Specialised milk feeds for term and preterm infants

Good nutrition is important at all stages of life but none more so than during infancy. The aim of this article is to provide a summary of the nutritional qualities of breast milk, breast milk fortifier and the various types of infant formulas and indications for their use. With the exception of preterm formulas, specialist infant formulas are made to meet the nutritional needs of term infants. As such these formulas should be used with caution alongside regular close growth monitoring and routine biochemistry to monitor bone health in preterm infants.

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Key points

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1. During the period of transition from parenteral nutrition (PN) to enteral feeds, consider the use of PN containing concentrated amino acids and early breast milk fortification (half fortification).
2. Post-hospital discharge use of breast milk fortifier boluses can support ongoing breastfeeding and optimum growth in breastfed preterm infants.
3. Amino acid formulas do not contain sufficient minerals to adequately support growth and optimal bone health. Close monitoring is essential when infants receive these feeds as a sole source of nutrition.

Infants are born at a time of rapid growth and formation of body tissues and organs, yet immature metabolism means they are unable to cope with either excess or lack of nutrients. Consideration of both the quantity and quality of nutrients is critically important. There is good evidence that feeding infants maternal breast milk (MBM) confers many advantages to infants and mothers;[1] as well as containing just the right nutrients for human development for infants born at term, breast milk contains many factors that promote immune function and enable healthy intestinal development. Breast milk and breastfeeding should be the preferred milk feed and all mothers should be encouraged and supported to breastfeed irrespective of the gestational age of their infant.[2] However, preterm infants and those with congenital abnormalities or metabolic disorders may require nutrient supplementation or special feeds, with some needing a period of intravenous nutrition until the gut is able to support their needs. Measuring growth and biochemistry is crucial to optimising nutrition in high-risk infants.[3-5] The aim of this article is to provide a summary of the nutritional qualities of MBM, breast milk fortifier (BMF) and the various types of infant formula and indications for their use.

Summary of nutritional needs of preterm infants (≤37 weeks gestational age)

Preterm infants need relatively high amounts of nutrients to support growth and development. In particular, for infants born around the threshold of viability, metabolic immaturity and complications of extreme prematurity mean that while nutritional requirements are high, meeting these needs can be challenging. It is currently recommended that the growth of preterm infants should aim to approximate the *in utero* growth of infants of the equivalent gestation.[6-8] Detailed recommendations on their nutrient intake have been published with the aim of trying to achieve this.[2,3]

Energy

Recommendations are 110-130kcal/kg/day for relatively well very low birthweight (VLBW) infants, although there is limited evidence to support specific energy requirements for infants who are sick or growth restricted. Total energy post-discharge should approach 100-120kcal/kg/day[2,3] for satisfactory functional development.

Protein

Recommendations for initial intakes of protein are 2.0-2.5g/kg/day with a gradual increase to 3.5g/kg/day by the end of the first week of life.[2] Infants at full enteral nutrition need 3.5-4.5g/kg/day, which can only be achieved using either fortified maternal/donor breast milk or preterm formula.[2,3] An ideal protein-energy

percentage (%PE) for growth resulting in lean body mass accretion in preterm infants (rather than deposition of adipose tissue), has been shown to be 12.7-13.8%. Therefore enriching products with modular additions of fat and carbohydrate alone often results in a lower %PE of 4.5-6%, which does not favour optimal growth in growth-faltering preterm infants.[2]

Calcium, phosphorus and vitamin D

Calcium requirements are estimated as being 120-200mg/kg/day, with an ideal ratio of Ca:P being 1.6:1-1.8:1. Vitamin D requirements have been estimated as being 10-25µg/day, which should be sufficient to maintain serum levels at >50nmol/L.[2,3]

Transition from parenteral nutrition to enteral feeds

For many preterm infants the period of transition from parenteral nutrition (PN) to enteral feeds often results in inadequate nutritional delivery and subsequent nutrient deficit particularly relating to protein, micronutrients and minerals. In recent years there has been a considerable amount of work undertaken towards optimising the early initiation and composition of PN, including the use of bedside nutritional guidelines to reduce variation in nutritional practice.[4,9] Using concentrated PN formulations containing amino acids (protein) at 3.5g/100mL in addition to the earlier fortification of breast milk at 80mL/kg/day has been shown to prevent growth faltering that was previously experienced during this transitional period. It is recommended that tapering off PN should not be commenced before at least 80mL/kg/day of breast milk is reached.[9-11]

Practice point: consider the use of concentrated PN providing protein at 3.5g/100mL during transitional periods of PN to enteral feeds. Consider commencing breast milk fortification (half fortification) at 80-100mL/kg/day MBM.[12]

Infant feeds

The variety of infant feeds available for preterm and term infants are described in the following sections, with a summary of their nutrient content and how they meet nutritional requirements given in **TABLE 1**.

