

Issues in establishing vitamin D recommendations for infants and children¹⁻³

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ABSTRACT

In 1963, the American Academy of Pediatrics Committee on Nutrition recommended 400 IU of vitamin D per day for all infants and children. After the late 1970s, this became an inconsistent recommendation, particularly for breast-feeding infants. In 2003, however, the Committee on Nutrition of the American Academy of Pediatrics recommended 200 IU/d vitamin D for all infants and children. This was in response to the vitamin D adequate intake recommendations made by the Institute of Medicine in 1997, the increasing number of reports of nutritional rickets in certain populations of American infants, and the Healthy People 2010 goal of having 75% of infants breast-fed for the first 6 mo of life. In making these recommendations, many issues were taken into consideration, including the following. 1) Vitamin D deficiency is more than rickets, which is the final stage of the deficient state among growing children. 2) Adequate sunlight exposure cannot be determined exactly for every subject. 3) There is new awareness of the hazards of ultraviolet-B light exposure in childhood and the subsequent development of skin cancer in adulthood. 4) There is decreasing intake of vitamin D-fortified foods among older children and adolescents. More research is needed in the pediatric population to determine the recommended dietary allowance of vitamin D. A new definition of vitamin D deficiency that would make use of normal serum concentrations of 25-hydroxyvitamin D₃ in a given population is needed. The recommended intake of 200 IU/d may not be enough. More data are needed to support the adequacy of the present and possibly even higher recommended vitamin D daily intakes. *Am J Clin Nutr* 2004; 80(suppl):1759S–62S.

KEY WORDS Vitamin D, infants, children

INTRODUCTION

In the first half of the 20th century, vitamin D deficiency was recognized as a significant problem in the pediatric population, with many cases of rickets being reported in the United States. Eventually, cow's milk and infant formula were fortified with vitamin D, and nutritional rickets became less evident. In 1963, the Committee on Nutrition of the American Academy of Pediatrics (AAP) (1) recommended that all infants (including breast-fed infants) receive 400 IU (10 μg) of vitamin D per day, starting in the first 2 wk of life. The committee also recommended 400 IU/d for all other children and adolescents, approximating the amount of vitamin D in 1 teaspoon of cod liver oil. The estimated daily requirement was 100–200 IU/d, and the committee recommended an intake of twice the daily requirement. This recommendation was supported by the knowledge that 400 IU/d had

been shown to prevent rickets and > 400 IU/d did not increase rickets prevention. It was also observed that rickets could be successfully treated with 300–400 IU of vitamin D per day and that a daily oral intake of > 500 IU did not improve the response of rickets to vitamin D therapy. The report did not comment on the vitamin D concentrations in human milk but noted an increase in vitamin D deficiency in the African American population even at that time. The committee also acknowledged that sunlight exposure could not be relied on to improve vitamin D status. Certainly, the observations of this committee were prescient for the time, because measurements of specific vitamin D metabolites in milk and human serum were not yet available.

In 1977, a report from the laboratory of Elsie Widdowson in Cambridge, England, described a new form of water-soluble vitamin D in human milk (2). This metabolite, vitamin D sulfate, was present at concentrations of 400–950 IU/L (2). Subsequently, the idea that breast-fed infants did not need supplemental vitamin D gained credibility. This led the AAP to become somewhat ambiguous regarding the vitamin D needs of breast-fed infants. A 1978 statement on breast-feeding from the AAP Committee on Nutrition (3) listed vitamin D only as a possible supplement for breast-fed infants. In 1981 (4), the same committee stated that arguments could be made for treating breast-fed infants with vitamin D during the first 6 mo of life, but there was disagreement about whether all breast-fed infants needed such supplementation.

Subsequent studies, using improved technology, found little or no vitamin D sulfate in human milk (5, 6), thus dispelling the myth of a water-soluble form (7). In addition, the biological activity of vitamin D sulfate was found to be < 5% of the activity of vitamin D₃ in mobilizing calcium from bone and < 1% of the activity in supporting bone calcification or in stimulating intestinal absorption of calcium (8, 9).

