# Nutrition in preterm infants before and after hospital discharge

There is accumulating evidence that nutrition has important effects on both short- and long-term outcomes. Good nutrition may ameliorate short-term morbidities such as respiratory disease, but also plays a key role in determining longer term developmental outcome. This article reviews key nutritional concepts involved in early neonatal care, and also discusses nutrition management after initial hospital discharge.

**Nicholas D Embleton**
BSc, MD, FRCPCH
Consultant Neonatal Paediatrician
n.d.embleton@ncl.ac.uk

**Robert J Tinnion**
BMedSci, MRCPCH
Higher Specialist Trainee in Neonatal Medicine
Newcastle Neonatal Service
Royal Victoria Infirmary
Newcastle upon Tyne

**Keywords**

nutrient intakes; preterm infant; nutritional requirements; post-discharge nutrition; growth monitoring

**Key points**

**Embleton N.D, Tinnion R.J.** Nutrition in preterm infants before and after hospital discharge *Infant* 2009; 5(6): 174-78.

1. Nutrition is the cornerstone of neonatal practice.
2. Nutrition affects both short-term (eg growth) and long-term (eg cognitive attainment) outcomes.
3. Policies should promote the use of breast milk.
4. The UK-WHO 0-4 year growth charts recently developed should be used (www.growthcharts.rcpch.ac.uk).

Long-term survival in preterm infants has increased dramatically in the last 20 years. The focus of neonatal care has now shifted from efforts concentrated purely on preventing death, to those that maximise long-term outcome. Parents and staff are interested in a range of outcomes. Although morbidities such as chronic lung disease (CLD) are not that uncommon, most infants born preterm do not have persisting 'medical' problems throughout childhood. The focus of neonatal care should therefore be on neuro-developmental outcome. We have known for a long time that the advantages of breast milk for all babies are overwhelming, but there is now emerging evidence that early nutrition affects not only neuro-cognitive outcomes[1,2], but also motor outcomes such as the presence or severity of cerebral palsy[3,4]. This means that everyone involved in providing care for preterm infants should be aware of the critical importance of good nutrition in both the short and long term. This article will focus on nutrient requirements rather than on other 'technical' aspects of feeding such as rates of feed increase.

## Defining nutritional status

'Nutrition' does not simply relate to dietary intake: it is not possible to determine optimal nutrient provision just by calculation from a reference table. Many neonatal staff incorrectly assume that by providing full volumes (eg 150mL/kg/day) of parenteral nutrition (PN) or milk, they will be meeting that baby's needs. Unfortunately, this is not true. The needs of a 2kg baby born at 35 weeks' gestation, are different to those of a baby weighing 2kg at 35 corrected weeks who has CLD, but who started off weighing 500g when born at 23 weeks. Nutrient needs must reflect:

- what has happened before – was the baby very intrauterine growth restricted (IUGR), or has growth *ex-utero* been poor?
- what is happening now – does the baby have additional needs because of CLD, or increased losses due to an intestinal stoma?
- the outcomes we are trying to achieve – should we monitor the 'success' of nutrition by weight gain, or might there be longer-term outcomes that suggest alternative growth trajectories?

Taking a systematic approach and treating each baby as unique is an important starting point in trying to guide practice. This does not mean that guidelines or references are unhelpful, quite the opposite. All the evidence currently available suggests that morbidities such as necrotising enterocolitis (NEC) or poor weight gain are less common in units that have standardised approaches to feeding and nutrition[5].

Nutrient requirements can be divided into macro- and micronutrients. Macronutrients include protein, energy (both fat and carbohydrate) and water. Micronutrients include electrolytes (sodium etc), minerals (calcium, phosphorus etc), vitamins (both fat and water soluble) and trace elements (iron, zinc etc). Most practitioners do not need a detailed knowledge of individual nutrient requirements, but it is useful (and not difficult!) to know macronutrient needs: most stable growing preterm infants need about 110-120kcal/kg/day and 3.5-4g/kg/day of protein[6,7].

