East of England Perinatal Network

Clinical Guideline: Enteral Feeding – Vitamin supplementation

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For use in: EoE Neonatal Units
Guidance specific to the care of neonatal patients.

Used by: Medical staff, Neonatal Nurse Practitioners, Dietitians, Nursery Nurses

Key Words: vitamins, enteral feeding, Abidec, Folic acid

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Approved by:

Neonatal Clinical Oversight Group	
Clinical Lead Mark Dyke	

Audit Standards:

Audit points
All babies born at <34 weeks gestation:
Receiving unfortified expressed breast milk or donor breast milk are given 0.6ml Abidec and 50 micrograms folic acid daily (the latter until term).
Receiving fortified expressed breast milk, preterm formula, term formula, specialist formulas or NEPDF are given 0.6ml Abidec daily.
Who are discharged exclusively breast feeding receive 0.6ml Abidec daily until 1 year corrected age.
Who are discharged on term, specialist formulas or NEPDF receive 0.6ml Abidec daily until 6 months corrected age.

1. Introduction

The third trimester of pregnancy is a time of rapid nutrient accretion, peak bone formation and the time when vitamin stores are laid down, infants born prematurely therefore have lower stores and higher requirements for vitamins than those born at term. Additionally low levels of specific enzymes and carrier proteins lead to lower absorption and transportation of some nutrients.

A number of vitamins have been studied in relation to prematurity, notably Vitamin A, Vitamin D, Vitamin E and Folic Acid. These form the basis of supplementation recommendations.

The gestation below which additional vitamins are required is unclear and supplementation practice has in the past varies across the EOE Network. International guidelines from Koletzko (2014) provide recommendations for vitamin intakes in ELBW and VLBW infants and ESPHGAN (2010) for infants <1800g but neither make any delineation by degree of prematurity.

As infants born >33 weeks are most likely to establish breast feeding quicker than more premature infants, by consequence they will correct any nutrient deficit within a shorter period of time. For these reasons these guidelines should apply at the earliest to infants <34 weeks gestation.

Vitamin supplements should commence once an enteral feed volume of >100ml/kg/day has been achieved alongside a reciprocal reduction in aqueous and lipid PN. Vitamins are contained within the lipid fraction of PN so care should be taken to ensure parenteral lipid provision is 5ml/kg/day or less before commencing enteral vitamin supplements. In contrast, consideration should be given to earlier enteral supplementation if PN weaning practice involves the cessation of lipid prior to that of aqueous PN.

Vitamin supplementation is necessary for many infants born prematurely. The evidence base for the exact requirement is limited for most vitamins, and although the quantities required are extremely small they are all essential to many basis life processes. As such they should be included in any enteral supplementation guidance. (1)
The following guidelines are based on a combination of careful analysis of the vitamin content of available feeds and formulas, available evidence and best practice.

The available evidence used to support these recommendations can be found in Appendix 2.

2. Vitamin supplementation regimen

Guidelines apply to all preterm infants <34 weeks gestation on full enteral feeds according to the milk they are receiving. Care should be given to changes in milk types and modifications made to the vitamin supplement regimen as appropriate.

Dalivit should not be used as an interchangeable alternative for Abidec due to its far higher vitamin A content. (Appendix 2)

Milk type	**Vitamin supplement**	**Dose**
In the Neonatal Unit		
Unfortified breast milk	Folic Acid Abidec	50micrograms/day 0.6ml/day
EBM+ SMA Breast Milk Fortifier (BMF) EBM + Nutriprem Human Milk Fortifier (HMF)	Abidec	0.6ml/day
Nutriprem 1 Hydrolysed Nutriprem SMA Gold Prem 1	Abidec	0.6ml/day
Term formula Specialist formulas Nutrient dense term formulas	Abidec	0.6ml/day
At time of discharge		
SMA Gold Prem 2 Nutriprem 2	Abidec	0.6ml/day until 6 months corrected age
Breast feeding	Abidec	0.6ml/day until 1 year corrected age
Term formula Specialist formulas Nutrient dense term formulas	Abidec	0.6ml/day until 6 months corrected age

Vitamin supplementation in infants with conjugated hyperbilirubinaemia...

