

Vitamin D in Health and Disease: A Hot Topic

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In the field of nutrition, vitamin D is a “hot topic.” If you enter “vitamin D” into the PubMed search engine, 45,000 entries appear. Currently, articles are being published on this important vitamin at a rate of almost 100 each month. For those of us caring for neonates and interested in infant nutrition, the big vitamin D story is the changed recommendations of the American Academy of Pediatrics (AAP) in 2008.¹ In the previous AAP recommendation, all infants were to begin 200 international units (IU)/day of vitamin D in the first 2 months after birth, and a daily intake of 200 IU was recommended for children and adolescents.² Since the initial publication of these recommendations (2003), numerous cases of rickets, thought to be caused by inadequate vitamin D intake and decreased sun exposure, have been reported.^{2,9} Many cases of deficiency involved exclusively breastfed infants and/or infants and children with darker skin pigmentation.^{3,7-9} Rickets, the extreme manifestation of vitamin D deficiency, has also been seen in the pediatric population.^{4,5}

There are two forms of Vitamin D: D₂, ergocalciferol (made by plants) and D₃, cholecalciferol (made by mammals). For humans, the main source of vitamin D activity is D₃, which is made in the skin from the action of ultraviolet light, which converts 7-dehydrocholesterol into previtamin D₃. This is further converted through the heat of the skin to vitamin D₃, which is transported to the liver for conversion into 25-OH-D. When assaying for deficiency states, 25-OH-D is the form to be requested in the screening test. 25-OH-D undergoes another conversion in the kidney (and other tissues) to 1,25-OH₂-D. This form may be normal or even elevated in deficiency states, so that it is not requested in screening tests.¹

Box 1: Recommendations on Prevention of Rickets and Vitamin D Deficiency¹

Breastfed (and partially breastfed) infants should be supplemented with 400 IU/day of vitamin D beginning in the first few days of life. Supplementation should be continued until the infant is weaned and consuming at least 1 L/day or 1 quart/day of vitamin D fortified formula or whole milk. Whole milk should not be used until 12 months of age.

All non-breastfed infants, as well as older children who are ingesting <1,000 ml/day of vitamin D fortified milk, should receive a vitamin D supplement of 400 IU/day.

Adolescents who do not obtain 400 IU/day through vitamin D fortified milk and vitamin D fortified foods should receive a vitamin D supplement of 400 IU/day.

Serum 25-OH-D levels for infants and children should be ≥ 50 nmol/L.

Children with increased risk of vitamin D deficiency (e.g., chronic fat malabsorption; antiseizure medications) may continue to be vitamin D deficient despite an intake of 400 IU/day. Higher doses of vitamin D may be necessary to achieve normal vitamin D status in these children.

Pediatricians and other healthcare providers should strive to make vitamin D supplementation readily available to all infants and children, especially for those most at risk.

Dietary sources of vitamin D are limited to vitamin D-fortified milk as well as natural D in fatty fish, certain fish oils, liver from aquatic mammals, and egg yolks from chickens fed vitamin D.¹⁰ In school we were always taught that vitamin D was the “sunshine vitamin.” Sunlight is a source of vitamin D, but it is affected by many factors, especially the pigmentation of the skin. People with darker skin require more time in the sun to generate the same vitamin D from the skin than a person of lighter pigmentation is able to generate from the same exposure.¹¹⁻¹³ Sunscreen, which is recommended, lessens the skin exposure to ultraviolet (UV) light, as do the amount of clothing, latitude or altitude, cloud cover, extent of air pollution and other factors.^{13,14} The AAP has guidelines to *reduce* the sun exposure of children, and recommends that infants under 6 months of age be kept out of direct sunlight.¹⁵ Epidemiological studies now suggest that the age at which direct sunlight exposure is initiated may be more important than the total sunlight exposure (over a lifetime) in

determining risk of skin cancer.^{16,17} Following these guidelines, supplementation would be necessary in infancy as well as in childhood and adolescence.¹

What, then, is new about the AAP 2008 guidelines? Recommendations for levels of vitamin D supplementation have doubled and vitamin D supplementation is now recommended to begin soon after birth, instead of 2 months of age. Excerpts from the new AAP recommendations¹ are listed in Box 1. Note that the changes are really quite easy — just remember 400 IU!!