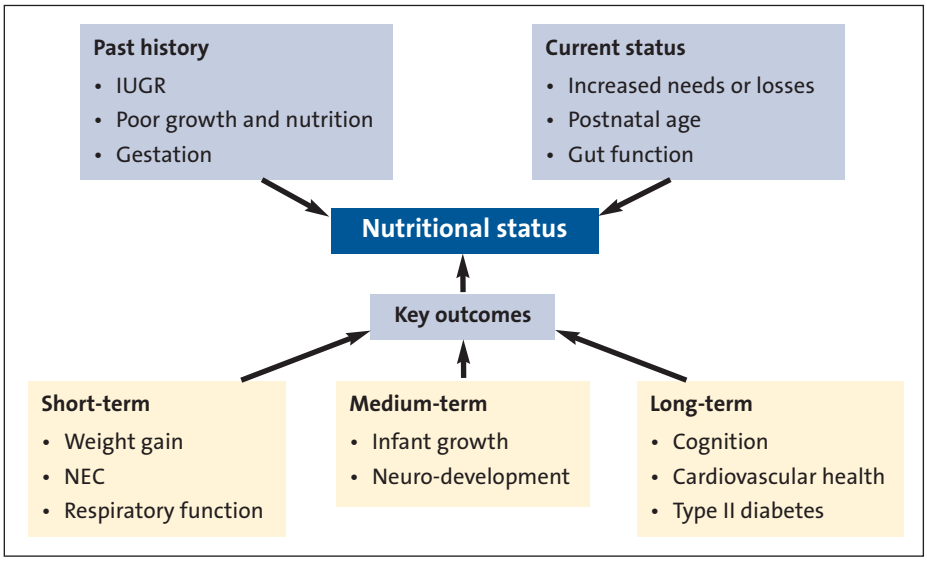


**FIGURE 1** Nutritional status and key outcomes.

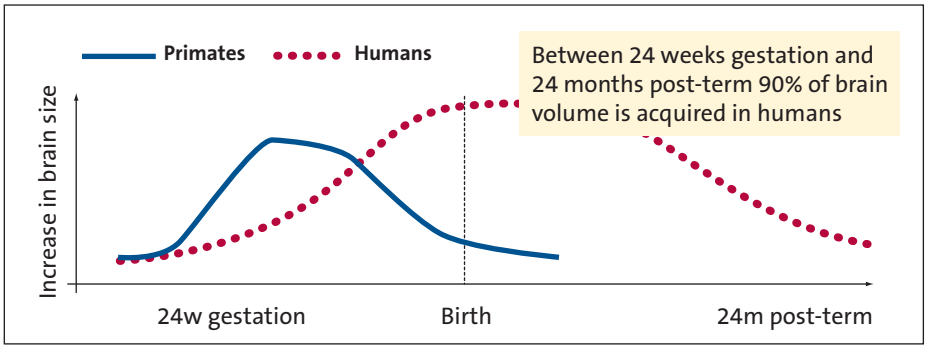


**FIGURE 2** Brain growth spurt in primates and humans.

## Key outcomes of good nutritional care: growth and brain development

There are now good data to show that nutritional practices affect short-term (eg growth, respiratory health etc), medium-term (eg neuro-developmental status) and long-term (eg risk of adult type II diabetes) outcomes (see **FIGURE 1**). In the last 10 years there has been an explosion of research looking at the area of programming and Developmental Origins of Health and Disease (DOHaD)[8]. Within this exciting new area we are starting to realise that how you grow in the first few weeks and months affects diseases that occur decades later. Term-born babies who weighed less than 5.5lb (2.5kg) compared to those weighing more than 8lb (3.6kg) have an excess risk of cardiovascular disease equivalent to that of being a lifetime smoker[9].