Infants with an increasing conjugated bilirubin >50micromol/l may have a degree of fat malabsorption, thereby indicating a need for additional supplements of fat soluble vitamins. The following supplementation regimen is suggested for these infants within the neonatal unit.

All other vitamin supplementation should be stopped when this regimen is implemented.

Preparation	**Dose**	**Provision**
Dalivit	0.6ml/day	5000 units vitamin A 400 units vitamin D
Alpha- tocopherol acetate suspension	10mg/kg/day (2)	14.9 units vitamin E / kg
Phytomenadione	1mg daily (3)	

When an infant is commenced on Ursodeoxycholic acid measure serum Vitamin D.

- Where level is <75 nanomol/l commence additional vitamin D to a **total*** of 1000units/day.
- Continue to measure serum vitamin D every three weeks whilst on supplementation.
- Where serum level is very low (eg <25nanomo/l) consideration could be given to the provision of a therapeutic dose of vitamin D accompanied by ongoing close monitoring of serum vit D levels.

Total* vitamin D = 0.6ml Dalivit + vitamin D from feed + additional vitamin D as colecalciferol or ergocalciferol.

Feed type	**Vit D content /100ml**	**Feed type**	**Vit D content /100ml**
Preterm breastmilk	8 IU (0.2 microgram)	EBM + SMA BMF	168 IU (4.2microgram)
Nutriprem 1	124 IU (3.1 microgram)	Pepti Junior	52 IU (1.3microgram)
Hydrolysed Nutriprem	124 IU (3.1 microgram)	Infatrini Peptisorb	68 IU (1.7microgram)
SMA Gold Prem 1	148IU (3.7 microgram)		
EBM +Nutriprem HMF	208 IU (5.2 microgram)		

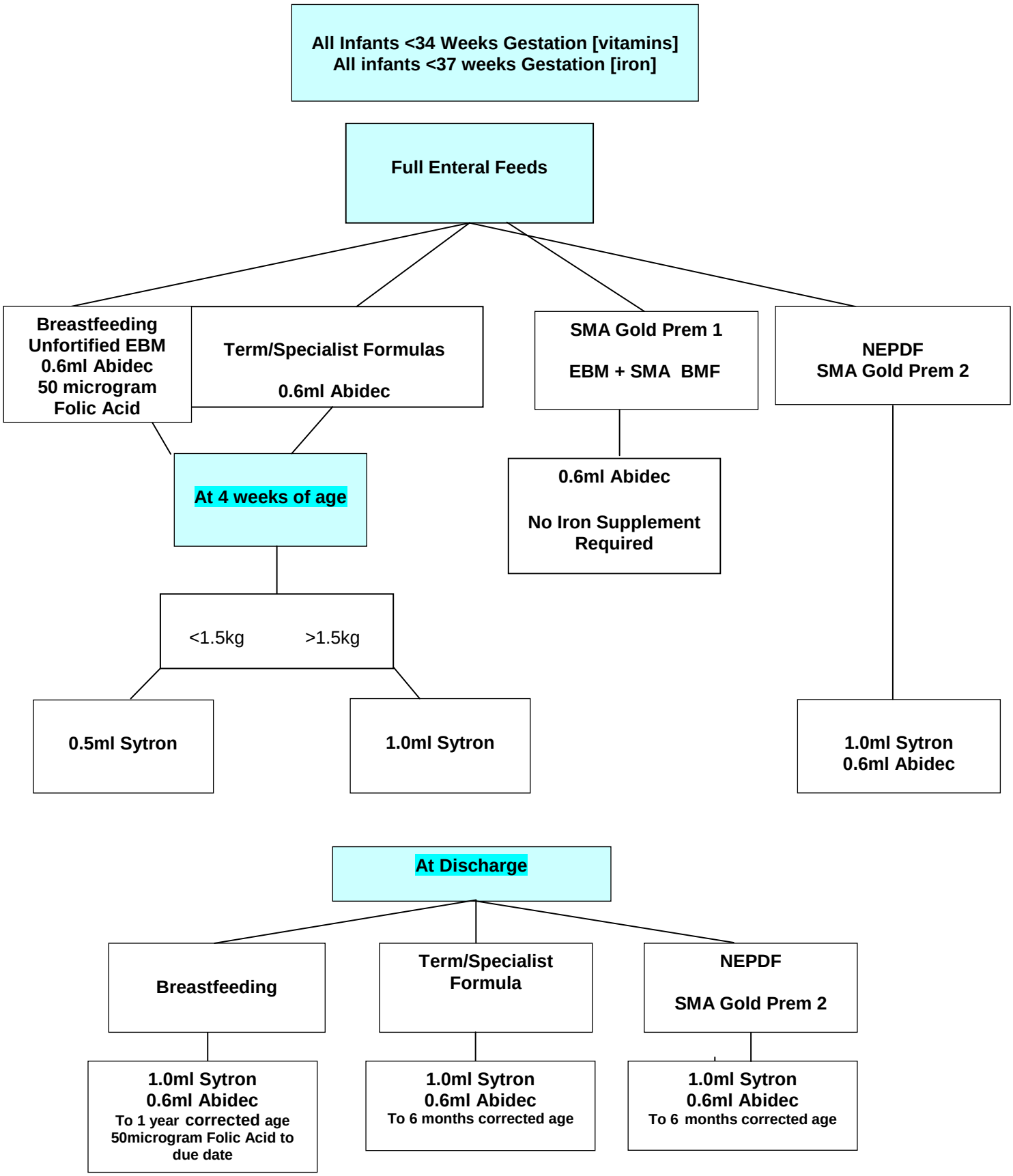
Example:

A 1.5kg infant receiving 150ml/kg Nutriprem 1:

Vit D provision Dalivit 400 IU/day
Nutriprem 1 1.5 x 150ml = 225ml, 2.25 x 124 IU = 279 IU/day
400+279 = 679 IU/day

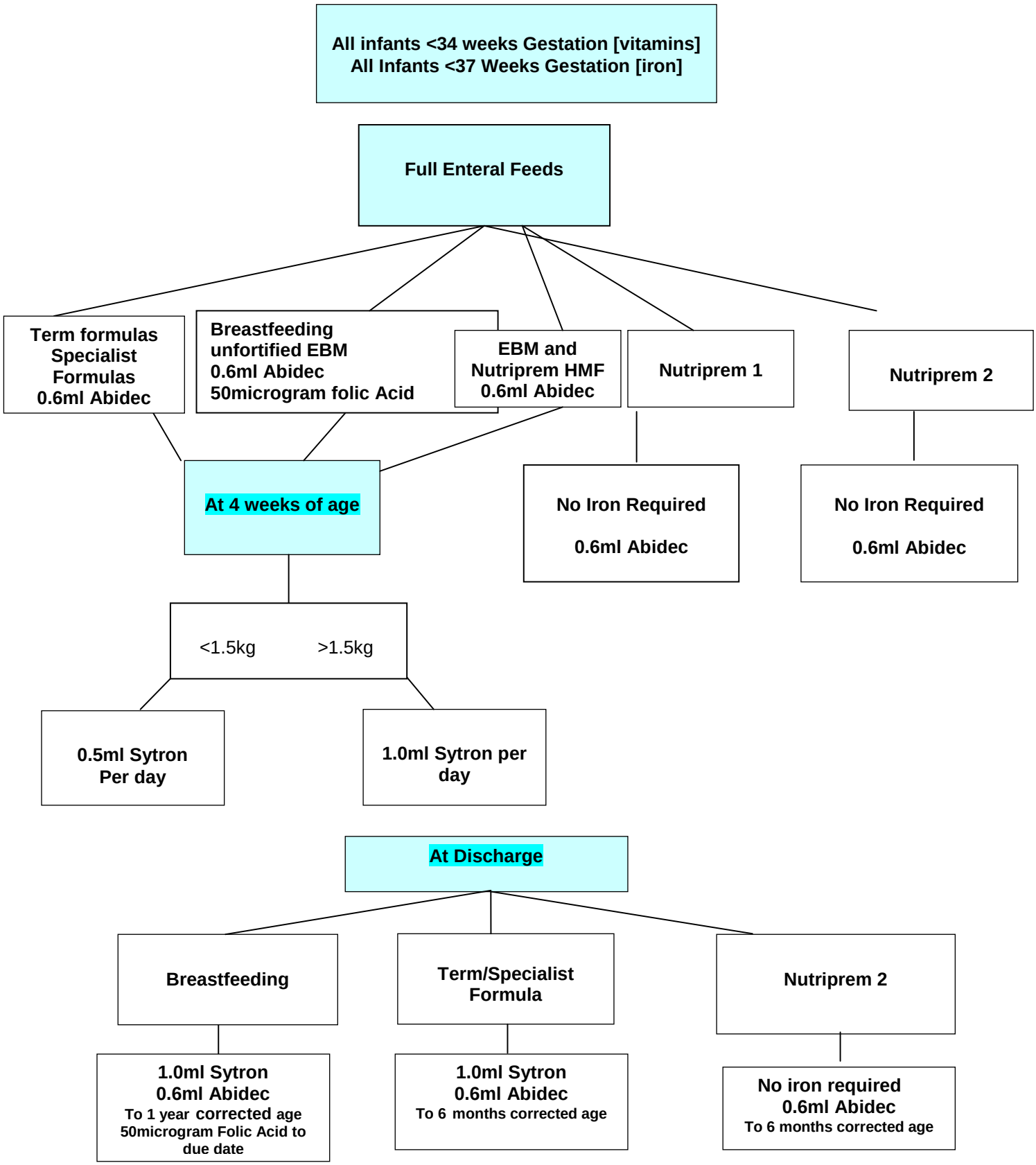
Additional Vit D required is 1000 - 679 = 321 IU from colecalciferol or ergocalciferol.

3.0 Algorithm for Iron & Vitamin supplementation – SMA range of feeds



Infants born ≥37 weeks and <2.5kg should be considered for iron supplementation from 4 weeks of age, especially if exclusively breastfeeding.

Algorithm for Iron and vitamin supplementation –Nutriprem range of feeds



Infants born ≥37 weeks and <2.5kg should be considered for iron supplementation from 4 weeks of age, especially if exclusively breastfeeding.

Composition of available vitamin supplements

Dalivit should not be used as an interchangeable alternative for Abidec or Healthy Start Vitamins due to its high vitamin A content.

	Vit A	Vit D	Vit C	Vit B1	Vit B2	Nic Acid	Vit B6
Abidec	IU micrograms	IU micrograms	mg	mg	mg	mg	mg
0.3ml	666 200	200 5	20	0.2	0.4	4.0	0.4
0.6ml	1333 400	400 10	40	0.4	0.8	8.0	0.8
Dalivit							
0.3ml	2500 750	200 5	25	0.5	0.2	2.5	0.25
0.6ml	5000 1500	400 10	50	1.0	0.4	5.0	0.5
Healthy Start							
5 drops	660 200	280 7	20				
10 drops	1320 400	560 14	40				

Appendix 2 - Evidence to support recommendations:

Vitamin A

Vitamin A is required for growth and differentiation of epithelial tissues, including the lungs and the retina. Preterm infants have low vitamin A levels at birth, which appears to persist at discharge (7) and may contribute to an increased risk of developing Chronic Lung Disease. A Cochrane review undertaken in 2011 concluded that large doses of vitamin A given intramuscularly showed a small decrease in oxygen dependency in infants at 36 weeks, but only to infants born < 1000g.(8) Supplementation of vitamin A may reduce the incidence of Retinopathy of Prematurity (ROP), Intra Ventricular Haemorrhage (IVH) and Necrotising Enterocolitis (NEC) whereas excess vitamin A can raise intracranial pressure, cause skin and mucosal membrane changes and vomiting.