Breast milk

Breast milk contains a myriad of nutritive components that aid the maturation of the neonatal gut. In all circumstances the feed of choice is breast milk and where possible mothers should be encouraged to provide their own breast milk.[13] Where breastfeeding is not possible due to prematurity or otherwise, expressed breast milk (EBM) should be encouraged and, for mothers who are not able to provide MBM, the use of donor breast milk (DBM) should be considered until the infant is at least of 35 weeks' gestational age.[4,12] While MBM and DBM are the feed of choice for term and preterm infants and meet the nutritional needs of the term infant, they do not meet the nutritional needs of preterm infants and need to be supplemented.

Breast milk fortifiers

BMFs are specifically designed to supplement breast milk providing additional protein, micronutrients and minerals such as calcium and phosphate.[3] The milk protein in BMF available in the UK is bovine with varying degrees of hydrolysis. In a hospital setting, one sachet of BMF is added to each 50mL of MBM to provide 120kcal and 3.9g protein per 150mL, meeting the nutritional requirements of infants ≤35 weeks' gestation. BMF can be added to MBM or DBM.

The ongoing increased nutritional requirements after discharge for formula-fed babies have been recognised by the recommendation of post-discharge formula, which has increased protein and minerals compared to term formula.[14] An increasing trend towards earlier discharge particularly for the late preterm group (≤35 weeks' gestation at birth) means that a proportion of breastfed infants can experience faltering growth related to stopping fortifier (with a consequent reduction in protein and mineral intake) prior to discharge. This can lead to the introduction of infant formula to supplement growth and reduced confidence in a mother to continue breastfeeding. Although BMF products in the UK are currently not prescribable by GPs in the community, as a food supplement they can be provided by the neonatal unit, community neonatal nurses or dietitians for use at home in this group of infants. The neonatal unit at Princess Anne Hospital, Southampton, uses this approach routinely. Families are taught to make up fortifier boluses (colloquially known as a bombs or shots) with one sachet in 5-10mL EBM given four times a day with a breastfeed until 44-48 weeks' corrected gestation.[15]

Practice point: preterm infants <1.8kg receiving MBM or DBM as their only source of nutrition require BMF in order to meet their nutritional requirements. Post-hospital discharge, the use of BMF boluses in breastfed preterm infants (born at ≤35 weeks' gestation) up to 48 weeks' gestational age can support ongoing breastfeeding and optimum growth.

Preterm protein powder

For preterm babies weighing <1,000g, a protein intake of 4.0-4.5g/kg/day is recommended.[3] Extensively hydrolysed protein supplements have been developed for extremely low birth weight infants ≤1,000g whose needs are not being met through fortified breast milk or preterm infant formula. The protein powder contains a whey and casein protein hydrolysate providing 0.8g per 1g sachet, which can be added to fortified breast milk or preterm infant formula to provide a protein intake of 3.6-4.1g per 100kcal.[16]

Practice point: protein supplementation of MBM may benefit those infants who require additional protein and those who are felt to be intolerant of BMF.

Preterm infant formula

Where fortified MBM is not available, preterm infant formula should be provided for preterm infants <1.8kg at birth. A range of preterm infant formulas have been variably formulated to meet the recommended nutritional requirements of infants ≤1.8kg and ≤1kg containing 120kcal and 3.9g protein per 150mL in those formulas for infants ≤1kg and providing 120kcal and 4.4g protein per 150mL for infants ≤1.8kg. In general, preterm infant formulas usually contain:

- protein, either as whole protein or partially hydrolysed whey and casein protein
- carbohydrates, including maltodextrin and lactose
- fats – long-chain polyunsaturated fatty acids, arachidonic acid, docosahexaenoic acid and, in some, medium-chain triglycerides
- prebiotics (in the form of galacto- or fructo-oligosaccharides), nucleotides, vitamins and minerals.