What products are available for supplementation? There are new vitamin D-only medications. In the past, a multivitamin or an ADC multivitamin was recommended because the vitamin D-only preparation was over 10 times as expensive and carried the concern about being administered in drops (having a potential for overdose, which occurred in at least one case).¹⁸ There continues to be a wide variation in dosing, since some products have a 1 drop dosage and others are 1 ml. Some vitamin D preparations are alcohol-based, while

Table 1: Vitamin Preparations Containing Vitamin D

Product	Manufacturer	Dosage	Preparation	Cost
Bio-D-Mulsion	Biotics Laboratory www.bioticsresearch.com	1 drop contains 400 IU	Corn Oil	1 oz (750 drops) \$11.50
Bio-D-Mulsion Forte	Biotics Laboratory www.bioticsresearch.com	1 drop 2000 IU per drop	Corn Oil	1 oz (750 drops) \$19.00
Baby D drops	Carlson Labs www.carlsonlabs.com	1 drop contains 400 IU	Safflower Oil	11 ml \$16.98
D drops 1000 IU	Carlson Labs www.carlsonlabs.com	1 drop contains 1000 IU	Safflower Oil	11 ml \$18.98
D drops 2000 IU	Carlson Labs www.carlsonlabs.com	1 drop contains 2000 IU	Safflower Oil	11 ml \$19.98
Just D Infant Vitamin Drops	Sunlight Vitamins Unit Drug Co. www.sunlightvitamins.com	1 ml contains 400 IU	Corn Oil	50 ml \$12
Multivitamin	Several manufacturers	1 ml contains 400 IU	Variable preparations that include glycerin and water, may also contain propylene glycol and/or polysorbate 80	@ \$5.70
Vitamins A,D,C	Several manufacturers	1 ml contains 400 IU	Variable preparations that include glycerin and water, may also contain propylene glycol and/or polysorbate 80	@ \$5.70
Gummy Vitamins	Several manufacturers	Varies: 1 gel contains 120 or 240 IU. Dose may be 2 gummies	Glucose syrup, sucrose, gelatin	\$4-10 @ 70 gummies

Adapted from Wagner CL, Greer FR, and the Section on Breast feeding Medicine: Prevention of rickets and vitamin D deficiency in infants, children, and adolescents, *Pediatrics* 2008; 122:1142 and Company Web sites

others are oil-based and, according to a study by Martinez et al.,¹⁹ are preferred by newborns and older infants. A list of vitamin preparations described in the AAP recommendations¹ is given in Table 1. Healthcare providers need to ask, and be vigilant about, the different dosages used in the community for vitamin D supplementation.

What about pregnant women? Research suggests that doses of vitamin D exceeding 1,000 IU/day may be needed by some women.¹ As many current prenatal vitamins only include 400 IU of vitamin D, it is conceivable that some mothers may be vitamin D deficient and if the mother is, her neonate will also be deficient.¹

Breast milk is known to be very low in vitamin D (25-OH-D), at less than 25 IU/Liter, although when breast milk was assayed for water-soluble fractions of vitamin D activity, more was found (40–50 IU/L).²⁰ There is a direct relationship between maternal and infant levels of 25-OH-D.¹⁶ When mothers of breastfed infants were given mega-doses of vitamin D, the vitamin D content of their milk increased.¹⁷ However, more research is needed before such doses of vitamin D become a universal recommendation.

What other research about vitamin D is available? Recent studies have implicated vitamin D insufficiency as a risk factor for a variety of chronic diseases,

including: (a) multiple sclerosis, (b) type I and II diabetes, (c) osteoporosis, (d) various cancers, (e) psychiatric illness, and (f) cardiovascular disease.²¹ The review by Lucas et al.²¹ describes future health implications of prenatal and early-life vitamin D status and the relationships between vitamin D insufficiency and chronic disease. The “Barker Hypothesis” postulates that adult diseases have their origins in fetal and infant life.²² During this critical time of early life there is a heightened susceptibility to certain disorders.²² Clearly, we need to be aware that some people may be deficient, and since we are now prudent about sun exposure, the need for supplementation for all ages is an important issue. ●