Measuring how much a baby weighs and plotting gain over time is a cornerstone of neonatal practice, as is serial measurement of head growth (circumference). While increase in head circumference closely parallels increase in brain volume (but not necessarily brain function), weight gain alone does not necessarily equate to growth. Babies may put on weight because of excess fluid retention, and an inappropriate balance of protein and energy may result in excess fat accumulation. Optimal growth can be conceptualised as the combination of weight gain and appropriate body composition. There are several techniques for measuring body composition, but none are readily available in clinical practice. However, the simple addition of measuring length (using a length board or mat, or using knemometry to measure knee-heel length) adds useful information: a baby whose weight gain is following a centile line, but whose length is falling away, will not be developing appropriate body composition.

Growth charts for use in the UK have been developed this year (2009) by the Royal College of Paediatrics and Child Health (RCPCH) using WHO standards (www.growthcharts.rcpch.ac.uk). Previous charts included data from formula-fed infants who may gain weight more quickly in the early weeks, so these new charts are designed to reflect the optimal growth of healthy breastfed infants. These will, then, make weight patterns in later infancy appear different to what many have been accustomed, so training and education will be needed. There is a separate 'Low birth weight' section for preterm infants and instructions on how to correct for gestation that require careful attention.

If optimal growth is defined by using growth charts and aims to promote appropriate composition, data on fetal growth can then be used to determine how much of a nutrient (eg protein or iron etc) a preterm baby might need on a daily basis[6,10,11]. Parents and staff want to see their baby growing 'normally' but much of neonatal care is, quite correctly, focused on optimising neuro-developmental outcome. This is partly determined by brain growth – both volume and complexity – and is nutritionally dependent. In humans, brain growth is most rapid in the period immediately before and after delivery, in contrast to other primates where the brain growth spurt occurs well before delivery (**FIGURE 2**)[12]. Between 24 weeks' gestation and two years' post-term the brain acquires 90% of its final volume. Inadequate nutrient provision in this period will irreversibly affect brain function[1].

There are good data from the controlled trials of Lucas and co-workers to show that differences in nutrient intakes over just a few weeks affect long-term outcome[3,13,14]. Babies who were fed a term formula prior to discharge, compared to a preterm formula, had lower (ie worse) developmental scores in infancy and lower cognitive scores in later childhood[3]. These longer-term effects resulted from marginally sub-optimal intakes (about 20% less energy and protein) rather than from very restricted intakes. Following these few weeks of study intervention, all babies were fed the same after discharge. There were no persisting differences in growth, but despite this, and the short nature of the intervention, cognitive deficits were still apparent years later[3]. In addition, the lower intake groups also seemed to have higher rates of cerebral palsy.

## Accumulation of nutrient deficits

Unfortunately, it is all too easy to provide marginally inadequate nutrition despite the evidence that this may permanently affect brain outcome[2]. Several studies have shown that there is a delay in providing adequate nutrition. This results in a