Practice point: where MBM is not available, infants ≤1.8kg should be provided with preterm infant formula aiming to meet protein intake of 3.5-4.5g/kg/day, in addition to micronutrient and mineral requirements depending on gestational age.

Preterm post-discharge infant formula

Breastfeeding at discharge is the preferred goal for all infants. While the available evidence supporting their use is variable,[17] nutrient-dense post-discharge infant formulas provide 150kcal and 3.9g protein per 150mL compared to 100kcal and 1.95g per 150mL of standard term infant formula. Improved nutritional status and optimum growth during infancy in preterm infants is associated with improved cognitive and long-term outcomes.[18]

Practice point: although there is not consistent evidence available to support the use of nutrient-dense post-discharge infant formula over standard term infant formula, where infants have a slowing growth trajectory in hospital or during the first few weeks post-discharge, providing a formula with additional nutrients may be of benefit to individual infants, particularly those with extreme prematurity.

Standard infant formula

For infants ≥1.8kg and where breast milk is unavailable, a standard infant formula should be chosen.

Specialist infant formula

With the exception of preterm formulas, specialist infant formulas are composed to

		Koletzko 2014[2] recomm-endations per day	Term breast milk	Breast milk with full strength fortifier	Preterm infant formula	Preterm infant formula 1kg	Term infant formula	Hydrolysed preterm infant formula	Extensively hydrolysed casein term infant formula	Extensively hydrolysed whey term infant formula	Amino acid infant formula	Nutrient energy dense infant formula
			Per 100mL/kg/day									
Energy	Kcal	110-130	64	80	80	80	66	80	68	66	67	100
Protein	g	3.5-4.5	1.2	2.6	2.6	2.9	1.3	2.6	1.9	1.6	1.8	2.6
% PE		12.7-13.8	7.5	13	13	14.5	7.8	13	11	11	11	10.4
Carbohydrates	g	11.6-13.2	7.4	9.6	8.4	8.1	7.3	8.4	7.5	6.8	7.2	10.3
Fat	g	4.8-6.6	3.6	3.5	3.9	4	3.4	4	3.4	3.5	3.4	5.4
Calcium	mg	120-200	35	91.4	94	116	50	104	77	50	66	80
Phosphorus	mg	60-140	15	52.2	62	77	28	58	53	28	47	40
Ca:P ratio		1.6:1-1.8:1	2.3:1	1.7:1	1.5:1	1.5:1	1.7:1	1.8:1	1.4:1	1.7:1	1.4:1	2:1
Vitamin D	µg	10-25	0	5.18	3	3.7	1.2	3	1	1.3	1.2	1.7
			Per 150mL/kg/day									
Energy	Kcal	110-130	96	120	120	120	99	120	102	99	100.5	150
Protein	g	3.5-4.5	1.8	3.9	3.9	4.35	1.95	3.9	2.85	2.4	2.7	3.9
Carbohydrates	g	11.6-13.2	11.3	14.4	12.6	12.2	11	12.6	11.3	10.2	10.8	15.5
Fat	g	4.8-6.6	5.4	5.25	5.85	6	5.1	6	5.1	5.25	5.1	8.1
Calcium	mg	120-200	52.5	137.1	141	174	75	156	115.5	75	99	120
Phosphorus	mg	60-140	22.5	78.3	93	115.5	42	87	79.5	42	70.5	60
Vitamin D	µg	10-25	0	7.77	4.5	5.55	1.8	4.5	1.5	1.95	1.8	2.55
			Per 180mL/kg/day									
Energy	Kcal	110-130	115	144	144	140	118.8	144	122.4	118.8	120.6	180
Protein	g	3.5-4.5	2.2	4.7	4.68	5.2	2.34	4.68	3.42	2.88	3.2	4.68
Carbohydrates	g	11.6-13.2	13.5	17.3	15.12	14.5	13.14	15.1	13.5	12.24	12.96	18.54
Fat	g	4.8-6.6	6.5	6.3	7.02	7	6.12	7.2	6.12	6.3	6.12	9.72
Calcium	mg	120-200	63	164.5	169.2	208	90	187.2	138.6	90	118.8	144
Phosphorus	mg	60-140	27	94	111.6	138	50.4	104.4	95.4	50.4	84.6	72
Vitamin D	µg	10-25	0	9.3	5.4	6.6	2.16	5.4	1.8	2.34	2.16	3.06
			Per 200mL/kg/day									
Energy	Kcal	110-130	128	160	160	160	132	160	136	132	134	200
Protein	g	3.5-4.5	2.4	5.2	5.2	5.8	2.6	5.2	3.8	3.2	3.6	5.2
Carbohydrates	g	11.6-13.2	14.8	19.2	16.8	16.2	14.6	16.8	15	13.6	14.4	20.6
Fat	g	4.8-6.6	7.2	7	7.8	8	6.8	8	6.8	7	6.8	10.8
Calcium	mg	120-200	70	182.8	188	232	100	208	154	100	132	160
Phosphorus	mg	60-140	30	104.4	124	154	56	116	106	56	94	80
Vitamin D	µg	10-25	0	10.36	6	7.4	2.4	6	2	2.6	2.4	3.4

