infants (Table 2).

Enteral feeding will usually be established using orogastric or nasogastric tubes. Oral feeding starts to develop from 32 weeks, however because of immature suck-swallow-breathe, most infants will not be able to breast or bottle feed totally until somewhere between 35 and 40 weeks gestation. Some units will send infants home while still tube fed, or on oxygen or both; policies differ locally depending on the services and support available to families in the community. Adequate nutritional intake should be assessed as part of thorough discharge planning. For a baby

who has been on breast milk fortifier and is moving on to breastfeeding, they need to be able to take enough milk from the breast to support growth. Since breast milk fortifier is not prescribable in the community, there are limited options available if the infant does not thrive. Some units will supply breast milk fortifier for parents to mix with some expressed breast milk; alternatively, families may be advised to add formula powder to breast milk or give top-up feeds of post discharge or nutrient dense formula.

For infants who have been on preterm formula on the unit, they will typically be discharged on a nutrient enriched post discharge formula (NEPDF), which is typically half way in composition between a preterm and standard formula (~75kcals/100mls; 2.0g protein/100mls). These also contain higher concentrations of vitamins and minerals to meet the ex-preterm infant's continuing higher requirements. If an infant is breast milk fed or has a standard term formula they will need additional vitamin and iron supplements.

If an infant is unable to take sufficient volume of breast milk or a NEPDF to gain weight satisfactorily, a term nutrient dense formula may be used (90 - 100kcals/100mls; 2.0 - 2.6g protein/100mls). These are not entirely suitable for preterm infants, but may be useful where infants are struggling to manage volumes, in conjunction with vitamin and iron supplements.

Preterm infants are born at a nutritional disadvantage and the current evidence suggests that current neonatal care is not successful in helping them to overcome those early disadvantages.

However, much work is going on to improve this situation in the future. Dietitians are not currently universally members of the neonatal team; as the key role of nutrition becomes more recognised it is to be hoped that will change in the years to come. In the meantime, robust, standardised evidence based enteral feeding guidelines will help to ensure that preterm infants receive the best possible nutrition from their first day of postnatal life.

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Questions relating to: *Improving outcomes by optimising nutrition for preterm infants* Type your answers below and then **print for your records** or print and complete answers by hand.	
Q.1	Describe the main reasons why the nutritional requirements of preterm infants are greater than those of infants born at term.
A	
Q.2	What would be the protein, energy, sodium, potassium, calcium and phosphate requirements be for a preterm infant weighing 1,500g and for an infant born at term weighing 3,750g?
A	
Q.3	What are the risks of growth retardation in preterm infants?
A	
Q.4	Outline the cognitive deficits associated with intrauterine growth.
A	
Q.5	What are the benefits of having standardised feeding regimes in neonatal units?
A	
Q.6	Describe the role of enteral feeding in the nutritional management of a preterm infant.
A	
Q.7	Why is mothers' breast milk the feed of choice on a neonatal clinic?
A	
Q.8	What evidence is there for the recommendation of the use of breast milk fortifiers (BMF)?
A	
Q.9	Describe the considerations involved in discharge planning.
A	
Please type additional notes here . . .	