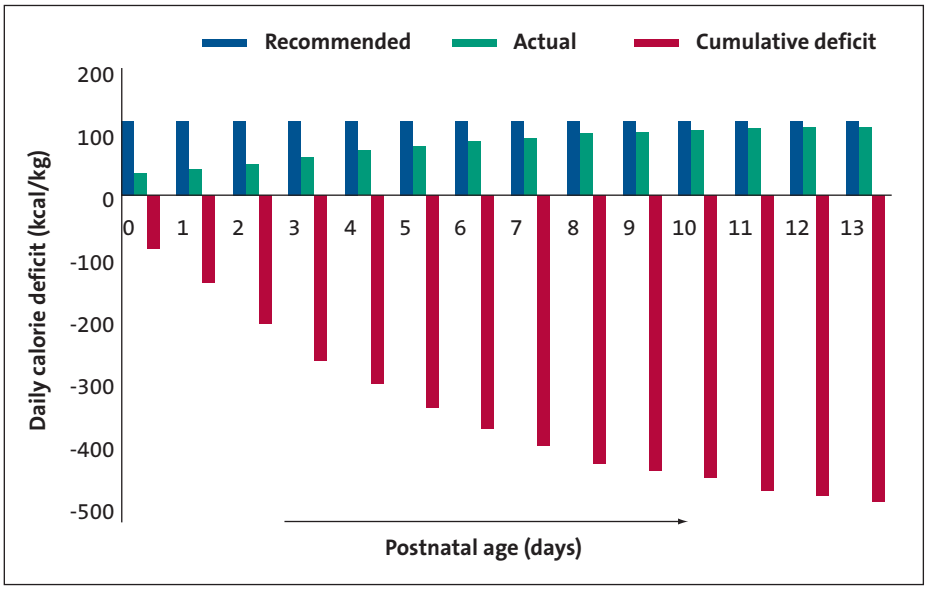


**FIGURE 3** Nutrient deficits in the first two weeks of life. Recommended energy intakes (blue bar) are ~120kcal/kg; the green bar depicts the actual amount of energy received, and the red bar is the cummulative deficit. By two weeks of age, the nutrient deficit is equivalent to only having received 70% of requirements. Based on Embleton et al. *Pediatrics* 2001[15].

nutrient deficit that tends to increase over time and is strongly associated with poor growth (**FIGURE 3**)[15]. Inadequate nutrient provision occurs for several reasons: sometimes because clinicians are cautious about starting and increasing parenteral nutrition (PN); sometimes because PN is not available or not thought to be useful; or because fluids are restricted.

Two small studies conducted in the late 1960s suggested that high levels of protein might be harmful, but these studies used protein intakes much higher than currently recommended, and bear little relationship with current practice[16,17]. Despite this, and because of largely unfounded concerns about 'metabolic immaturity', many clinicians seem to remain 'protein-phobic'. In addition, some babies may not control their glucose levels in the early postnatal period, some might need insulin, and therefore the amount of energy provided needs careful consideration[6]. Clinicians also start and introduce lipids slowly despite any evidence to show that such an approach results in better tolerance. Nutrient deficits are partly the result of metabolic limitations (such as hyperglycaemia) but often occur because of clinical practices that lack a strong evidence base.

## Nutrition in the first few days

When all the data currently available are considered there seems to be no good reason why parenteral protein (in the form of amino acids) and lipids can not start on the first day[6,7,18]. Although babies have individual nutrient needs, it is far more effective (and safe) to use standardised PN bags with standard compositions of amino acid (which are utilised to form protein), dextrose (for energy) and electrolytes. Less than 10% of babies probably need 'individualised' PN prescriptions. Precise requirements might be difficult to define, but many nutritional experts would recommend at least 2-3g/kg/day protein and 1-2g/kg/day lipid in the first 1-2 days (some would recommend and give more), increasing to 3-4g/kg/day protein and 3-3.5g/kg/day lipid within the subsequent 1-2 days[6,7,11,18]. If babies are very unwell, acidotic or septic then they will not metabolise and utilise nutrients effectively so it might be sensible not to increase from the initial starting amounts until they are more stable.

Milk feeds are usually started and increased slowly because of the risk of necrotising enterocolitis (NEC), and feeds are often stopped because of concerns that a baby may be developing NEC[19,20]. Often these concerns arise because of large 'aspirates' (gastric residuals) but there are almost no data to support the commonly-held belief that this sign alone indicates the presence of early NEC. There are too few data to make firm recommendations about how best to provide enteral nutrition, but there is overwhelming evidence that we should use mother's own expressed breast milk (EBM)[6,21]. There are also some data that suggest donor EBM might be protective against NEC, but this is not available at every unit and it will never provide as much advantage as own mother's fresh EBM[22]. One of the simplest and most important nutritional strategies to promote is one that encourages the provision of EBM.

## Nutrition in stable growing preterm infants

There are several authoritative recommendations on nutrient requirements in preterm infants[6,11] and ESPGHAN are due to publish new guidelines very shortly that update their 1987 recommendations[23]. Assuming a baby is able to tolerate full enteral feed volumes what should we be giving? If EBM is available then intake should be maximised – this might mean giving more than the standard 150mL/kg/day. Our current practice is to increase feeds up to 175mL/kg/day and review growth. Most babies <1500g will require much more protein and energy than can be provided by EBM alone (even at intakes of 175-200mL/kg/day) but adding a commercial breast milk fortifier (BMF) will meet most babies' needs[24]. Although there are small differences in composition for the currently available low birthweight (LBW) formulas there are no data to show superiority of any individual brand.