TABLE 1 Current recommendations for nutrition of preterm infants (based on Koletzko et al[2]) and a comparison of various feeds. Fields within the table with no colour do not meet the recommendations within the given feed volume. Yellow fields indicate nutritional requirements will be met provided this volume of feed is delivered and blue fields exceed the recommendations within the volume of feed.

meet the nutritional needs of term infants. As quality evidence supporting the use of hydrolysed protein infant formula is poor (particularly relating to improved feed tolerance and reduced risk of necrotising enterocolitis, NEC),[19] they should be used with caution in preterm infants, with close growth monitoring and regular routine biochemistry to monitor bone health. However, for a multitude of reasons, some preterm infants may require a specialist infant formula. These commonly include those arising from surgical pathology, either congenital (eg gastroschisis) or from NEC and the formation of a stoma. Other at-risk infants are those born with congenital heart disease requiring surgical intervention beyond the premature period; these infants may have higher energy requirements or be fluid restricted. In those with congenital or acquired surgical pathology, breast milk remains the preferred option with the best available evidence suggesting this will be well tolerated in the majority of infants. For infants with stomas, providing continuous over bolus milk feeds may ensure better tolerance, in addition to allowing greater luminal contact with the feeds, which may promote intestinal adaptation.[20]

Cows' milk protein allergy (CMPA) may also be a consideration for ongoing feed intolerance. This is an uncommon finding with estimated incidence of 2.4% for immunoglobulin E (IgE)-mediated and 1.7% for non-IgE mediated[21] although it may form part of the differential diagnosis in cases of 'feed intolerance'. It is important to consider the impact on nutritional intake of a change to specialist formula particularly for preterm infants with this diagnosis and therefore it is important not to over-interpret non-specific symptoms. A specialist paediatric dietitian with neonatal competencies should review all infants with suspected CMPA to ensure that requirements for macro- and micro-nutrients are adequately supplemented. There is a well-recognised pathway for the diagnosis and management of CMPA that involves challenge with feed containing cows' milk protein to confirm the diagnosis.[22,23] For breastfed infants, an exclusion diet should be considered and recommended under dietetic supervision. A decision to stop breastfeeding should not be undertaken lightly given the life-long benefits of breastfeeding to both mother and child.

The various types of specialist infant formulas available are as follows:

Extensively hydrolysed infant formula (eHF)

These formulas are suitable for infants with CMPA and contain extensively hydrolysed protein (casein and whey). They can lead to faster gastric emptying than a whole protein feed[24] and so may also reduce vomiting and reflux.[25] The type of fat within a feed may also be important and factors such as the length of the remaining bowel, capacity of the bowel, surgical history, and overall likelihood for fat malabsorption should be considered.[26] A component of the fat content as medium-chain triglycerides[27] may facilitate faster gastric emptying compared to those products with long-chain fats alone,[28] which may decrease the incidence of fat malabsorption. Some extensively hydrolysed infant formulas contain >50% palm olein oil from coconut oil,[29] which can result in the formation of insoluble calcium soaps from unabsorbed palmitic acid.[30] Palm olein oil free formulas may therefore be preferable. Calcium citrate is a more bioavailable source of calcium compared to that of calcium carbonate, so eHF that contains calcium citrate is preferable.[31]