The 1980 Infant Formula Act (10) established a minimum of 40 IU/100 kcal and a maximum of 100 IU/100 kcal for vitamin D in infant formulas. Therefore, a 20-kcal/ounce formula would supply 265–660 IU/L of vitamin D to the formula-fed infant (10). The 10th edition of the recommended dietary allowances (RDAs) recommended 300 IU/d vitamin D for infants < 6 mo of

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age and 400 IU/d for all infants and children > 6 mo of age (11). For breast-fed infants not exposed to sunlight, a RDA of 200–300 IU/d was made.

In 1997, the Food and Nutrition Board of the Institute of Medicine (IOM) (12) established the daily adequate intake (AI) of vitamin D at 200 IU/d, to cover the needs of all infants and children, regardless of sunlight exposure. AI is used when there is insufficient evidence for calculation of a RDA. AI is a value based on experimentally derived intakes or approximations of observed mean nutrient intakes by a group of healthy people. This intake is expected to meet or exceed the amount needed to maintain a nutritional state of adequacy for essentially all members of a specific healthy population. For infants and children, this would include normal growth, maintenance of normal circulating nutrient concentrations, and other aspects of nutritional well-being and general health. The AI for infants is based on data from the United States, Norway, and China that show that an intake of vitamin D of ≥ 200 IU/d prevents physical signs of vitamin D deficiency and maintains serum 25-hydroxyvitamin D₃ [25(OH)D₃] concentrations at ≥ 27.5 nmol/L (11 ng/mL) (12). The IOM acknowledges that there are fewer data available for older children and adolescents, but the AI for that population should remain the same, pending additional research.

In 2003, the Committee on Nutrition and Section of Breast Feeding Medicine of the AAP (13) published new recommendations for vitamin D supplementation for infants and children. This was largely in response to the IOM's 1997 AI recommendations, the increasing number of reports of nutritional rickets among certain populations of American infants (14–17), and the Healthy People 2010 goal of having 75% of infants breast-fed for the first 6 mo of life (US Department of Health and Human Services Office of Disease Prevention and Health Promotion, www.healthypeople.gov). In making this recommendation, the following factors were taken into consideration.

DEFINITION OF VITAMIN D DEFICIENCY

Clinical rickets is the final stage of vitamin D deficiency, and the deficiency must be present for many months before rickets can be diagnosed (18). 25(OH)₂D₃ is the most plentiful circulating serum metabolite and is indicative of overall vitamin D status. According to the IOM, the lower limit of the normal range may be as low as 20 nmol/L (8 ng/mL) or as high as 37.5 nmol/L (15 ng/mL). In general, a serum 25(OH)₂D₃ concentration of < 27.5 nmol/L (11 ng/mL) is considered deficient for children. Exclusively breast-fed white infants, born in winter in Wisconsin, exhibited mean 25(OH)₂D₃ concentrations of < 10 ng/mL at 6 wk of age if given no vitamin D supplements (19). A recent report from Alaska showed that 41 of 133 infants attending Supplemental Nutrition Program for Women, Infants, and Children clinics had low (< 15 ng/mL) or low-normal (25 ng/mL) 25(OH)₂D₃ levels. Forty of the 41 infants were being breast-fed or were previously breast-fed (20). If the normal range of values for 25(OH)₂D₃ were known, more meaningful and precise recommendations for vitamin D intake could be made. In optimal calcium and bone metabolism studies among adults, conflicting studies suggested that 25(OH)₂D₃ concentrations should be ≥ 37.5 nmol/L (15 ng/mL) (21, 22), ≥ 50 nmol/L (20 ng/mL) (23), or perhaps even higher (≥ 78 nmol/L or 31 ng/mL) (24). Although vitamin D is essential for bone health, many types of cells in the body have vitamin D receptors, and vitamin D likely

is functionally important in other ways. Epithelial cells other than those of renal origin are capable of synthesizing 1,25-dihydroxyvitamin D₃ from 25(OH)₂D₃ (25, 26). Vitamin D may also play a role in cancer prevention, in that it appears to moderate colonic and prostate cell proliferation through vitamin D receptors (27, 28).