Preterm babies fed at 160-180mL/kg/day of either LBW formula or fortified EBM will have most of their nutrient needs met. However, there are a few important considerations:

1. Babies may not receive their full intake if they are vomiting or if feeds are frequently stopped. Always review what the baby received, not what was prescribed.
2. Most breast milk fortifiers in the UK do not contain iron. If the baby was <1.5-2kg at birth, is mainly receiving fortified EBM and has not been transfused recently, start supplemental iron at 4-6 weeks of age (~2mg/kg/day iron).
3. Several authorities recommend more vitamin D (<800iU/day) than is currently provided in LBW formula or BMF (both provide about 300-400iU/day). There is also some evidence that many preterm babies receive inadequate vitamin A[6]. While we do not know for certain what is best, it seems prudent (and safe) to provide additional vitamin D (and maybe also vitamin A) using commercial multivitamin drops.

4. Weigh babies at least weekly and plot using the new charts. As a general rule most babies gain about 30g/day – if their weight gain is falling off the centile line, they need nutritional review and not the simple addition of more calories. Current formula and BMF may not provide sufficient protein for the smallest preterm infants[7,25,26].
5. The frequent combination of IUGR, poor postnatal growth and ongoing additional needs mean that nutritional status must continue to be a focus of ongoing care for infants born preterm even when they can feed 'ad-lib' and are discharged.

## Nutrient needs at discharge

Despite the improvements in nutritional care in the last few years, a substantial proportion of preterm babies have still to catch up their nutritional and growth deficits by the time they are ready for discharge[15]. In addition, even those infants who have grown well are likely to have additional ongoing needs, and many with apparently normal growth might be relatively deficient in calcium and phosphorus and other micronutrients[6,11]. It remains a matter of intense debate as to how fast these babies should grow and whether continued catch-up growth should be promoted. In term infants, rapid weight gain in the first few weeks and months appears to increase the risk of later metabolic disease. In near term and term IUGR infants, promoting fast growth might be harmful, but preterm infants have had a very different nutritional course and we do not know for certain what might be best. Given the concerns that inadequate nutrition may prevent optimal cognitive outcome, our current recommendation is not to restrict or restrain growth.

Although we may not know how much preterm infants need after discharge, 95% of them will feed on demand and determine their own intakes. Despite the fact that breast milk contains lower nutrient densities than LBW formula, the benefits for optimising neuro-cognitive and metabolic outcome are so strong that there are very few good reasons to recommend the alternative use of any formula supplements after discharge (**FIGURE 4**). Breast fed babies will, however, continue to benefit from supplemental vitamin D and iron. Such provision should continue until the baby receives adequate amounts from weaning foods, and some

**FIGURE 4** Breast milk is the preferred milk for preterm babies, but may need fortification.

authorities now recommend continuing vitamin D supplements for all babies throughout infancy. There is just one small trial looking at the use of BMF after discharge[27], but despite ESPGHAN recommendations[28] we do not currently recommend the routine use of any supplements other than vitamins and iron.

Many mothers, however, are no longer providing EBM at discharge, and some find it difficult to continue breastfeeding. For babies receiving formula there are three options: term milk, LBW formula or a post-discharge formula (PDF). There is fairly strong evidence that otherwise well infants regulate their intake on total calories consumed, so the real question is not how much to give them, but what the optimal ratio of nutrients should be[29]. The main advantage (if there is one) of either a LBW or PDF are the higher protein:energy ratios, but they also provide additional minerals that improve bone mineral density in preterm infants. Of these, a PDF is preferable as it more closely meets estimated requirements. Appreciating that babies feeding on demand regulate their intake by caloric intake is important: if weight gain is slow then simply adding more calories (as a carbohydrate or fat supplement) to the milk will often lead to decreasing volume intakes, and in so doing, will further decrease intake of the other essential nutrients such as protein and minerals. Dieticians can be a useful resource. In babies at high risk of cerebral palsy, providing additional energy after discharge may improve outcome[4]. Current data do not show an advantage of PDF use in terms of developmental outcome[30].

