

Newborn Critical Care Center (NCCC) Clinical Guidelines

Recommendations for the Supplementation of Vitamin D

BACKGROUND

Vitamin D (calciferol) refers to 2 secosteroids - vitamin D₂ (ergocalciferol) and vitamin D₃ (cholecalciferol). Vitamins D₂ and D₃ are considered prohormones and undergo 25-hydroxylation in the liver to 25-hydroxy vitamin D (25-OH-D, calcidiol), which is the major circulating form of vitamin D. From the liver, 25-OH-D is transported to the kidney for hydroxylation to form 1,25-dihydroxy vitamin D (1,25-OH₂-D, calcitriol). Calcitriol is the biologically active form of vitamin D, which stimulates intestinal absorption of calcium and phosphorous, renal reabsorption of filtered calcium, and the mobilization of calcium and phosphorous from bone.

TOXICITY

- Hypercalcemia, leading to depression of the central nervous system and ectopic calcification
- Hypercalciuria, leading to nephrocalcinosis and nephrolithiasis
- **The highest daily intake should be 1000 IU/day for infants 0 to 6 months of age**

DEFICIENCY

The manifestations of vitamin D deficiency are related to the effects on calcium metabolism. The most common clinical features are hypocalcemia, hypophosphatemia, tetany, osteomalacia, and rickets. The diagnosis of rickets is made on the basis of a history of inadequate intake and clinical findings and is confirmed by biochemical indices and radiographic findings.

ASSESSMENT

The best indicator of vitamin D status is serum 25-OH-D concentration. Other potentially useful tests include serum calcium, phosphorous, alkaline phosphatase, and parathyroid hormone concentrations. Parathyroid hormone generally is elevated in rickets associated with vitamin D deficiency. **The recommend target for serum 25-OH-D concentration is ≥ 50 nmol/L (20ng/mL).**

PREVENTION AND TREATMENT

The vitamin D content of human milk is low (22 IU/L), and most infant formulas and cow milk contain 400 IU/L. At the present time, the AAP recommends vitamin D supplementation at 400 IU/day for all breast-fed infants and all non-breast-fed infants. Supplementation should be continued until infants are taking at least **ONE LITER** of formula (or whole milk if older than 12 months) per day.

DAILY SUPPLEMENTATION FOR INFANTS ON FULL ENTERAL FEEDINGS	
Type of Feeding	MVI or Vitamin D Supplement
MBM	1 mL/day or 400 International Units/day
Term Infant Formula	1 mL/day or 400 International Units/day
MBM with HMF	0.5 mL/day or 0.25 mL twice daily
MBM/DBM with Prolacta	1 mL/day or 0.5 mL twice daily
Preterm Formula (SSC 24, 26)	0.5 mL/day
Discharge Formula (Neosure)	1 mL/day
Special Formulas (Elecare, Alimentum)	1 mL/day

SPECIAL CONSIDERATIONS

Infants with diseases associated with fat malabsorption like cystic fibrosis, short bowel syndrome or receiving medications which interfere with fat absorption such as antiepileptics and infants with renal disease or cholestasis are at risk for Vitamin D deficiency and may require higher dose of vitamin D supplementation.

Deficiency can be treated with oral vitamin D supplementation in addition to Vitamin D provided in enteral feeding at a dose range of 600-1000 IU/day. 25-OH-D concentrations should be measured at 3-month intervals.

- For infants with **cholestasis** (direct bilirubin >2 mg/dL), consider AquADEK (1 mL/day), which provides 400 IU of vitamin D. This will provide the recommended vitamin D3 goals with a water miscible vitamin source for better absorption.
- Preterm infants with **rickets** may require an increase in vitamin D supplementation (up to 1000 IU/day) as well as addition of calcium and phosphorus supplementation.
- Routine management of preterm with birth weight < 2kg should include human milk fortifiers with minerals or formulas designed for preterm infants.
- Routine evaluation is indicated for infants with birth weight < 1500grams:
 - Biochemical testing should usually start at 4-5 weeks after birth.
 - Serum alkaline phosphatase > 800 IU/L or clinical evidence of fractures should lead to radiographic evaluation for rickets.
 - Persistent serum phosphorus concentration < ~4 mg/dL should be evaluated, consider phosphorus supplement.
 - For former preterm infants who are discharged on exclusive unfortified breastmilk, a follow up alkaline phosphatase level is recommended 2-4 weeks after discharge.

References:

1. Kleinman RE, Greer FR et al. AAP Pediatric Nutrition, 8th Ed. Fat-Soluble Vitamins, Vitamin D. AAP, 2019; 21.1; p642-646.
2. Koletzko B, Poindexter B, Uauy R. Nutritional Care of Preterm Infants. Calcium, Phosphorus, Magnesium and Vitamin D Requirements of the preterm infant. By Karger 2014; Vol.110; 144-148.
3. Abrams SA and the AAP Committee on Nutrition. Calcium and Vitamin D Requirements of Enterally Fed Preterm Infants. Pediatrics. 2013; 131: e1676-e1683.