SUNLIGHT EXPOSURE

Vitamin D is synthesized naturally in the skin after exposure to ultraviolet-B (UV-B) radiation from the sun. For any given infant or child, however, the amount of sunlight exposure (total surface area of the skin exposed for a given amount of time) needed to prevent vitamin D deficiency and rickets is difficult to determine; this is greatly influenced by the environment, including weather conditions, air pollution, time of year, and degree of latitude of the exposure. Vitamin D synthesis is influenced by skin pigmentation and, for individuals, it is difficult to determine how much skin pigmentation blocks vitamin D synthesis and how much provides adequate protection from UV-B light exposure (see below). Furthermore, the correct use of sunscreens dramatically blocks UV-B light exposure of the skin (29).

HAZARDS OF UV-B LIGHT EXPOSURE

There is growing concern regarding UV-B light exposure in childhood and its relationship to skin cancer (basal and squamous cell carcinoma and malignant melanoma) in later years (30). There is a positive correlation between the occurrence of malignant melanoma among adults and the degree of sunlight exposure in childhood (31, 32). The Centers for Disease Control and Prevention, with the support of many organizations, including the AAP and the American Cancer Society, launched a major public health campaign to decrease the incidence of skin cancer by urging people to limit exposure to UV light and to use sunscreens (33). The Committee on Environmental Health of the AAP (34) recommended that infants < 6 mo of age for whom the use of sunscreens is not currently recommended) be kept out of direct sunlight, that children's activities in general minimize sunlight exposure, and that protective clothing and sunscreens be used at all times.

DIETARY INTAKE OF VITAMIN D

Fortified dairy products are the single most important dietary source of vitamin D for older infants and children. Other than dairy products, vitamin D is present in fortified cereals and juices and in fatty fish and fish liver oils. It does not naturally occur as a nutrient to a significant degree in any infant food, including human milk (6, 35). In fact, vitamin D is not technically a nutrient but is a precursor of a steroidal hormone (prohormone) that is synthesized in the skin. Among older children and adolescents, decreasing vitamin D intake is related to replacement of milk by soft drinks, fruit juices, and/or fruit drinks (36, 37). There is also the concern that dairy products are fattening and are responsible for lactose intolerance in some populations (38).

PRACTICAL CONSIDERATIONS FOR VITAMIN D SUPPLEMENTATION

Several other points are worthy of consideration regarding recommendation of the ideal vitamin D supplement. These include the following.

The supplement should prevent vitamin D deficiency and rickets for all infants and children, including those with chronic diseases, who may have decreased vitamin D absorption. No ethnic group or minority should be singled out, given the increasing difficulty of defining these groups, although appropriate educational materials should be readily available for those caring for these groups. There should be no risks attributable to use of the supplement. The supplement should be safe to keep in the home, given the possibility of accidental ingestion.

The ideal supplement should contain vitamin D only. Supplements presently available for infants contain additional vitamins.


For breast-fed infants, supplements should be started in early infancy and continued until there is an intake of ≥ 200 IU/d from fortified foods. Such supplementation should not interfere with the establishment of breast-feeding.

The vitamin D status of the mother during pregnancy and lactation should be taken into consideration by infant health care providers in establishing the need for supplementation. A supplement should be given to all children and adolescents who are not receiving ≥ 200 IU/d from fortified foods. The supplement should be given as part of a daily routine, to maximize compliance. For infants receiving vitamin D-fortified formulas (≥ 500 mL/d), there is no need for vitamin D supplements.

The vitamin D supplement should be cost-effective. This includes not only the cost of the supplement but also the cost of treating potential overdoses and missed subjects who require additional further medical care.

FUTURE RESEARCH QUESTIONS

Vitamin D research in the pediatric population should be directed toward establishing a RDA, rather than an AI. This would require collecting information on normal serum concentrations of $25(\text{OH})_2\text{D}_3$ from infancy to adolescence. Is a serum $25(\text{OH})_2\text{D}_3$ concentration of < 27.5 nmol/L (11 ng/mL) appropriate for defining the deficient state among infants and children? Should the cutoff value be 37.5 nmol/L (15 ng/mL) or 50 nmol/L (20 ng/mL)?

Is an AI of 200 IU/d for vitamin D enough, particularly with the likelihood of decreased sunlight exposure if sunscreens are used as recommended and if sunlight is purposely avoided? Is one AI or RDA appropriate for all pediatric patients? Is 200 IU/d enough for all ages and racial/ethnic groups? How do various environmental conditions and geographic locations affect the AI or RDA for vitamin D? 

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