There are too few data to determine exactly which preterm babies will benefit from a PDF. Babies with risk factors for poor growth will benefit most:

- babies <1750g birth weight
- IUGR babies
- babies with continuing additional needs (CLD or a stoma)
- babies with poor *ex-utero* growth (below birth centile).

Most preterm babies have a combination of these risk factors, but there will be a few preterm babies <34 weeks, who might have been relatively well, and may have very little to gain by using an enriched formula post-discharge.

Preterm infants seem to establish demand feeding sometime between 35 and 37 weeks corrected age, and this appears to be driven in part by the establishment of neuronal circuitry that determines appetite. As appetite appears to be satiated by caloric intake, and because of the importance of adequate energy intake for brain growth, it seems sensible not to change formula in the weeks immediately following discharge unless there is a good reason to do so. Our current practice is to continue a PDF until the baby is receiving at least 2-3 solid meals per day. At this stage, milk nutrients provide a lower proportion of overall intake. There are just a few babies with ongoing poor growth, or complex ongoing medical needs who might benefit from a PDF until 9-12 months' corrected age.

## Conclusions

In contrast to respiratory, cardiac or neurological disease, nutritional morbidity is often hidden. Little attention was paid to its importance in the early years of modern neonatal practice. Nowadays, we care for many preterm babies with minimal respiratory or neurological morbidity but good nutritional status remains essential for every baby. The accumulating evidence continues to encourage use of breast milk, and highlights the long-term adverse effects that poor nutritional care might cause. Nutritional management should start as soon as the baby is born, and continue into the post-discharge period if optimal outcome is to be achieved.

## References


1. **Cooke R.W.I.** Are there critical periods for brain growth in children born preterm? *Arch Dis Child: Fetal Neonatal Ed* 2006; **91**(1): 17-20.
2. **Isaacs E.B., Gadian D.G., Sabatini S. et al.** The effect of early human diet on caudate volumes and IQ. *Pediatr Res* 2008; **63**(3): 308-14.
3. **Lucas A., Morley R., Cole T.J.** Randomised trial of early diet in preterm babies and later intelligence quotient. *BMJ* 1998; **317**(7171): 1481-87.
4. **Dabydeen L., Thomas J.E., Aston T.J., Hartley H., Sinha S.K., Eyre J.A.** High-energy and -protein diet increases brain and corticospinal tract growth in