Amino acids infant formula

Some infants, such as those with surgical pathology as a result of surgical resection with small bowel stoma, may not tolerate eHF and so may require amino acid infant formula. Some amino acid feeds contain medium-chain triglycerides and infants with short bowel syndrome or high output stoma may tolerate these better than those only derived from long-chain fats.[32] Amino acid feeds are high in glutamate and may therefore impact on the infant's ability to consume sufficient calories orally due to early satiety. Therefore, breast milk, eHF or standard infant formula should be encouraged where possible.[33]

Practice point: as amino acid formulas do not contain sufficient minerals to adequately support growth and optimal bone health, close monitoring is essential and recent recommendations suggest that where infants or children receive these feeds as a sole source of nutrition, a regular review (3-6 months) of nutritional markers (including parathyroid hormone, vitamin D, calcium, phosphorus, alkaline phosphatase, iron studies and zinc) should be completed alongside growth monitoring.[34]

Nutrient and energy dense infant feeds

Infants born with congenital heart disease requiring future surgical intervention have nutritional requirements estimated at 10% higher than otherwise healthy infants. The amount of energy a term infant requires is dependent on the type of cardiac lesion and ranges 110-130kcal/kg/day. Although additional calories and protein are often prescribed, it is common for infants not to achieve feeding targets either due to feeding difficulties or fluid restrictions leading to growth failure. Post-surgery catch-up growth may be required. Therefore, while breast milk is best and where possible should be encouraged, a combination of fortified breast milk or energy/nutrient dense formula feeds may help promote growth.[35,36] These feeds contain 100kcal and 2.6g protein per 100mL, which is available as either whole or extensively hydrolysed whey protein. Fats within these products are either as long-chain fatty acids or a 50% mix of long-chain and medium-chain triglycerides. They are also nutrient dense containing higher amounts of micronutrients and minerals. This is important because medications, particularly diuretics, reduce total body stores (especially sodium) affecting growth; supplementation may be required.[36,37]

Micronutrient supplementation – hospital and beyond

Maternal breast milk provides insufficient vitamins (particularly vitamin A and D) and iron for preterm infants. Preterm infants have low levels of fat soluble vitamins, particularly A and D.[2]

Practice point: while in hospital, preterm infants should be commenced on a once daily multivitamin supplement once tolerating 60mL/kg/day enteral feeds. This should be continued post-discharge irrespective of the mode of feeding. In addition, for those infants discharged home breastfeeding, iron should be started from day 28 and continued until the introduction of iron-rich complementary food.

Enteral feeding practices

There is no consensus about ideal feeding practices, however it has been demonstrated that standardised feeding regimes may be very important tools to prevent and minimise NEC in preterm infants and maximise growth.[4,38] Breast milk is the feed of choice and can be fortified from as early as 80-100mL/kg/day.

Healthy preterm infants with normal renal intake may be able to tolerate up to 200mL/kg/day of enteral feed, although this target will depend on the type of feed and corresponding growth. Whatever the choice of feed, it is important to ensure it meets nutritional requirements and that growth and nutritional status including biochemical parameters are monitored after making changes to feeds.

Conclusion

Breast milk and breastfeeding continue to be the preferred milk feed and all mothers should be encouraged and supported to breastfeed irrespective of the gestational age of their infant.[2] Where this is not possible due to congenital abnormalities, bowel complications of prematurity or metabolic disorders, a specialist infant formula may be required. With the exception of preterm formula, specialist infant formulas are made to meet the nutritional needs of term infants. Where possible, preterm infants with a previous history of feeding intolerance should continue to be challenged to more suitable formula such as breast milk with fortifier or preterm infant formula to ensure their nutritional needs are met. Where this is not feasible, close growth monitoring, supplementation of micronutrients (particularly phosphate and vitamins) and regular routine biochemistry is essential to ensure optimal bone health and growth among preterm infants deriving their sole source of nutrition from specialist infant formula.

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