The most recent recommendations for vitamin A requirements in preterm infants are 400 -1,100 microgram RE/kg/day or 1,330 – 3,330 IU/kg/day (9), this figure, published in 2014 is unchanged from the recommendations made by ESPGHAN in 2010 (10). Higher oral doses of 5000units/day do not seem to show any clinical benefit (11).
The requirements post discharge are unknown though low levels have been reported in infants until 6 months corrected age who were discharged on term formulas, whereas normal levels were identified in infants fed NEPDF to 2 months corrected age(12).

Vitamin **D**

Vitamin D is essential for the absorption of calcium and phosphorus and is therefore vital in bone formation. Supplementation is of no benefit if there are inadequate supplies of these two minerals, though its exact mechanism is unknown. Bronner et al (13) showed that calcium absorption in low birth weight infants was directly proportional to the calcium intake and independent of daily vitamin D supplementation. In contrast Devlin et al (14,15) showed that calcium absorption increases from 50% to 71% when AGA preterm infants <1500g were fed banked human milk alone or supplemented with vitamin D without calcium fortification, demonstrating that vitamin D affected calcium absorption rates.
Preterm infants are able to hydroxylate vitamin D so do not need the active form (16). Supplementation with excess active vitamin D may cause calcium resorption of the bone so should only be considered where there is clear biochemical deficiency or poor absorption eg. significant cholestatic liver disease.
Historically 400 IU/day of vitamin D has been considered adequate for optimal absorption in the presence of sufficient calcium, phosphorus and magnesium (17). Koo demonstrated that 800 IU/day is no better than 400 IU/day, but that 200 IU/day was inadequate for the prevention of osteoporosis and rickets of prematurity (18). In 2010 ESPGHAN recommended 800 -1000 IU/day (9) based on the prevalence of vitamin D deficiency in pregnant women (19) and the international consensus to increase circulating vitamin D levels in the general population (20), however the most recent recommendations suggest that 400I IU/day is adequate in the presence of sufficient quantities of calcium, phosphorus and magnesium, but that provision should increase up to 1000 IU/day if there is a likelihood of maternal depletion (21)

B vitamins and Folic Acid

Recommended levels for most B vitamins are provided by routine vitamin supplementation or formula composition, however Folic acid deficiency (in the form of growth retardation, anaemia and small intestine morphology) can be expected in the preterm infant not fed fortified breast milk or preterm formula due to poor intrauterine stores, rapid growth and low levels of folic acid in preterm breast milk. Folic acid is not present in standard vitamin supplements so needs to be supplemented separately.
Unfortified breast milk contains approx 3micrograms/100ml so does not meet the current recommendations of 35-100micrograms /kg/day (9).Recommendations for Folic acid are based on low plasma and red cell folate levels in preterm formula fed infants without Folic acid supplementation as compared to those given a supplement of 50microgram/day who had levels comparable to breast fed term infants (22).

Vitamin E

Vitamin E is a biological antioxident with a role in the prevention of haemolytic anaemia and may protect against Bronchopulmonary dysplasia (BPD), ROP and IVH. A Cochrane Review stated that “vitamin E supplementation in preterm infants reduces the risk of intra cranial haemorrhage but increases the risk of sepsis.”(23) a second study concluded that vitamin E reduces the risk of severe retinopathy and blindness in those studied but it increases the risk of sepsis. It has also been associated with a higher risk of NEC. (24)
Evidence for supplementation of vitamin E is conflicting, however as minimum requirements for vitamin E are met from both human and formula milk there is little clear evidence to support routine supplementation.(24)

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