term and preterm infants after perinatal brain injury. *Pediatrics* 2008; **121**(1): 148-56.
5. **Patole S.K., de Klerk N.** Impact of standardised feeding regimens on incidence of neonatal necrotising enterocolitis: a systematic review and meta-analysis of observational studies [see comment]. *Arch Dis Child: Fetal Neonatal Ed* 2005; **90**(2): 147-51.
6. **Tsang R., Uauy R., Zlotkin S., Koletzko B., eds.** Nutritional Needs of the Preterm Infant: Scientific Basis and Practical Guidelines. Digital Educational Publishing. 2005.
7. **Embleton N.D.** Optimal protein and energy intakes in preterm infants. *Early Hum Dev* 2007; **83**(12): 831-37.
8. **Lucas A.** Long-term programming effects of early nutrition – implications for the preterm infant. *J Perinatol* 2005; **25** Suppl 2: S2-6.
9. **Barker D.J., Winter P.D., Osmond C., Margetts B., Simmonds S.J.** Weight in infancy and death from ischaemic heart disease [see comments]. *Lancet* 1989; **2**(8663): 577-80.
10. **Ziegler E.E., O'Donnell A.M., Nelson S.E., Fomon S.J.** Body composition of the reference fetus. *Growth* 1976; **40**(4): 329-41.
11. **Klein C.J.** Nutrient requirements for preterm infant formulas. *J Nutr* 2002; **132**(4): 1395S-1577S.
12. **Dobbing J.** Undernutrition and the developing brain. The relevance of animal models to the human problem. *Am J Dis Child* 1970; **120**(5): 411-15.
13. **Lucas A., Gore S.M., Cole T.J. et al.** Multicentre trial on feeding low birthweight infants: effects of diet on early growth. *Arch Dis Child* 1984; **59**(8): 722-30.
14. **Lucas A., Morley R., Cole T.J. et al.** Early diet in preterm babies and developmental status at 18 months. *Lancet* 1990; **335**(8704): 1477-81.
15. **Embleton N.D., Pang N., Cooke R.J.** Postnatal malnutrition and growth retardation: An inevitable consequence of current recommendations in preterm infants? *Pediatrics* 2001; **107**(2): 270-73.
16. **Goldman H.I., Freudenthal R., Holland B., Karelitz S.** Clinical effects of two different levels of protein intake on low-birthweight infants. *J Pediatr* 1969; **74**(6): 881-89.
17. **Goldman H.I., Liebman O.B., Freudenthal R., Reuben R.** Effects of early dietary protein intake on low-birthweight infants: evaluation at 3 years of age. *J Pediatr* 1971; **78**(1): 126-29.
18. **te Braake F.W., van den Akker C.H., Riedijk M.A., van Goudoever J.B.** Parenteral amino acid and energy administration to premature infants in early life. *Semin Fetal Neonatal Med* 2007; **12**(1): 11-18.
19. **Embleton N.D.** When should enteral feeds be started in preterm infants? *Paediatr Child Health* 2008; **18**(4): 200-01.
20. **Flidel-Rimon O., Branski D., Shinwell E.S.** The fear of necrotizing enterocolitis versus achieving optimal growth in preterm infants – An opinion. *Acta Paediatr* 2006; **95**(11): 1341-44.
21. **Singhal A., Cole T.J., Lucas A.** Early nutrition in preterm infants and later blood pressure: two cohorts after randomised trials [see comment]. *Lancet* 2001; **357**(9254/): 413-19.
22. **Lucas A., Morley R., Cole T.J., Gore S.M.** A randomised multicentre study of human milk versus formula and later development in preterm infants. *Arch Dis Child: Fetal Neonatal Ed* 1994; **70**(2): F141-46.
23. **Wharton B.A.** Nutrition and Feeding of Preterm Infants. Committee on nutrition of the preterm infant, ESPGAN: Blackwell Scientific Publications, 1987.
24. **Lucas A., Fewtrell M.S., Morley R. et al.** Randomized outcome trial of human milk fortification and developmental outcome in preterm infants [comment]. *Am J Clin Nutr* 1996; **64**(2): 142-51.
25. **Cooke R., Embleton N., Rigo J., Carrie A., Haschke F., Ziegler E.** High protein pre-term infant formula: Effect on nutrient balance, metabolic status and growth. *Pediatric Res* 2006; **59**(2): 265-70.
26. **Embleton N.D., Cooke R.J.** Protein requirements in preterm infants: effect of different levels of protein intake on growth and body composition. *Pediatric Res* 2005; **58**(5): 855-60.
27. **O'Connor D.L., Khan S., Weishuhn K. et al.** Growth and nutrient intakes of human milk-fed preterm infants provided with extra energy and nutrients after hospital discharge. *Pediatrics* 2008; **121**(4): 766-76.
28. **Aggett P.J., Agostoni C., Axelsson I. et al.** Feeding preterm infants after hospital discharge: A commentary by the ESPGHAN Committee on Nutrition. *J Pediatric Gastroenterol Nutr* 2006; **42**(5): 596-603.
29. **Cooke R.J., Griffin I.J., McCormick K. et al.** Feeding preterm infants after hospital discharge: effect of dietary manipulation on nutrient intake and growth. *Pediatric Research* 1998; **43**(3): 355-60.
30. **Cooke R.J., Embleton N.D., Griffin I.J., Wells J.C., McCormick K.P.** Feeding preterm infants after hospital discharge: growth and development at 18 months of age. *Pediatric Res* 2001; **49**: 719-22.